

**UNIVERSITY OF MIAMI
EVELYN F. MCKNIGHT BRAIN INSTITUTE
ANNUAL PROGRESS REPORT
JANUARY 1, 2018 - DECEMBER 31, 2018**



THE EVELYN F. **McKNIGHT** BRAIN INSTITUTE®
UNIVERSITY OF MIAMI
Preserving memory, enhancing life

**PRESENTED TO THE MCKNIGHT BRAIN RESEARCH FOUNDATION
BOARD OF TRUSTEES**



January 15, 2019

J. Lee Dockery, M.D.
Michael L. Dockery, M.D.
Nina Ellenbogen Raim, M.D., J.D.
Richard S. Isaacson, M.D.
Susan Pekarske, M.D.
Amy Porter
Gene R. Ryerson, M.D.
Madhav Thambisetty, M.D., Ph.D.
Robert M. Wah, M.D.
Melanie Cianciotto
Trustees, The Evelyn F. McKnight Brain Research Foundation, Inc.

SunTrust Banks, Inc.
Foundations & Endowments Specialty Practice
Mail Code FL-ORL-2100
200 S Orange Ave., SOAB-10
Orlando, Florida 32801

Dear Trustees,

This has been a special year in that we enjoyed a visit from the Trustees and Dr. Tatjana Rundek was appointed the *Evelyn F. McKnight Brain Institute Scientific Director* and the *Evelyn F. McKnight Endowed Chair for Memory and Learning in Aging*.

We would like to thank you for providing the Endowed Chair and for making it possible for us to have a McKnight Brain Institute at the University of Miami. We are pleased to send you this report for 2018 entailing our accomplishments, achievements, awards and research updates. In addition, we have included our goals and plans for 2019. Thank you.

Yours Sincerely,

Ralph L. Sacco, M.D., M.S.
Executive Director
Evelyn F. McKnight Brain Institute

Tatjana Rundek, M.D., Ph.D.
Scientific Director
Evelyn F. McKnight Brain Institute

RLS/TR/SSM/bd

cc: Susan Fox Rosellini

Evelyn F. McKnight Brain Institute 2018 Annual Report

Table of Contents

1. Summary of Scientific and Educational Achievements Since Last Report and Introduction.....	2
1.1. Appointment of Scientific Director.....	2
1.2. Accomplishments Towards Last Year Goals.....	4
1.3. Notable Scientific and Educational Activities.....	7
1.3.1. MBI Related Grants and Other Prestigious Awards	7
1.3.2. Participation in MBRF Inter-Institutional Events.....	9
1.3.3. Clinical and Population-Based Research.....	10
1.3.4. Basic and Translational Science research.....	11
1.4. Evelyn F. McKnight Brain Institute Strategic Plan.....	12
1.4.1. Development of MBI Strategic plan.....	12
1.4.2. Strategic Plan - Phase I.....	15
1.4.3. UM Medical School Research Strategic Plan.....	18
1.5. The McKnight Brain Research Foundation Visits the University of Miami and the Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging Ceremony.....	19
1.5.1. Overview of the Evelyn F. McKnight Brain Institute Research Symposium.....	22
1.5.2. The Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging Ceremony.....	25
2. Publications in Peer Reviewed Journals.....	27
3. Publications (Other).....	37
4. Presentations at Scientific Meetings.....	38
5. Presentations at Public (Non- Scientific) Meetings and Events.....	42
6. Awards (Other).....	44

6.1. Trainee Awards.....	44
6.2. Faculty Grants and Awards.....	46
7. Faculty - Included at the end of the report.	
8. Trainees - Included at the end of the report.	
9. Clinical/Translational Programs.....	49
9.1. Update on Existing Clinical Studies.....	49
9.1.1. Update on Population-Based Research.....	49
9.1.2. Update on Basic and Translational Science Research.....	62
9.2. Future Research Plans.....	66
9.2.1. Upcoming Population-Based Research.....	66
9.2.2. Upcoming Basic and Translational Science Research.....	67
9.2.3. Upcoming Education Program.....	68
10. Technology Transfer.....	69
11. Budget Update - Included at the end of the report.	
12. Educational Programs Focusing on Age-Related Memory Loss.....	69
12.1. General Education Program.....	75
12.2. Education of Trainees: Undergraduate, Medical and Doctoral Students, Post-Doctoral Students and Fellows.....	76
13. Collaborative Activities With other McKnight Brain Institutes, Institutions and Research Programs	79
14. Collaborative Activities With Non McKnight Brain Institutes, Institutions and Research Programs	80
15. Briefly Describe Plans for Future Research and/or Clinical Initiatives.....	81
16. If applicable, please provide endowment investment results for the report period. Included at the end of the report.	
17. Were any funds used for a Prohibited Purpose during the report period?.....	85
18. Do you recommend any modification to the Purpose or mandates in the Gift Agreement?	
19. Did all activities during the report period further the purpose?.....	85

- 20. Please describe any negative events (loss of personnel, space, budget, etc.) that occurred during the report period and the possible impact on carrying out the Gift Agreement..... 85**

- 21. Please provide any general comments or thoughts not covered elsewhere – a response is not required. Please respond only if you would like to add something not otherwise covered elsewhere.....85**

- 22. What do you consider your most important scientific achievement this year?.....86**

- 23. Signature, date, and title of person submitting the report. 89**



THE EVELYN F.
McKNIGHT BRAIN INSTITUTE®
UNIVERSITY OF MIAMI
Preserving memory, enhancing life



**UNIVERSITY OF MIAMI
EVELYN F. McKNIGHT BRAIN INSTITUTE**

**ANNUAL PROGRESS REPORT
JANUARY 1 – DECEMBER 31, 2018**

1. Summary of Scientific and Educational Achievements Since Last Report

Introduction

We start the summary of our achievements with (1) the changes occurring after the formal appointment of Scientific Director, (2) accomplishments towards the goals set forth for the last year, (3) followed by our notable scientific and educational activities, and (4) concluding with the description of the first phase of the Evelyn F. McKnight Brain Institute (MBI) strategic planning completed in 2018.

1.1. Appointment of Scientific Director

In January 2018, **Tatjana Rundek, MD, PhD** was formally appointed as Scientific Director of the Miami Evelyn F. McKnight Brain Institute, after she served as Interim Scientific Director and after the national search for a new Scientific Director was concluded. She was considered to be a competitive and best-suited candidate for the position by the Search Committee. She immediately started in her role as Scientific Director with great enthusiasm and rigorous plans for a successful year. At the first McKnight research meeting there was a sense of excitement and camaraderie, which continued and grew throughout the year. Regular weekly staff and research meetings entailed briefings on progress of current projects, brainstorming of new ideas, mentoring and planning of research projects for all members, from the trainees to junior and mid-level faculty. Dr. Rundek made the McKnight Brain Institute's members, collaborators and trainees eager to morph their interests and expertise into important science and collaborative research projects around the common theme of age-related memory loss and brain health. Plans for abstracts, posters, manuscripts and/or grant submissions were reviewed for science and feasibility, realistic research goals were set and the progress towards these goals was frequently reviewed. Although these meetings were productive and organized, she always fostered a free forum to explore ideas, encouraged junior members to participate in discussions and share their views, and hear group opinions.

Dr. Rundek successfully recruited collaborative partners from other departments, centers and institutes and fostered more productive multi-disciplinary collaborations within our McKnight Brain Institute and across the University of Miami. From multiple discussions with the Evelyn F. McKnight Executive Director Dr. Ralph L. Sacco and McKnight research team, the Scientific Advisory Board members, the leadership of the Miller School of Medicine including the new Dean and senior Executive Dean for Research, leaders of the Brain Bank, Center for Cognitive Neuroscience and Aging, the Miami Project, and Chairs of the Department of Psychology, Geriatrics and Genomics, it was clear that the direction, vision and mission, branding, and future research and educational plans for our McKnight Brain Institute needed to be revised and revitalized with important input from a broad range of scientists, partners, collaborators and

stakeholders interested in ameliorating age related memory loss and improving brain health. In order to accomplish this objective, ***we prepared and conducted the first phase of the McKnight Brain Institute strategic planning*** in June of 2018 with the help and coaching provided by the Miami Clinical Translational Science Institute (CTSI). This was the first strategic plan conducted for our MBI and its continuation to the next phase with clear definition of our strategic goals and their implementation, measurable outcomes and timeline will continue to be the focus of our MBI major activities in 2019.

Through the team and collaborative vision of Dr. Rundek, our Executive Director Dr. Sacco, the Scientific Advisory Board members and the conclusion of the first phase of our strategic planning, our McKnight Brain Institute's first order of business was to ***extend our Scientific Advisory Board*** and develop ***a unified framework of cognitive aging and brain health***. We will capitalize on the scientific strengths of our McKnight Brain Institute, UM Centers and Institutes, and to leverage our institutional infrastructure and resources, as well as the recently developed University of Miami Miller School of Medicine Research Strategic Plan. Our research focus on vascular, metabolic, and sensory drivers of cognitive aging and brain health is our major strength that will define our scientific framework, steer research and educational directions, and set research and educational goals and priorities to further the mission of our MBI.



PRESS RELEASE:

[Dr. Tatjana Rundek Named Scientific Director of Evelyn F. McKnight Brain Institute](#)

Tatjana Rundek, M.D., Ph.D., FAAN, professor of neurology and public health sciences and executive vice chair for research and faculty affairs in the Department of Neurology, has been named scientific director of the Evelyn F. McKnight Brain Institute and Evelyn F. McKnight Chair for Learning and Memory in Aging at the University of Miami Miller School of Medicine. She has served as the interim scientific director since October 2016.

The Evelyn F. McKnight Brain Institute at the University of Miami was established in 2007 with a donation from the McKnight Brain Research Foundation and a match from the Schoninger Foundation and other UM donors. Its mission is to discover and explore normal memory changes that happen with age, investigate the causes of age-related disorders of brain function and memory, and develop ways to prevent them.

"I am dedicated to our McKnight Brain Institute's mission to accelerate discovery of the causes, treatment, and prevention of age-related memory loss and cognitive decline, and to enhance brain health through translational and patient-oriented research," said Rundek, who also serves as director of the Clinical Translational Research Division in Neurology, and director of the Master of Science Degree in Clinical Translational Investigations.

"Dr. Rundek is a wonderful choice as scientific director," said Ralph L. Sacco, M.D., M.S., executive director of the McKnight Brain Institute, professor and chair of neurology, Olemberg Chair in Neurological Disorders, senior associate dean for clinical and translational science and director of UM's Clinical and Translational Science Institute. "Her passion for team science and developing new ideas in a truly collaborative manner is very special. I am looking forward to great things under Dr. Rundek's leadership."

As interim director Rundek created the Miami McKnight Brain Institute Small Pilot Collaborative Award. The program gave small grants to junior faculty or post-doctoral trainees with promising potential to become successful investigators in age-related memory loss and cognitive decline, supporting research and advancing the McKnight Brain Institute collaborative research project pipeline.

"Dr. Rundek's background and training, both as a clinician and a research scientist, make her uniquely qualified to advance the research initiatives in cognitive aging leading to the understanding of and alleviation of age-related memory loss, not only at the University of Miami, but throughout the universal scientific community," said J. Lee Dockery, M.D., chair of the Board of Trustees for the McKnight Brain Research Foundation.

1.2. Accomplishments Towards Last Year Goals

In our previous Annual Progress Report, we included several goals and aspirations for our McKnight Brain Institute (MBI) for 2018. We have accomplished all the planned goals and more since last year's progress report, including:

- First, we planned to reassess and revise our MBI research and education program. We have immediately started several new initiatives for our research direction in collaboration with the newly named *Center for Cognitive Neuroscience and Aging* (previously: Center for Aging) under the new leadership of Dr. David Loewenstein, PhD. Dr. Rundek and Dr. Loewenstein have established bi-monthly meetings to continue our current collaborations and discuss and strategize new avenues of research and educational collaborations. As Dr. Loewenstein is a co-Director of the Clinical Core of the 1FLADRC (PI: Todd Golde, UF) he introduced Dr. Rundek to Dr. Ranjan Duaara, (Mt. Sinai, Miami Beach) a Director of the 1FL ADRC Clinical Core and both Dr. Rundek and Dr. Loewenstein have established monthly research meetings with the research team at Mt. Sinai. These collaborations have already resulted in a successful grant application.
- Our major objective was to prepare and conduct the strategic planning meeting and align our MBI strategic goals with the recently completed University of Miami Miller School of Medicine Strategic plan. We conducted the MBI retreat and completed the first phase of MBI strategic planning with the help of coaching experts from our Clinical Translation Science Institute (**Section 1.4**).
- As a result of our retreat, we have immediately expanded the McKnight Scientific Advisory Board to include a broader representation of scientists, leaders, partners and collaborators focused on age-related cognitive functioning and brain health to help extend our research and educational mission and accomplish our strategic goals.
- We have successfully continued our current research and educational projects by focusing on successful and promising projects and collaborations, including an extension of the *McKnight Frailty Registry* (as a subset of the Cognitive Disorders Clinical and Biorepository Registry) led by Dr. Bonnie Levin, the *small vessel disease project* (brain and eye) led by Dr. Noam Alperin in Radiology and Dr. Hong Jiang in Neuro-ophthalmology; *sleep disorders and cognition* led by Dr. Alberto Ramos, and *neuroplasticity assessment using Transcranial Magnetic Stimulation (TMS)* led by Dr. Joyce Gomes-Osman. Our *basic science projects continued to focus on treatments for improving cognitive outcomes* using novel white matter stroke behavioral models in rats (Dr. Kunjan Dave and Dr. Miguel Perez-Pinzon). We have continued evaluating synergistic effects of physical exercise and resveratrol treatment on post-stroke cognitive function in middle aged rats with the goal of improving post-stroke cognitive function. In parallel, our clinical research has expanded to the investigation of the effect of aerobic exercise on synaptic functioning using TMS assessments.

- Two grants that were submitted to the NIH last year using preliminary data from the McKnight Frailty Registry (Dr. Jiang's retinal and brain hemodynamic proposal, and Drs. Alperin/Rundek's proposal on MR imaging of cerebral small vessel perfusion), received excellent scores but were not funded and will be resubmitted this year.
- Two R21 grant proposals on *sleep and cognitive performance across the lifespan* submitted last year (both by Dr. Alberto Ramos) were awarded funding by the NHLBI. A R01 using a large cohort from the Hispanic Community Health Study-Study of Latinos (HCHS-SOL) and based on the framework of these R21 grants was just submitted. It includes institutions that are homes to national leaders in sleep medicine (University of Miami, University of Chicago, Albert Einstein in NY, UCSD and MGH).
- In collaboration with other McKnight Brain Institutes, we successfully continued our collaborative projects, including the *MBAR-McKnight Brain Aging Registry*. Drs. Bonnie Levin and Sarah Getz (Co-Investigators) were awarded the first MBRF Cognitive Aging and Memory Intervention Core Inter-institutional Pilot Grant in collaboration with UF and the University of Arizona for the research project *Uncovering Risk Profiles of Deception and Mitigating Susceptibility to Scamming in Midlife and Older Age: A Novel Intervention Tool*.
- As part of other collaborations, we successfully continued with projects on cognitive trajectories in aging in NOMAS (Northern Manhattan Study) and the Brain Hemodynamic Study in the Einstein Aging Study in the Bronx. We would like to highlight the investigations on the associations between subclinical brain infarcts (SBI) and white matter hyperintensity volume (WMHV), cognition and functional trajectories. The results showed that SBI moderated the association between cognition and functional trajectories, with 3-fold greater functional decline among those having SBI compared to those not having SBI. This highlights the strong and independent association between subclinical brain imaging markers and patient-centered functional trajectories over time. This work will continue in the next year by including the network of inflammation biomarkers as important mediators between cognitive performance and functional trajectories over time.
- In the last year we have successfully started new research initiatives. These involved collaborations with the Center for Cognitive Neuroscience and Aging (Director: Dr. Loewenstein) and the Mount Sinai Wien Center (Dr. Duara) on two major initiatives that include (1) investigations of brain vascular phenotypes in cognitive decline, and (2) a collaboration on 1FL ADRC Clinical Core and Educational Component. We have submitted the proposal on *Brain Vascular Imaging Phenotypes (VIP) and cognitive and neurodegenerative profile* to the Florida DOH and just received the notification of an award for 2-year funding (PI: Dr. Rundek). In respect to the 1FL ADRC, UM will apply for the competitive renewal together with UF in May of 2019. The current 1FL ADC Clinical Core under the direction of Dr. Duara (Mt. Sinai) will be extended and will include a Co-Director at UM (Dr. Loewenstein) with Dr. Rundek as a co-investigator. In addition, Dr. Rundek will serve on the 1FL ADC Recruitment Core. One of the main changes in the 1FL ADC re-submission is in the Educational/Training Core leadership, where Dr. Rundek will serve as an educational/training Co-Director together with Dr. Glenn Smith from UF.

- Another novel research initiative our MBI started last year included *novel functional interventions to improve synaptic functioning and cognitive performance in aging* using oral supplementation (Souvenaid) that increases brain levels of DHA, choline and uridine. This exciting new research initiative is led by Dr. Christian Camargo, our prior MBI fellow, under the mentorship of Dr. Rundek and Dr. Richard Wurtman, our recently appointed voluntary professor Emeritus. *Dr. Richard J. Wurtman, MD* who has been Professor Emeritus at MIT for over 40 years is known as the father of ‘the melatonin role in sleep’.
- We have extended our MRI capabilities by partnering with the Department of Psychology (Dr. Phil McCabe, Department Chair) at the Coral Gables Campus where a research 3T MRI resides. We have started our MRI scans in that facility, which significantly increased a number of available MRI slots for our studies and reduced waiting and scheduling time for our participants that we experienced in the clinical MRI facilities at the Medical School Campus. We have also started *a new collaboration on resting brain networks* using resting state MRI in collaboration with Dr. Roger McIntosh, PhD from the Department of Psychology, who is an expert in fMRI. Dr. McIntosh is now our newest MBI collaborator.
- Another important and major partnership and collaboration is currently in progress with the University of Arizona MBI under the leadership of Dr. Carol Barnes. She leads a large U19 application to the NIA (deadline: Jan 25, 2019) to investigate main drivers of cognitive aging across the lifespan: *Precision Aging Network (PAN): Closing the Gap Between Cognitive Healthspan and Human Lifespan*. Dr. Rundek and Dr. Levin will lead the Miami Clinical Project (*In-depth Profiles of Resilience and Risk*) and serve on the PAN Executive committee.
- Lastly, with the respect of our educational goals, we have enrolled the second MBI research fellow last July (Dr. Anita Seixas Dias Saporta, MD) after Dr. Christian Camargo completed his MBI clinical and research fellowship. Anita has a strong clinical background in MRI and electrophysiology with a particular research interest in multimodality brain imaging and aging. She will continue her fellowship for another year. *As our McKnight trainee Michelle Caunca, MD/PhD Student successfully obtained a F30 NIH award last year (primary mentor: Dr. Rundek)* we have resources to accept another MD/PhD student to our McKnight cognitive graduate training program. Dr. Rundek serves on the MD/PhD Program Admission Committee and has already interviewed a number of candidates for the MD/PhD program and identified a highly promising MD/PhD candidate to join our MBI on the cognitive aging projects and work on her PhD thesis in our MBI. Her MBI appointment is pending official admission to the MD/PhD program at the University of Miami, Miller School of Medicine.
- Dr. Joyce Gomes-Osman has just been awarded a NCATS CTSI KL2 award. This is a 2-year training award that will protect 75% of Joyce’s time to obtain research training and provides some funds for resources needed to conduct research on *Assessing cognitive improvements, brain neuroplasticity and the role of genetic factors after aerobic exercise in sedentary adults*. Joyce’s primary mentor is Dr. Rundek.
- Dr. Christian Camargo has been retained and advanced to a faculty position of an Instructor in the Department of Neurology. He has submitted a grant on the use of Souvenaid to improve synaptic functioning in cognitive aging to the AAN/McKnight funding. He just

received a provisional award notice for 2-year funding (pending responses to the reviewers' comments with the deadline of Jan 18). Christian's primary mentor is Dr. Rundek.

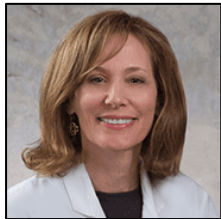
- As we are currently planning and preparing a major education/training application to the NIA as a part of the 1FL ADC Educational Core in collaboration with UF, we have postponed our plans for a T32 training grant proposal in cognitive aging and brain health. Our Scientific Advisory Board also recommended that we postpone this application after reviewing our current educational activities.

1.3. Notable Scientific and Educational Activities

In the following section we provide more details on several of our noteworthy MBI progress and accomplishments in 2018.

1.3.1. MBI Related Grants and Other Prestigious Awards

Drs. Bonnie Levin and Sarah Getz (Co-Investigators) were awarded the first McKnight Brain Foundation Inter-Institutional Collaborative Pilot Grant in 2018 for the research project *Uncovering Risk Profiles of Deception and Mitigating Susceptibility to Scamming in Midlife and Older Age: A Novel Intervention Tool*.



The University of Miami neuropsychologists Bonnie Levin, PhD and Sarah Getz, PhD were awarded a grant for this important research project at the Evelyn F. McKnight Brain Institute. The research is a collaboration with the McKnight Brain Institutes at the Universities of Florida and Arizona. This collaboration will specifically examine scamming in middle



and older life, a pressing public health problem associated with decreased functional independence, increased financial dependency, lower quality of life and a host of negative health outcomes. This project will attempt to understand the cognitive, socio-affective and neurobiological mechanisms underlying increased susceptibility to being deceived and poor decision-making. Currently, there are no effective interventions to reduce scam susceptibility and the goal of this multi-site collaboration is to develop and validate a decision-supportive device to reduce online scam susceptibility in late midlife and older age.

Dr. Joyce Gomes-Osman is awarded a Mentored Translational Research Scholars Program Award (KL2) from the University of Miami Clinical Translational Science Institute (CTSI)

Congratulations to Dr. Joyce Gomes-Osman for being awarded a Mentored Translational Research Scholars Program Award (KL2)! This program is designed to support the research career development of early stage investigators at the assistant professor level for two years and will include: (1) 75% salary support up to the NIH Salary Cap; (2) \$2,500 for travel and training-related activities; (3) \$30,000 for research expenses. Joyce's primary mentor is Dr. Rundek.



Dr. Joyce Gomes-Osman is leveraging the preliminary data from her previously awarded *McKnight Pilot Grant* for an innovative study that will investigate mechanisms

underlying cognitive benefits after an 8-week exercise intervention in sedentary adults over 55 years of age. In this study, she will combine the use of a non-invasive assessment of synaptic neuroplasticity by Transcranial Magnetic Stimulation (TMS), neuropsychological outcome measures, and examine potential effect modifications by genetic brain-derived neurotrophic factor (BDNF) and apolipoprotein E (APOE) factors.

This KL2 Award will greatly help her advancing academic career by protecting her time for research, enabling additional training and mentorship from a multi-disciplinary group of established researchers at UM Miller School of Medicine (Drs. Rundek and Loewenstein) and Harvard (Dr. Alvaro Pascual-Leone), combining the fields of clinical and translational research in aging, genetics, neurophysiology and cognition.

Dr. Christian Camargo just received a provisional award notice for 2-year funding from the **AAN McKnight Clinical Translational Research Scholarship in Cognitive Aging and Age Related Memory Loss** (pending responses to the reviewers' comments with the deadline of Jan 18) to study the effect of an oral nutrient on synaptic function and cognition in aging: *Reducing the Effects of Aging on Cognition with Therapeutic Intervention of an Oral Nutrient - The REACTION Study*. He is proposing a pilot study with a parallel group design of a multi-nutrient oral supplement on improved cognitive performance in participants with age-related cognitive complaints and age-matched participants without cognitive complaints. The nutrient Souvenaid is an example of such a treatment to increase synaptic plasticity. Its key ingredient, Fortasyn-Connect, contains a patented combination of phospholipids, DHA and choline. The formulation is based on the biochemical properties of synaptic membranes intimated after years of rigorous research by one of his mentors, Dr. Richard Wurtman from MIT. Christian's primary mentor is Dr. Rundek.



Dr. Rundek just received a notice of award from FL DOH for a 2-year funding to study vascular contribution to neurodegeneration: ***Brain Vascular Imaging Phenotypes (VIP) and cognitive and neurodegenerative profile - The VIP Study***. This research was a result from a new initiative and collaboration with the Center for Cognitive Neuroscience and Aging (Director: Dr. Loewenstein) and the Mount Sinai Wien Center (Director: Dr. Duara) started in 2018. The objective of the proposal is to determine the impact of novel brain vascular imaging phenotypes (VIP) of small vessel disease and modifiable vascular comorbidities on cognitive and neurodegenerative profiles. To achieve this goal, the investigators will leverage brain MRI, clinical and neurocognitive data from the NIH-funded 1FL ADRC control population. This unique study will determine the impact of the modifiable vascular risk factors, comorbidities and vascular brain imaging phenotypes on cognition and the signatures of AD pathology in the 'non-AD affected' 1FL ADRC population. The proposed study is of high impact for the health of the Florida population, as it will help to close the gap in our understanding of the mechanisms by which vascular phenotypes contribute to neurodegeneration and inform strategies to reduce AD risk specifically tailored to high vascular risk individuals in the diverse Florida population.

Dr. Ralph Sacco was **elected to the prestigious National Academy of Medicine (NAM)** this year. This extraordinary honor reflects his height of professional achievement and commitment to

service in health and medicine. Dr. Sacco received the honor “for his instrumental involvement in policies promoting ideal cardiovascular health, brain health, stroke prevention, and non-communicable disease targets,” according to the Academy. See [Section 22](#) for additional information and the press release.

Dr. Rundek just received the 31st annual *In the Company of Women Outstanding Woman in Science and Technology* award. She was one of 2 winners who are sharing this year’s award. The award is given to recognize Miami-Dade County women leaders and their contributions to the community. Awardees are women who exemplify professional development, community responsibility, leadership and vision, who made contributions to women’s progress and the promotion of pluralism.



1.3.2. Participation in MBRF Inter-Institutional Events

The Miami Evelyn F. McKnight Brain Institute participation in the 10th Annual McKnight Inter-Institutional Meeting at the University of Alabama at Birmingham, April 5-6, 2018.

These were the presentations given by our Trainees, Collaborators and Members:

- *Intervention Opportunities for Cognitive Decline: Report from the National Academy of Medicine*, **Ralph Sacco, MD, MS, FAHA, FAAN**
- *McKnight Brain Aging Registry I: Clinical Update*, **Bonnie Levin, PhD**
- *Cognitive, Cultural and Affective Dimensions of Frailty*, **Katalina McInerney, PhD, Assistant Professor and Sarah Getz, PhD Neuropsychology Postdoctoral Fellow**
- *Sleep and Neurocognitive Aging in Population Based Studies*, **Alberto Ramos, MD, MSPH, Associate Professor and Sleep Research Director**
- *Retinal Microvascular and Microstructural Changes in Normal Aging and Alzheimer’s Disease* **Hong Jiang, MD, PhD Assistant Professor of Clinical Neuro-ophthalmology & Neurology**
- *Post-Stroke Physical Exercise Improves Cognitive Outcomes in Young and Elderly Animals*, **Kunjan Dave, PhD, Research Associate Professor**

The Miami MBI participation in the McKnight Brain Research Foundation Poster Reception at the Society for Neuroscience (SFN) meeting, San Diego, CA, November 4th, 2018.

Below are the poster presentations given by our Trainees, Collaborators and Members:

- **Dr. Ami Raval** “Monitoring post stroke frailty in nicotineexposed female rats”
- **Dr. Milena Pinto** “Lack Of Cytochrome C In Adult Forebrain Neurons In Vivo Leads To A Decrease In Cytochrome C Oxidase, Increased Oxidative Stress But No Overt Cell Death”
- **Ashish Rehni** mentored by **Dr. Kunjan Dave** “Exposure to recurrent hypo- glycemia modulates endoplasmic reticulum stress in hippocampus of insulin treated diabetic rats”



- **Austin Choi** mentored by **Dr. Antoni Barrientos** “Biogenetic features and function of the mitochondrial ribosome in health and mitochondrial encephalomyopathies”
- **Jordyn Rice** mentored by **Dr. Joyce Gomes-Osman** “Dual-task performance is related to a neurophysiological measure of plasticity in individuals with memory disorders”
- **Jordyn Rice** mentored by **Dr. Joyce Gomes-Osman** “Effects of a 4-week Aerobic Exercise Intervention on TMS Neuroplasticity Measures and Cognition in Healthy Sedentary Adults: an Ongoing Pilot Study”
- **Jordyn Rice** mentored by **Dr. Joyce Gomes-Osman** “Timed Up-and-Go Performance and Dual-Task Effects are Correlated with Distinct Neuropsychological Measures of Executive Function in Healthy Older Adults”
- **Kristen Sanders** mentored by Dr. Tasuku Akiyama "Anxiety-like behavior and Fos expression in amygdala elicited by itch mediators in mice"

1.3.3. Clinical and Population-Based Research

Dr. Joyce Gomes-Osman’s paper *Exercise for cognitive brain health in aging: A systematic review for an evaluation of dose* was published in *Neurology: Clinical Practice* in June 2018. It received wide coverage internationally from newspapers and magazines as well as radio and television interviews. See Section **9.1** for further information.

Under the direction of **Dr. Bonnie Levin**, significant work was done on the Cognitive Disorders Clinical and Biorepository Registry (referred to in the remainder of this report as the McKnight Frailty Registry). This database holds almost 400 records of subjects with memory complaints. Each participant who met study inclusion criteria was evaluated by Dr. Levin’s team with a detailed cognitive and frailty assessment battery and is included in the database. This database presents a valuable resource for generating research hypotheses relevant to age-related memory loss and cognitive decline and have already led to a great number of posters, presentations, abstracts and grant and manuscript submissions in 2018.

Dr. Tatjana Rundek received an NIH award to conduct a Family Study of Carotid Atherosclerosis and Stroke Risk (the 3rd cycle of funding). We propose to expand our prior genetic investigations to conduct a methylome-wide-association-study (MWAS) to identify differential DNA methylation regions (DMRs) associated with subclinical stroke precursors, stroke and CVD. The proposed investigations would provide new insights relevant to the development of novel clinical strategies for prevention and treatment of stroke and CVD, as our ultimate goal is to reduce stroke risk and race- ethnic disparities in stroke and CVD. Besides clinical aims, we plan to evaluate the functional impact of DNA sequence variation and DMRs using CRISPR-Cas9 technology. To achieve our goals we will leverage the rich data already collected in the past cycle of Family Study and add new data collection to detect vascular events (stroke, myocardial infarction, vascular death). We will validate the findings in an independent sample from the ongoing longitudinal Northern Manhattan Study (NOMAS). The innovative aspects of our proposal include novel discoveries of modifiable epigenetic sites for stroke, CRISPR-Cas9 technology to model specific genome-editing, a unique population of Dominicans, a family study design, and an available independent population for validation studies. Findings from our study may lead to the most promising molecular strategies for risk stratification, prevention and

treatment of stroke. The plan is to extend our genomic and epigenetic investigations to age-related cognitive performance in high-cerebrovascular-risk families.

Dr. Noam Alperin's paper *Effect of Sleep Quality on aMCI Vulnerable Brain Regions in Cognitively Normal Elderly Individuals* was accepted for publication in the leading sleep journal, SLEEP. It describes the first assessment of the effect of poor sleep quality on several MRI phenotypes in cognitively intact elderly subjects. Faced with aging global populations, the medical community has become increasingly interested in developing interventions to slow or prevent age-related cognitive decline. Sleep quality has been targeted as a factor that may help modulate the course of amnesic mild cognitive impairment and Alzheimer's, but the relationship between sleep, cognition, and dementia disorders is still poorly understood. His study reports that patterns of cortical and deep gray matter atrophy related to poor sleep quality impact in AD-prone regions of the cortex even in a population rigorously deemed unaffected by cognitive impairment, psychological disorders or dementia. The study emphasizes a role for sleep intervention in fighting neurodegeneration and potentially slowing age-related cognitive decline.

Dr. Sun Xiaoyan our MBI Educational Director has taken on a significant role in the University of Miami Brain Bank. She became a Co-Director of the Brain Bank and took a lead in making the final disease diagnosis from the brain pathology specimens and available clinical information. Dr. Sun's new position will help in establishing a strong partnership between our MBI and the Brain Bank in research proposals and educational activities.

Dr. Elizabeth Crocco was named the Clinical Director of the Center for Cognitive Neuroscience and Aging (CNSA) directed by Dr. David Loewenstein.

Dr. David Loewenstein and his NIA-supported team of researchers at the Center for Cognitive Neurosciences and Aging and the University of Miami developed *the Loewenstein-Acevedo Scales for Semantic Interference and Learning (LASSI-L) test*. Traditional memory measures are subject to individual differences in learning strategies, cognitive reserve and other sources of variability that may effectively lower the signal-to-noise ratio, hampering the assessment of the earliest stages of cognitive deficits in AD, and the ability to track changes over time. The LASSI-L is a sensitive cognitive 'stress' test that overcomes these challenges and can assess cognitive deficits associated with early biological changes in neurodegeneration. The preliminary findings using LASSI-L show that semantic intrusion on the LASSI-L could differentiate amnesic MCI patients with high and low amyloid loads and may have significant implications for screening for enrollment in novel clinical trials for cognitive improvements. The results were published in the September 4, 2018 issue of *Neurology*.

1.3.4. Basic and Translational Science Research

Dr. Milena Pinto has resubmitted her K01 award project in and will receive notice regarding funding in 2019.

Dr. Ami Raval was appointed Associate Research Professor.

1.4. The Evelyn F. McKnight Brain Institute Strategic Planning

Our major goal set last year was to hold a one-day **Evelyn F. McKnight Brain Institute Strategic Planning Retreat**, in order to steer our Institute's research and educational priorities for the next 5 years, focus energy and resources towards these priorities, strengthen clinical oriented research in age-related memory loss, ensure that our research team members and collaborators work toward the common goals, and to assess and adjust the Institute's direction in response to a changing research and funding environment.

1.4.1. Development of MBI Strategic Plan

Preparation for the **Strategic Planning Retreat** began immediately after Dr. Rundek was appointed as Scientific Director in Jan 2018. Dr. Rundek spent a significant amount of time to conduct a thorough search across departments, disciplines, centers, institutes and schools to learn about the age-related research being done at all University of Miami campuses. She explored potential research partnerships and collaborations with our MBI and identified key players and leaders within the University as potential partners for advancing our MBI mission and programs. She met with most of these leaders and scientists personally and invited them for collaborations with our research and education programs in age-related memory loss and cognitive decline.

Multiple disciplines were considered including geriatrics and public health, psychology, psychiatry, radiology, nuclear medicine, basic science, genetics, exercise physiology, aging/neuroscience, psychology, and representative partners were invited to be part of the MBI Strategic Planning Retreat.

Task Force Working Groups

We have created 3 task force working groups consisting of multi-disciplinary teams and based on their expertise in aging and cognitive function, leadership ability and propensity to brainstorm and bring forth novel ideas. The three task force groups were (members of the each group are listed below - 'Today's exercise'):

- (1) Clinical Interventions**
- (2) Translational/Genetics/Brain Bank**
- (3) Imaging**

These 3 task force groups consisted of scientists and leaders in age-related research across UM campuses and our MBI members and collaborators, as listed below. The task force groups had an experienced group leader-scientist in age-related research, who are also leaders of one of the UM Centers, Institutes or Departments. In addition, each working group had a facilitator experienced in research administration and coaching. We also included a junior faculty or trainee in each working group to foster their learning experience and include them in discussions, decision-making and research networking.

The Retreat was held on June 1st, 2018. **Phase I of our MBI Strategic Plan was completed.**

The Retreat was structured in 3 parts:

- (1) It started with an initial group meeting and presentation of the history, mission and vision and current state of our MBI programs, preliminary SWOT analysis, and a charge to the 3 task force working groups (Clinical Interventions, Translational/Genetics/Brain Bank and Imaging),
- (2) Breakout sessions with each group directed to review our MBI vision and mission, SWOT, and to propose several goals and strategies for their achievement, tactics and metrics, and milestones, and
- (3) It ended with all regrouping to share and review each group’s goals and strategies.

TODAY’S EXERCISE

Goals

1. Discuss and add to SWOT analysis – 30 minutes
2. Fill out template for each Focus Area
3. Give 15 minute presentation to the group

Clinical/Interventions (Rm. 1381)	Imaging (Rm. 1380)	Translational/Genetics/Brain Bank (Rm. 1340)
Group leader: Norman Altman Facilitator: Daru Ransford	Group leader: David Loewenstein Facilitator: Susan Fox-Rosellini	Group leader: Bill Scott Facilitator: Sheela Dominguez
Barry Baumel	Noam Alperin	Antoni Barrientos
Michael Benatar	Mike Georgiou	Susan Blanton
Olveen Carrasquillo	Hong Jiang	Kunjan Dave
Katalina Fernandez-McInerney	Phil McCabe	Dalton Dietrich
Joyce Gomes-Osman	Pradip Pattany	Savita Pahwa
Neil Schneiderman	Alberto Ramos	Milena Pinto
Joe Signorile	Anita Saporta	Ami Raval
Adina Zeki Al Hazzouri	Xiaoyan Sun	Peggy Pericak-Vance



University of Miami
Evelyn F. McKnight Brain Institute
Strategic Planning Meeting
June 1st, 2018

AGENDA

8:30am - 9:00am	Breakfast
9:00am - 9:15am	Introduction - Sacco, Rundek, Attendees
9:15am - 9:30am	McKnight Brain Research Foundation (MBRF) and IOM Report - Sacco
9:30am - 9:45am	McKnight Brain Institute History, Mission and Vision - Rundek/Sacco
9:45am - 10:00am	Miller School of Medicine Neuroscience Strategic Plan - Sacco/Ransford/Dominguez
10:00am - 10:30am	SWOT Analysis - Rundek Assignment of Working Groups - Rundek/ Ransford/Dominguez/Rosellini <ul style="list-style-type: none">- Clinical/Intervention Group- Imaging Group- Translational/Biomarker/Brain Bank
10:30am - 12:00pm	Working Group Meetings
12:00pm - 12:45pm	Working Lunch/Prepare Presentations

1.4.2. Strategic Plan - Phase I

In Phase I of our Strategic Plan each working group accomplished the following:

- Reviewed the MBI vision and mission and the group SWOT analysis
- Established strategic SMART objectives (Specific, Measurable, Achievable, Realistic and Time-based) for the next 3-5 years; and
- Proposed a ‘big picture’ strategy for achievement of the SMART objectives.

Objective #1:

In the group discussion at the end of the Retreat, the main objective was to **expand our MBI Scientific Advisory Board** to include a broader cross-disciplinary representation of investigators and leaders involved in age-related memory research across our medical school Departments, Centers and Institutes, and across the schools at UM.

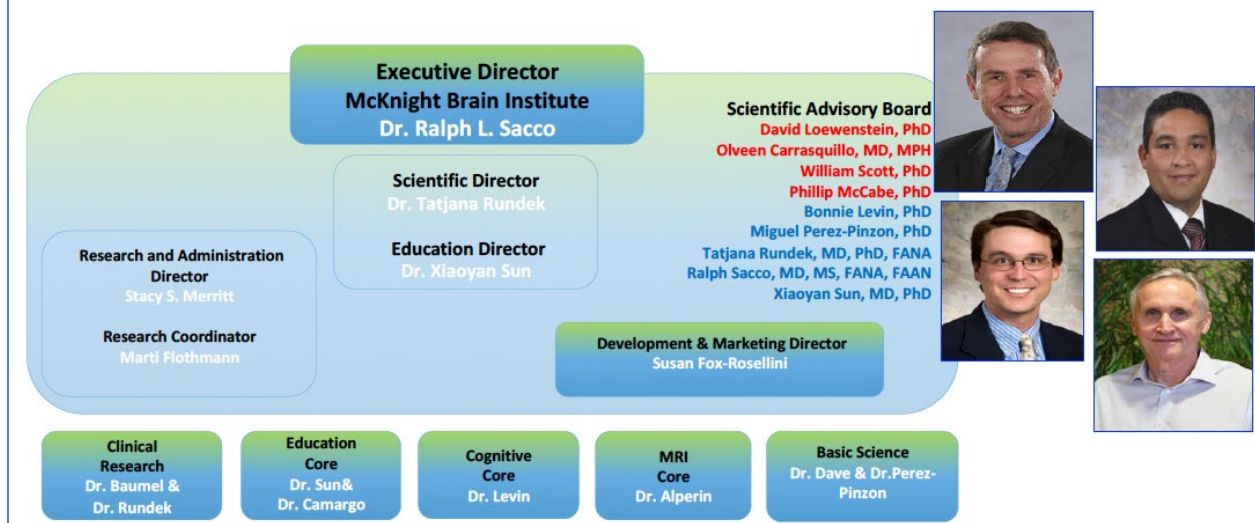
Completed Action:

In addition to the current Board members (Dr. Sacco, Dr. Rundek, Dr. Levin, Dr. Sun and Dr. Perez-Pinzon) the new MBI Scientific Advisory Board Members are:

- **Dr. David Loewenstein, PhD**, Professor, Director of the Center for Cognitive Neuroscience & Aging
- **Dr. Phillip McCabe, PhD**, Professor and Chairman of the Department of Psychology
- **Dr. William Scott, PhD**, Professor of Human Genetics, Neurology and Public Health Sciences, Director of the Brain Bank, and Vice Chair for Education and Training of the John P. Hussman Institute for Human Genomics; and
- **Dr. Olveen Carrasquillo, MD, MPH**, Professor of Medicine and Public Health Sciences, Chief of General Internal Medicine Division, Director of Community Engagement, UM CTSI.

These new Board Members were chosen based on their ability to complement the Board’s current Members and their knowledge-base; to employ novel approaches to identifying funding opportunities and challenges in age-related cognitive research; to be well-versed on memory and cognition changes in aging; to execute research on the aging population; and to possess experience in forming multi-disciplinary and multi-institutional collaborations. Their NIH biosketches are included with this report.

Miami McKnight Brain Institute - Organizational Chart



The entire Scientific Advisory Board was assembled in August and reconvened in November of 2018. The MBI Scientific Advisory Board has been charged to help conduct Phase II of the Strategic Planning in 2019, to align our Strategic Plan with the recently completed Miller School of Medicine Research Strategic Plan and to successfully lead the implementation of our Strategic Plan in the next 5 years.

Objective #2: to develop *a unified framework of cognitive aging and brain health* capitalizing on the scientific strengths of our McKnight Brain Institute, UM Centers and Institutes, and leveraging institutional infrastructure and resources and recently developed University of Miami Miller School of Medicine Research Strategic Plan.

Action: Development of our unified scientific framework of cognitive aging and brain health is in development. We focus on clinical and translational investigations of vascular, metabolic and sensory drivers of cognitive aging and brain health, that unifies the major strengths of our MBI and Institution and that will define our scientific framework, steer research and educational directions, and set research and educational goals and priorities to further the mission of our McKnight Brain Institute.

The 3 task force working groups have created a set of preliminary goals and strategies that will be discussed, revised and adopted in *Phase II of the MBI Strategic Plan* in 2019:

CLINICAL INTERVENTIONS	TRANSLATIONAL/GENETICS/BIO/BRAIN	IMAGING
<p>Goal 1- Develop screening program throughout UHealth for age-related memory loss (pre-screening before issues present) to increase research recruitment.</p> <p>Strategy 1 Utilize screening program to define the clinical population to engage with age-related disorders</p> <p>Strategy 2 Identify pre-screening issues</p> <p>Strategy 3 Partner with VA or Miami Jewish to develop screening programs to identify biomarkers and early indicators</p> <p>Strategy 4 Scientifically develop a cohort</p> <p>Goal 2- Increase communication for developing integrated treatment plans, referrals and research opportunities.</p> <p>Strategy 1 Redesign McKnight website that can integrate the various specialties and research opportunities</p> <p>Strategy 2 Re-evaluate and better clarify within org chart structure with the five arms (i.e. clinical/interventions). Hold regular meetings individually and with the other groups.</p> <p>Strategy 3 Notify members of ongoing activities</p> <p>Goal 3- Strengthen mentor programs through McKnight Institute.</p> <p>Strategy 1 Partner with CTSI on the Connection (network for early career faculty) through (1) information exchange, (2) networking, (3) group learning, and (4) mentorship required for team science</p> <p>Strategy 2 Identify scholars to apply for AAN McKnight scholar awards</p> <p>Goal 4- Develop a strong therapeutic trials program.</p> <p>Strategy 1 Identify and pilot an intervention trials for age-related cognitive decline (e.g. Souvenaid)</p> <p>Strategy 2 Identify leaders and apply for funding within multidisciplinary fields (e.g. exercise + neuromodulation, cognitive training + exercise)</p>	<p>Goal 1- Enable data sharing & improve communications for both informational purposes & to develop collaborations & new research opportunities.</p> <p>Strategy 1 Comprehensive inventory of all resources and assets (e.g. biological specimens, samples, data sets, pre-clinical model systems, assays)</p> <p>Strategy 2 Identify interdisciplinary Internal Advisory Committee members</p> <p>Strategy 3 Develop informatics infrastructure that's needed for sharing/linking data/extract integration</p> <p>Goal 2- Create a closer link between pre-clinical and clinical work.</p> <p>Strategy 1 Create opportunities for interactions that bring investigators together to develop team science research questions</p> <p>Strategy 2 Take advantage of strengths in cell therapies, biomarkers, pathophysiology, novel treatments, experimental systems</p> <p>Goal 3- Consolidate McKnight data collection efforts into unified framework that answers fundamental question about cognition.</p> <p>Strategy 1 Optimize what MCK is collecting - 1 group of people that is very well-characterized to answer defined research ?5</p> <p>Strategy 2 Leverage other data sources – use existing federated cohorts that are already being assembled (don't reinvent the wheel)</p> <p>Goal 4- Develop imaging capabilities to strengthen aging research, including small animal imaging, PET for research, and Cyclotron.</p> <p>Strategy 1 Develop business plan for proposed new imaging capabilities.</p> <p>Strategy 2 Identify/partner w/ other organizations on campus w/ the same needs to leverage resources</p>	<p>Goal 1- Expand research dedicated MRI imaging at the Coral Gables MRI Center.</p> <p>Strategy 1 Create and communicate comprehensive inventory of all resources available at the CG MRI Center.</p> <p>Strategy 2 Establish transportation between Medical and Coral Gables</p> <p>Strategy 3 Evaluate renewal/replacement of scanner</p> <p>Goal 2- Create research dedicated resources for Nuclear Med. & PET/CT scanner to strengthen aging research, including human and small animal imaging.</p> <p>Strategy 1 Develop business plan to justify need for Nuclear Medicine/PET Research capabilities on Medical Campus</p> <p>Strategy 2 Develop a survey to poll all possible users & projects</p> <p>Strategy 3 Define vascular contributions to cognitive decline & age related memory loss.</p> <p>Strategy 4 Develop pilot fund for scans & young investigator projects</p> <p>Goal 3- Develop partnerships to create unique radio lipids to develop new PET studies and proprietary protocols.</p> <p>Strategy 1 Identify functional neural signatures related to cognitive disorders and beyond</p>

We have already started to develop and implement some of the identified goals.

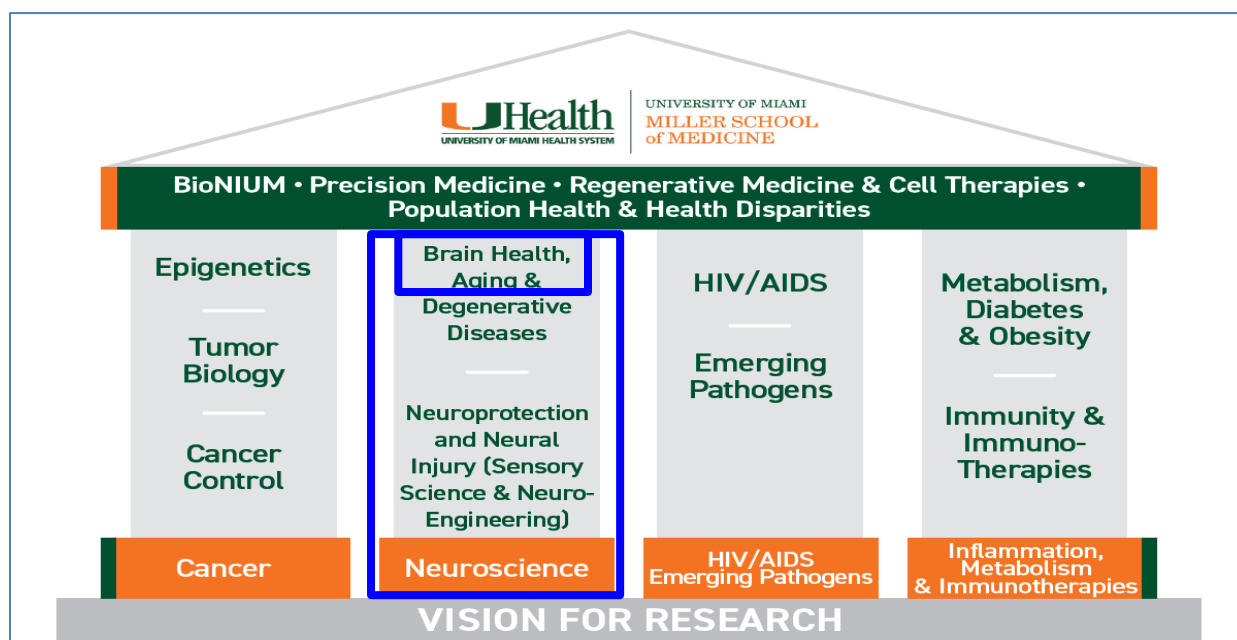
For example:

- **Clinical Interventional working group Goal #3:** We have established multiple mentorship teams across disciplines for several of our trainees: Dr. Gomes-Osman (Mentors: Drs. Loewenstein, Rundek) and Dr. Camargo (Mentors: Drs. Levin, Wurtman, Rundek) who have been successful in obtaining training and research grants in 2018;
- **Imaging working group Goal #1:** We have already started utilizing the research MRI facilities at the Coral Gables campus;
- **Translational working group Goal #3:** We have devised our preliminary unified framework and Logic Model around age-related memory loss, cognitive aging and brain health, which will be presented, discussed and finalized in the Phase II Strategic Planning and included in our MBI Strategic Plan document.

1.4.3. UM Medical School Research Strategic Plan

In November of 2017, Dean Dr. Edward Abraham at the time (now Chief Executive Officer of UHealth) charged our Research Deans and Leadership to execute the Miller School of Medicine Research Strategic Plan. Our new Dean, Dr. Henri Ford (appointed in June 2018) is now in charge of the Plan implementation.

Under this plan, Brain Health, Aging, and Degenerative Diseases are areas of focus under the Neuroscience pillar, one of the main strategically focused areas.



Alignment of our MBI Strategic Plan with the Miller School of Medicine Research strategic plan will create new opportunities for our McKnight Brain Institute to advance the goals and mission through strategically targeted collaborations and partnerships and by leveraging institutional infrastructure, resources and research support.

The next step is to conduct Phase II of the MBI Strategic Retreat in 2019, where the Phase I Retreat attendees will meet in smaller groups to review and refine the goals, priorities, strategies and tactics based on proposed goals and resources, the Medical School Strategic Plan, and feasibility. The Scientific Advisory Board will lead and implement the final strategies and directions of our MBI in the next 5 years. After completion of the Phase II Strategic Plan in 2019, we plan to prepare a separate document, *The MBI Strategic Plan Document*, where the details on unified goals, action plans, milestones and timelines will be provided.

1.5. The McKnight Brain Research Foundation Visits the University of Miami and the Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging Ceremony

In October of 2018, the MBRF Trustees visited our MBI, attended *the UM Evelyn F. McKnight Research Symposium*, and installed *the Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging*.

Dr. Rundek has received the second Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging at the University of Miami.

The Endowed Chair Ceremony was led by Dr. Sacco with participation of the UM President Dr. Julio Frenk, Dean of the University of Miami Miller School of Medicine Dr. Henri Ford, and the MBRF Trustee, Dr. Lee Dockery.

October 30th - 31st, 2018
The McKnight Brain Research Foundation Trustees,
Dr. Sacco, Dr. Rundek and the
UM President Julio Frenk and Medical School Dean Henri Ford





**University of Miami Miller School of Medicine
Evelyn F. McKnight Brain Institute
Research Symposium and Chair Installation
October 31st, 2018**

**Don Soffer Clinical Research Center
Michael S. Gordon Center for Research in Medical Education
1120 NW 14th Street, 1st Floor, Miami, Florida 33136**

8:00am - 8:30am	Breakfast
8:30am - 8:50am	Welcome, Introduction and Scientific Director Transition Ralph L. Sacco, MD, MS, FAHA, FAAN Professor and Olemberg Chair of Neurology Executive Director, Evelyn F. McKnight Brain Institute Director, Clinical and Translational Science Institute Senior Associate Dean for Clinical and Translational Science University of Miami, Miller School of Medicine President, American Academy of Neurology 2017-2019 Edward Abraham, MD Executive Vice President for Health Affairs and Chief Executive Officer of UHealth, University of Miami, Miller School of Medicine J. Lee Dockery, MD McKnight Brain Research Foundation Trustee
8:50am - 9:05am	Scientific Overview Tatjana Rundek, MD, PhD Professor of Neurology Scientific Director, Evelyn F. McKnight Brain Institute Executive Vice Chair of Research and Faculty Affairs Director, Clinical and Translational Research Division Department of Neurology Director, Master of Science in Clinical and Translational Investigation Research Update Session
9:05am - 9:20am	<i>A Treatment Strategy for Age-Related Cognitive Decline: Accelerating Synapse Formation with the Oral Multi-Nutrient Souvenaid</i> Christian Camargo, MD Collaborator, Evelyn F. McKnight Brain Institute Instructor, Clinician Department of Neurology


9:20am - 9:35am	<p><i>Resting-State Functional Brain Connectivity: A Potential Biomarker of Risk For Age-Related Cognitive Decline</i></p> <p>Roger McIntosh, PhD Collaborator, Evelyn F. McKnight Brain Institute Assistant Professor, Department of Psychology, Health Division</p>
9:35am - 9:50am	<p><i>Susceptibility to Deception: Decreasing Vulnerability in Age Related Memory Loss</i></p> <p>Sarah Getz, PhD Collaborator, Evelyn F. McKnight Brain Institute Instructor, Department of Neurology</p>
9:50am - 10:05am	<p><i>Exercise for Brain Health: Neuroplasticity and the Pursuit of Data-driven, Dose-specific Recommendations</i></p> <p>Joyce Gomes-Osman, PT, PhD Member, Evelyn F. McKnight Brain Institute Assistant Professor, Department of Physical Therapy and Neurology</p>
10:05am - 10:20am	<p><i>Sleep Quality Mediates the Relationship Between Cognitive Dysfunction and Frailty in Non-demented Older Adults</i></p> <p>Sonya Kaur, PhD Neuropsychology Research Fellow, Department of Neurology</p>
10:20am - 10:35am	<p><i>Subjective Fatigue and Cognition in Non-demented Older Adults</i></p> <p>Nikhil Banerjee Predoctoral Psychology Trainee, Clinical Health Psychology</p>
10:35am - 10:50am	<p><i>Whole Body Vibration Therapy after Ischemia Reduces Brain Damage In Reproductively Senescent Female Rats</i></p> <p>Ami Raval, PhD Collaborator, Evelyn F. McKnight Brain Institute Associate Research Professor, Department of Neurology</p>
10:50am - 11:00am	Questions
11:00am - 11:15am	Break
11:15am - 11:45am	<p>Chair Presentation</p> <p>Henri Ford, MD, MHA Dean and Chief Academic Officer University of Miami, Miller School of Medicine</p> <p>Chair Presentation</p> <p>President Julio Frenk, MD, MPH, PhD University of Miami, Miller School of Medicine</p> <p>J. Lee Dockery, MD McKnight Brain Research Foundation Trustee</p> <p>Tatjana Rundek, MD, PhD Professor of Neurology Scientific Director, Evelyn F. McKnight Brain Institute Executive Vice Chair of Research and Faculty Affairs Director, Clinical and Translational Research Division Department of Neurology Director, Master of Science in Clinical Translational Investigations</p>

1.5.1. Overview of the Evelyn F. McKnight Brain Institute Research Symposium

October 31, 2018

We decided to provide an opportunity for our MBI trainees and junior faculty to participate in the MBI Research Symposium, present their research and show their enthusiasm to be a part of the Symposium and our MBI.




Dr. Rundek presented the MBI scientific update with the current research portfolio and introduced our junior speakers.



Current MBI Research Project Portfolio


Clinical Studies

- MBI Clinical, Cognitive & Emotional **Frailty Registry**
- **Sleep** in Neurocognitive Aging
- **Fatigue** and Cognitive Aging
- **Brain Plasticity** using Transcranial Magnetic Stimulation (TMS) and Exercise
- **Vascular scores** and Cognitive Aging
- **McKnight Brain Aging Registry (MBAR)**






Soluble and Imaging Biomarkers

- **Systemic & Retinal** Microvascular Dysfunction
- **Biomarkers** for Early Diagnosis of Cognitive Impairment
- **Functional Brain Connectivity** and Risk for Age-Related Cognitive Decline
- **MRI Small Vessel** Perfusion Index
- **Genetic markers** of Cognitive Domains




Clinical Interventional

- **Deception** and Mitigating Susceptibility to Scamming
- Aerobic/resistance **exercise & cognitive training** post stroke (AHA Bugher)
- **Synaptic Function**- Clinical Trial with Souvenaid



Translational Interventional

- **Ischemic Preconditioning**: Mechanisms of Neuroprotection; Diabetes-Hypoglycemia
- **Whole Body Vibration** after Ischemia Reduces Brain Damage (Female Rats)



Cohort Studies

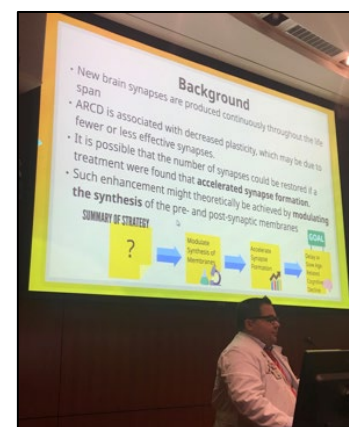
- Age-Related Cognitive Trajectories (NOMAS)
- Vascular contribution to cognitive impairment (Einstein Aging Study)
- HCHS/SOL-INCA (Neurocognitive Aging)

Here are the highlights of the McKnight Research Symposium presentations:

A Treatment Strategy for Age-Related Cognitive Decline: Accelerating Synapse Formation with the Oral Multi-Nutrient Souvenaid **Presented By Christian Camargo, MD**

Christian presented a pilot study of a multi-nutrient oral supplement for improved cognitive performance in participants with age-related cognitive complaints. The study is designed to test the feasibility and safety of *Souvenaid* for improvements in cognitive performance in age-related cognitive decline (ARCD).

Recent research has suggested that the underlying mechanism behind age-related cognitive decline is a *loss of synaptic plasticity*, the dynamic ability of synapses to strengthen or weaken their connections. Synaptic plasticity is essential for learning, memory and the formation of memory engrams in part, through its effects on dendritic spine morphology. A



landmark study has recently described the biological basis of memory engrams by utilizing *Souvenaid*, a specific *oral multi-nutrient*, as an example of a treatment to increase synaptic plasticity. The formulation is based on the biochemical properties of synaptic membranes intimated after years of rigorous research.

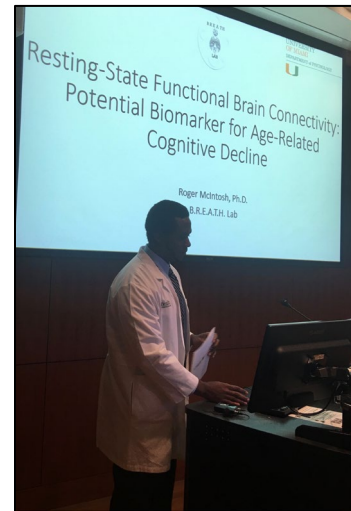
Resting-State Functional Brain Connectivity: A Potential Biomarker of Risk For Age-Related Cognitive Decline

Presented By Roger McIntosh, PhD

Roger eloquently presented some of our resting state functional brain connectivity research, addressing the risk for cognitive aging that was recently submitted for publication.

His first study evidenced preserved resting state functional connectivity (rsFC) of the hippocampus and parietal lobes in Super-Agers, versus age-matched controls, as it relates to lower cardiovascular disease risk.

His second study demonstrated that poorer performance on the Trails-making task was linked to aberrant patterns of intrinsic rsFC in the executive control network of individuals self-reporting high sleep disturbance versus those endorsing low sleep disturbance. He also presented results from an Honor's Thesis Study of one of his students, addressing whether cardiorespiratory fitness relates to differential patterns of intrinsic rsFC of the default mode network in post-menopausal women.



Susceptibility to Deception: Decreasing Vulnerability in Age Related Memory Loss

Presented By Sarah Getz, PhD

Sarah presented on the project scamming in elderly. Scamming, the cheating of people out of money or information, is a pressing public health problem associated with decreased quality of life, functional dependence and negative health outcomes. Individuals in late middle and late adulthood are at particular risk for scamming, but the cognitive, socio-affective, and neurobiological mechanisms underlying this increased risk with advanced age are unclear. There are currently no effective interventions to reduce scam susceptibility in these age groups. Therefore, the long-term goal of this research is to implement an effective intervention to reduce online scam susceptibility in late midlife and old age. Her specific goal is to quantify the cognitive, physical, and socio-affective correlates deception susceptibility, among cognitively healthy late middle and older adults. Within this aim, she will measure participants' actual behavioral response when faced with deceptive stimuli and their scam susceptibility.

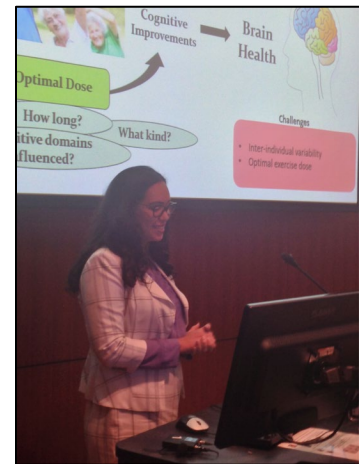
She will employ a selected test battery to identify correlates of self-reported level of scam susceptibility. She hypothesize that high scam susceptibility will be associated with evidence of executive dysfunction, increased frailty symptoms, and lower scores on affective ratings of social wellbeing (e.g., more negative affect, more loneliness).



Exercise for Brain Health: Neuroplasticity and the Pursuit of Data-driven, Dose-specific Recommendations

Presented By Joyce Gomes-Osman, PT, PhD

Joyce spoke about the theoretical concept of brain plasticity, defined as the capacity of the nervous system to adapt and change in response to changes in the environment and lifespan. She expanded upon this concept by presenting a more practical scientific paradigm used to quantify brain plasticity using non-invasive transcranial magnetic brain stimulation (TMS). In addition, she presented the preliminary results of our first McKnight pilot study that was awarded to her last year in which she investigated changes in brain plasticity in aging adults following a 4-week aerobic exercise intervention. Finally, she shared the results of an extensive quantitative systematic review that she carried out with the objective of outlining dose-specific recommendations of exercise to promote cognitive brain health.



Sleep Quality Mediates the Relationship Between Cognitive Dysfunction and Frailty in Non-demented Older Adults

Presented By Sonya Kaur, PhD

Sonya presented on the association of frailty with a host of negative outcomes including cognitive decline in older adults and how sleep quality may play an important role in understanding this association in older adults.

Her results showed that the relationships between frailty severity and measures of executive function, learning and memory were significantly mediated by poor sleep quality. Based on her research, interventions to improve sleep quality may be promising avenues to prevent or potentially reverse cognitive decline in frail older adults.

Subjective Fatigue and Cognition in Non-demented Older Adults

Presented By Nikhil Banerjee

Nick presented the association between self-reported fatigue and neuropsychological functioning in middle-aged and older adults, and the moderating role of physical activity. He showed that higher levels of fatigue were significantly associated with poorer attention/information processing, executive functioning, and psychomotor speed, even after controlling for depression, sleep quality, grip-strength, and gender. Participants endorsing moderate-severe fatigue faced higher odds of exhibiting attention/information processing and psychomotor speed/dexterity impairments than those without after controlling for covariates. Moderation analyses showed that fatigue was related to attention/information processing and psychomotor speed deficits among those reporting mean or lower levels of activity, but not high levels. Overall, these findings highlight fatigue as a distinct and important clinical marker of select cognitive deficits in non-demented older adults. High levels of physical activity may buffer this relationship, suggesting a potential avenue for targeted intervention efforts to promote healthy cognitive aging.

1.5.2. The Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging Ceremony (October 31, 2018).

Dr. Tatjana Rundek was deeply honored by receiving the second *Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging*.

PRESS RELEASE:

Dr. Tatjana Rundek was Awarded the Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging



L-r, back row: Michael Dockery, M.D., Madhav Thambisetty, M.D., Ph.D., Richard Isaacson, M.D., Gene Ryerson, M.D., and Amy Porter. L-r, front row: Dean Henri R. Ford, M.D., MHA, Ralph Sacco, M.D., MS, Tatjana Rundek, M.D., Ph.D., Lee Dockery, M.D., Melanie Cianciotto, President Julio Frenk

At a ceremony before many of the nation’s most prominent neurologists, renowned researcher, epidemiologist, mentor, and educator Tatjana Rundek, M.D., Ph.D., formally became the holder of the Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging.

Dr. Rundek, who is also the scientific director of the Evelyn F. McKnight Brain Institute (MBI) at the University of Miami Miller School of Medicine, said she is excited to lead the dedicated team of physician-scientists who are committed to understanding how aging influences memory.

“I am dedicated to the McKnight Brain Research Foundation [MBRF] mission of improving cognitive brain health,” said Dr. Rundek, professor of neurology and public health, executive vice chair of research and faculty affairs, director of the Clinical Translational Research Division in Neurology, and director of the Master of Science degree program in clinical translational investigations. “I see myself as a catalyst, along with the MBI team, to advance our innovative research and educational programs.”

One of four McKnight Institutes nationwide, MBI was established in 2002 with a generous donation from the MBRF and a match from the Bernard and Alexandria Schoninger Foundation and other UM donors to investigate and treat age-related cognitive decline. Through an additional gift, MBRF then established the Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging to support the scientific director of the institute, providing them the freedom to further their research in the field.

“Today’s installation is a well-deserved honor for Dr. Rundek and stands as a testament to the generosity of the Evelyn F. McKnight Brain Research Foundation,” said University of Miami President Julio Frenk. “We are so appreciative of their extraordinary philanthropy.”

“An endowed chair is one of the highest academic honors that we can confer on a faculty member,” said Henri R. Ford, M.D., MHA, dean and chief academic officer of the Miller School. “It is a tribute to the faculty member’s achievements and our sincere and utmost confidence that this individual is going to continue on a path of excellence.”

J. Lee Dockery, M.D., chair of the board of trustees of MBRF, said Mrs. McKnight would have been delighted with Dr. Rundek’s appointment as chair holder.

“Mrs. McKnight was a great champion of women and had a very successful career as a nurse, serving as a captain in the United States Air Force and as a Nurse in United States Congress —she created great things,” Dr. Dockery said. “Dr. Rundek would have certainly been her choice to take on this challenge.”

Ralph L. Sacco, M.D., MS, professor and chair of the Department of Neurology, has been Dr. Rundek’s colleague for 20 years. He said she embodies a commitment to excellence that is critical to the department’s success.

“Thanks to her innovation, her insight, and her collaboration, Tatjana truly embraces team science,” said Dr. Sacco, who is also the Olemberg Family Chair in Neurological Disorders and executive director of the institute. “She does it with grace and in a way that makes everyone feel a part of the team.”

While accepting the honor, Dr. Rundek thanked those who spoke on her behalf, as well as members of MBRF, her research team, and collaborators. “I like to say, ‘If you want to go fast, go alone. But if you want to go far, go together.’ This has been my motto,” Dr. Rundek said. “I look forward to working with all to do great things.”



2. Publications in Peer Reviewed Journals

Trainee (as first authors) Publications

Banerjee N, McInerney KF, Getz SJ, Sun-Suslow N, Gomes-Osman J, Bure-Reyes A, Sarno M, Dong C, Sun X, Rundek T, Levin BE. The relationship between fatigue and executive function in aging adults. *The Journal of Frailty and Aging*. 2018;7(1).

Caunca MR, Simonetto M, Hartley G, Wright CB, Czaja S. Design and Usability Testing of a Mobile-Friendly Website to Reduce Stroke Caregiver Burden. *Rehabilitation Nursing*. 2018. (In press)

d'Adesky ND, de Rivero Vaccari JP, Bhattacharya P, **Schatz M, Perez-Pinzon MA,** Bramlett HM, **Raval AP**.** Nicotine alters estrogen receptor-beta-regulated inflammasome activity and exacerbates ischemic brain damage in female rats. *Int J Mol Sci*. 2018;19(5).

**Denotes corresponding author

Doliner B, Dong C, Blanton SH, Gardener H, Elkind MSV, **Sacco RL,** Demmer RT, Desvarieux M, **Rundek T.** Apolipoprotein E Gene Polymorphism and Subclinical Carotid Atherosclerosis: The Northern Manhattan Study. *J Stroke Cerebrovasc Dis*. 2018;27(3):645-652.

Gardener H, Caunca M, Dong C, Cheung YK, **Alperin N, Rundek T,** Elkind MSV, Wright CB, **Sacco RL.** Ideal Cardiovascular Health and Biomarkers of Subclinical Brain Aging: The Northern Manhattan Study. *J Am Heart Assoc*. 2018 Aug 21;7(16):e009544.

Gardener H, Caunca MR. Mediterranean Diet in Preventing Neurodegenerative Diseases. *Curr Nutr Rep*. 2018;7(1):10-20.

Gardener H, Moon YP, **Rundek T,** Elkind MSV, **Sacco RL.** Diet Soda and Sugar-Sweetened Soda Consumption in Relation to Incident Diabetes in the Northern Manhattan Study. *Curr Dev Nutr*. 2018 Jan 30;2(5):nzy008.

Gardener H, Pepe PE, **Rundek T,** Wang K, **Dong C,** Ciliberti M, Gutierrez C, Gandia A, Antevy P, Hodges W, Mueller-Kronast N, Sand C, Romano JG, **Sacco RL.** Need to Prioritize Education of the Public Regarding Stroke Symptoms and Faster Activation of the 9-1-1 System: Findings from the Florida-Puerto Rico CRESD Stroke Registry. *Prehosp Emerg Care*. 2018 Oct 25:1-8. doi: 10.1080/10903127.2018.1525458. [Epub ahead of print]

Getz SJ, McInerney KF, Banerjee N, Gomes-Osman J, Sun-Suslow S, Merritt S, Gaztanaga W, Bure-Reyes A, Sarno M, Dong C, Sun X, Rundek T, Levin B. Low Emotional Reserve as a Risk Factor for the Frailty Syndrome Independent of Gender. *The Journal of Frailty and Aging*, 2018;7(1):114.

Getz SJ, McInerney KF, Sun-Suslow S, Banerjee NS, Bure-Reyes A, Sarno M, Levin BE. Low Emotional Reserve as a Risk Factor for the Frailty Syndrome. *Journal of the International Neuropsychological Society*, 2018;24(1).

Gomes-Osman J, Cabral DF, Morris TP, **McInerney K,** Cahalin LP, **Rundek T,** Oliveira A, Pascual-Leone A. Exercise for cognitive brain health in aging: A systematic review for an evaluation of dose. *Neurol Clin Pract.* 2018;8(3):257-265.

Gomes-Osman J, Indahlastari A, Fried PJ, **Cabral DLF, Rice J,** Nissim NR, Aksu S, McLaren ME, Woods AJ. Non-invasive Brain Stimulation: Probing Intracortical Circuits and Improving Cognition in the Aging Brain. *Frontiers in Aging Neuroscience.* 2018;1-25.

Headley A, De Leon A, **Dong C, Levin B, Loewenstein D, Camargo C, Rundek T,** Zetterberg H, Blennow K, Wright C, **Sun X.** "Neurogranin as a predictor of memory and executive function decline in MCI patients." *Neurology.* 2018;90(10):887-895

Khoury N, Koronowski KB, Young JI, **Perez-Pinzon MA.** The NAD(+)-Dependent Family of Sirtuins in Cerebral Ischemia and Preconditioning. *Antioxid Redox Signal.* 2018;28(8):691-710.

Khoury N, Xu J, Stegelmann SD, Jackson CW, Koronowski KB, **Dave KR,** Young JI, **Perez-Pinzon MA.** Resveratrol Preconditioning Induces Genomic and Metabolic Adaptations within the Long-Term Window of Cerebral Ischemic Tolerance Leading to Bioenergetic Efficiency. *Mol Neurobiol.* 2018. (In Press)

McInerney KF, Gomes-Osman J, Banerjee NS, Getz SJ, Sun-Suslow N. Bure-Reyes A, Sarno M, Merritt S, Gaztanaga W, Dong C, Sun X, Rundek T, Levin B. A comparison of frailty criteria in Hispanic/Latino and Non-Hispanic/Latino older adults in South Florida. *The Journal of Frailty and Aging,* 2018;7(1):114.

Rehni AK, Dave KR. Ameliorative potential of conditioning on ischemia-reperfusion injury in diabetes. *Cond Med.* 2018;1(3):105-115.

Rehni AK, Dave KR. Impact of Hypoglycemia on Brain Metabolism During Diabetes. *Mol Neurobiol.* 2018 Dec;55(12):9075-9088.

Rehni AK, Shukla V, Perez-Pinzon MA, Dave KR. Acidosis mediates recurrent hypoglycemia-induced increase in ischemic brain injury in treated diabetic rats. *Neuropharmacology.* 2018;135:192-201.

Ruetenik A. and Barrientos A. Exploiting Post-mitotic Yeast Cultures to Model Neurodegeneration. *Front. Mol. Neurosci,* 2018;11:400. doi: 10.3389/fnmol.2018.00400.

Seixas AA, Henclewood DA, Williams SK, et al. Sleep Duration and Physical Activity Profiles Associated With Self-Reported Stroke in the United States: Application of Bayesian Belief Network Modeling Techniques. *Front Neurol.* 2018;9:534.

Shukla V, Fuchs P, Liu A, **Cohan CH**, **Dong C**, Wright CB, **Perez-Pinzon MA**, **Dave KR**. Recurrent Hypoglycemia Exacerbates Cerebral Ischemic Damage in Diabetic Rats via Enhanced Post-Ischemic Mitochondrial Dysfunction. *Transl Stroke Res*. 2018. (In Press)

Sun-Suslow N, DaCosta AJ, **Banerjee N**, **Sarno M**, **Bure-Reyes A**, **Getz S**, **McInerney KF**, **Levin BE**. The association between indicators of physical frailty syndrome and cognitive functioning. *Journal of the International Neuropsychological Society*, 2018: 24 (1).

Cross-Disciplinary and Collaborative Publications

Alperin N, Wiltshire J, **Lee SH**, **Ramos, AR**, Hernandez-Cardenache R, Curiel Cid RE, **Rundek T**, **Loewenstein DA**. Effect of Sleep Quality on aMCI Vulnerable Brain Regions in cognitively Normal Elderly Individuals. *Sleep*. 2018 Dec 12. doi: 10.1093/sleep/zsy254. [Epub ahead of print]

Crocco EA, **Loewenstein DA**, Curiel RE, **Alperin N**, Czaja SJ, Harvey PD, **Sun X**, Lenchus J, Raffo A, Penate A, Melo J, **Sang L**, Valdivia R, Cardenas K. A Novel Cognitive Assessment Paradigm to Detect Pre-Mild Cognitive Impairment (PreMCI) and the Relationship to Biological Markers of Alzheimer's Disease. *Journal of Psychiatric Research*. 2018;96:33-38.

Dhamoon MS, Cheung YK, Bagci A, **Alperin N**, **Sacco RL**, Elkind MSV, Wright CB. Periventricular White Matter Hyperintensities and Functional Decline. *J Am Geriatr Soc*. 2018;66(1):113-119.

Dueker ND, Guo S, Beecham A, Wang L, **Blanton SH**, Di Tullio MR, **Rundek T**, **Sacco RL**. Sequencing of Linkage Region on Chromosome 12p11 Identifies PKP2 as a Candidate Gene for Left Ventricular Mass in Dominican Families. *G3 (Bethesda)*. 2018;8(2):659-668.

Gomes-Osman J, **Cabral D**, Morris TP, **McInerney K**, Oliveira A, **Rundek T**, Pascual-Leone A. Exercise for cognitive brain cognitive health in aging: a systematic review for an evaluation of dose. *Neurology: Clinical Practice*. 2018;1-9.

Gutierrez J, Kulick E, Park Moon Y, **Dong C**, Cheung K, Ahmet B, Stern Y, **Alperin N**, **Rundek T**, **Sacco RL**, Wright CB, Elkind MSV. Brain Arterial Diameters and Cognitive Performance: The Northern Manhattan Study. *J Int Neuropsychol Soc*. 2018;24(4):335-346.

Raval AP, **Schatz M**, Bhattacharya P, **d'Adesky N**, **Rundek T**, Dietrich WD, Bramlett HM. Whole Body Vibration Therapy after Ischemia Reduces Brain Damage in Reproductively Senescent Female Rats. *Int J Mol Sci*. 2018 Sep 13;19(9). pii: E2749. doi: 10.3390/ijms19092749.

Willey JZ, Moon YP, Dhamoon MS, Kulick ER, Bagci A, **Alperin N**, Cheung YK, Wright CB, **Sacco RL**, Elkind MSV. Regional Subclinical Cerebrovascular Disease Is Associated with Balance in an Elderly Multi-Ethnic Population. *Neuroepidemiology*. 2018;51(1-2):57-63.

Zeki Al Hazzouri A*, **Caunca MR***, Nobrega JC, Elfassy T, Cheung YK, **Alperin N**, **Dong C**, Elkind MSV, **Sacco RL**, DeCarli C, Wright CB. Greater depressive symptoms, cognition, and markers of brain aging: Northern Manhattan Study. *Neurology*. 2018;90(23).

*AZ and MRC shared first authorship.

Abbott SM, Weng J, Reid KJ, **Ramos AR**, et al. Sleep Timing, Stability and Blood Pressure in the Sueno Ancillary Study of the Hispanic Community Health Study/Study of Latinos (HCHS/SOL). *Chest*. 2018.

Ahn S, Lim J, Paik MC, **Sacco RL**, Elkind MS. Cox model with interval-censored covariate in cohort studies. *Biom J*. 2018;60(4):797-814.

Alperin N, Bagci AM. Spaceflight-Induced Visual Impairment and Globe Deformations in Astronauts Are Linked to Orbital Cerebrospinal Fluid Volume Increase. *Acta Neurochir Suppl*. 2018;126:215-219.

Asdaghi N, Wang K, Ciliberti-Vargas MA, Gutierrez CM, Koch S, **Gardener H**, **Dong C**, Rose DZ, Garcia EJ, Burgin WS, Zevallos JC, **Rundek T**, **Sacco RL**, Romano JG; FL-PR CRESD Investigators and Collaborators. Predictors of Thrombolysis Administration in Mild Stroke: Florida-Puerto Rico Collaboration to Reduce Stroke Disparities. *Stroke*. 2018;49(3):638-645.

Baird SW, Jin Z, Okajima K, Russo C, Schwartz JE, Elkind MSV, **Rundek T**, Homma S, **Sacco RL**, Di Tullio MR. Relationship between body mass and ambulatory blood pressure: comparison with office blood pressure measurement and effect of treatment. *J Hum Hypertens*. 2018;32(2):122-128.

Beer J, Snitz BE, Chun-Chou H, Chang J, **Loewenstein DA**, Ganguli M. Does a Cognitive Stress Test predict progression from Mild Cognitive Impairment to dementia equally well in Clinical versus population-based settings? *International Psychogeriatrics*. 2018;16:1-11.

Brown SC, Perrino T, Lombard J, Wang K, Toro M, **Rundek T**, Gutierrez CM, **Dong C**, Plater-Zyberk E, Nardi MI, Kardys J, Szapocznik J. Health Disparities in the Relationship of Neighborhood Greenness to Mental Health Outcomes in 249,405 U.S. Medicare Beneficiaries. *Int J Environ Res Public Health*. 2018;15(3).

Burman R, **Alperin N**, et al. Comparing invasive with MRI-derived Intracranial Pressure measurements in healthy elderly and brain trauma cases: A Pilot Study. *JMRI* 2018. (Accepted pending revisions).

Burman R, **Alperin N**, **Lee SH**, Ertl-Wagner B. Patient-specific cranio-spinal compliance distribution using lumped-parameter model: its relation with ICP over a wide age range. *Fluids Barriers CNS*. 2018;15(1):29.

Bushnell CD, Chaturvedi S, Gage KR, Herson PS, Hurn PD, Jiménez MC, Kittner SJ, Madsen TE, McCullough LD, McDermott M, Reeves MJ, **Rundek T**. Sex differences in stroke: Challenges and opportunities. *J Cereb Blood Flow Metab*. 2018;38(12):2179-2191.

Chen H, Cade BE, Gleason KJ, **Ramos AR**, et al. Multiethnic Meta-Analysis Identifies RAI1 as a Possible Obstructive Sleep Apnea-related Quantitative Trait Locus in Men. *Am J Respir Cell Mol Biol*. 2018;58(3):391-401.

Chen J, Patel SR, Redline S, **Ramos AR**, et al. Weekly sleep trajectories and their associations with obesity and hypertension in the Hispanic/Latino population. *Sleep*. 2018;41(10).

Corp DT, Youssef GJ, Clark RA, **Gomes-Osman J**, Yücel MA, Oldham SJ, Aldraiwiesh S, **Rice J**, Pascual-Leone A, Rogers MA. Reduced motor cortex inhibition and a 'cognitive-first' prioritisation strategy for older adults during dual-tasking. *Experimental Gerontology*. 2018;95-105.

Curiel RE, **Crocco EA**, Raffo A, Guinjoan SM, Nemeroff CB, Pina D, Penate A, **Loewenstein DA**. Failure to recover from proactive semantic interference differentiates amnesic mild cognitive impairment and PreMCI from normal aging after adjusting for initial learning ability. *Advances in Alzheimer's Disease*. 2018;7(02):50.

Del Brutto OH, Castillo PR, Sedler MJ, Del Brutto VJ, Zambrano M, Mera RM, Wright CB, **Rundek T**. Reasons for Declining Consent in a Population-Based Cohort Study Conducted in a Rural South American Community. *J Environ Public Health*. 2018;8267948.

Del Brutto OH, Mera RM, Del Brutto VJ, Zambrano M, Wright CB, **Rundek T**. Clinical and neuroimaging risk factors for cognitive decline in community-dwelling older adults living in rural Ecuador. A population-based prospective cohort study. *Int J Geriatr Psychiatry*. 2018 Nov 26. doi: 10.1002/gps.5037. [Epub ahead of print]

Della-Morte D, Dong C, Markert MS, Elkind MSV, **Sacco RL**, Wright CB, **Rundek T**. Carotid Intima-Media Thickness Is Associated With White Matter Hyperintensities: The Northern Manhattan Study. *Stroke*. 2018;49(2):304-311.

Della-Morte D, Gardener H, Dong C, Markert M, **Cabral D**, Elkind MSV, **Sacco RL, Rundek T**. Association Between Carotid Artery Function and Structure in the Northern Manhattan Study. *Front Neurol*. 2018;9:246.

Deng Y, Li M, Wang G, **Jiang H, Wang J**, Zhong J, Li S, Yuan J. The inter-visit variability of retinal blood flow velocity measurements using retinal function imager (RFI). *Eye Vis (Lond)*. 2018;5:31.

Devanand DP, Strickler JG, Huey ED, **Crocco E**, Forester BP, Husain MM, Vahia IV, Andrews H, Wall MM, Pelton GH. Lithium treatment for agitation in Alzheimer's disease (Lit-AD): clinical rationale and study design. *Contemporary Clinical Trials*. 2018;71:33-39.

Dhamoon MS, Cheung YK, DeRosa JT, Gutierrez J, Moon YP, **Sacco RL**, Elkind MSV, Wright CB. Association Between Subclinical Brain Infarcts and Functional Decline Trajectories. *J Am Geriatr Soc*. 2018;66(11):2144-2150.

Dhamoon MS, Cheung YK, Gutierrez J, Moon YP, **Sacco RL**, Elkind MSV, Wright CB. Functional Trajectories, Cognition, and Subclinical Cerebrovascular Disease. *Stroke*. 2018;49(3):549-555.

Fang C, Li C, Cabrerizo M, Barreto A, Andrian J, Rishe N, **Loewenstein D**, Duara R, Adjouadi M. Gaussian Discriminant Analysis for Optimal Delineation of Mild Cognitive Impairment in Alzheimer's Disease. *Int J. Neural Syst*. 2018 Apr 12:1850017. doi: 10.1142/S012906571850017X. [Epub ahead of print]

Fleysher R, Lipton ML, Noskin O, **Rundek T**, Lipton R, Derby CA. White matter structural integrity and transcranial Doppler blood flow pulsatility in normal aging. *Magn Reson Imaging*. 2018;47:97-102.

Gameiro GR, Jiang H, Liu Y, Deng Y, **Sun X**, Nascentes B, **Baumel B**, **Rundek T**, **Wang J**. Retinal tissue hypoperfusion in patients with clinical Alzheimer's disease. *Eye Vis (Lond)*. 2018;17(5):21.

Grassi M, **Loewenstein DA**, Caldirola D, Schruers K, Duara R, Perna G. A clinically-translatable machine learning algorithm for the prediction of Alzheimer's disease conversion: further evidence of its accuracy via a transfer learning approach. *Internat Psychogeriatrics*. 2018;1-9.

Grassi M, Perna G, Caldirola Schruers K, Duara R, **Loewenstein DA**. A clinically- translatable machine learning algorithm for the prediction of Alzheimer's Disease conversion in individuals with mild and pre-mild cognitive Impairment, *J of Alzheimer's Disease*. 2018;61(4) 1555-1573.

Haley A, Oleson S, Pasha E, Birdsill A, **Kaur S**, Thompson J, Tanaka H. Phenotypic heterogeneity of obesity-related brain vulnerability: one-size interventions will not fit all, *Annals of the New York Academy of Sciences*. 2018;1428:89-102.

Hall DA, **Ramos AR**, Gelfand JM, et al. The state of clinical research in neurology. *Neurology*. 2018;90(15):e1347-e1354.

Hoffer ME, **Levin BE**, Snapp H, Buskirk J, Balaban C. Acute findings in an acquired neurosensory dysfunction. *Laryngoscope Investigative Otolaryngology*. <http://doi.org/10.1002/lio2.231>

Hunter MD, Park Moon Y, DeCarli C, Gutierrez J, Wright CB, Di Tullio MR, **Sacco RL**, Kamel H, Elkind MSV. Electrocardiographic left atrial abnormality and silent vascular brain injury: The Northern Manhattan Study. *PLoS One*. 2018 Oct 12;13(10):e0203774.

Jiang H, Wei Y, Shi Y, Wright C, **Sun X**, Gregori G, Zheng F, Vanner E, Lam B, **Rundek T**, **Wang J**. Altered retinal microvasculature in mild cognitive impairment and Alzheimer's disease. *JNO*, 2018;38(3):292-298.

Jiang H, Liu Y, Wei Y, Shi Y, Wright CB, **Sun X**, **Rundek T**, **Baumel BS**, **Landman J**, **Wang J**. Impaired retinal microcirculation in patients with Alzheimer's disease. *PLoS One*. 2018 Feb 2;13(2):e0192154.

Kulick ER, Wellenius GA, Boehme AK, **Sacco RL**, Elkind MS. Residential Proximity to Major Roadways and Risk of Incident Ischemic Stroke in NOMAS (The Northern Manhattan Study). *Stroke*. 2018;49(4):835-841.

Lange MC, Ribas G, Scavasine V, Ducci RD, Mendes DC, Zétola VHF, Cabral N, **Rundek T**. Stroke recurrence in the different subtypes of ischemic stroke. The importance of the intracranial disease. *Arq Neuropsiquiatr*. 2018;76(10):649-653.

Leifer D, **Rundek T**. Atrial cardiopathy: A new cause for stroke? *Neurology*. 2018 Dec 5. pii: 10.1212/WNL.0000000000006749. doi: 10.1212/WNL.0000000000006749. [Epub ahead of print]

Lowenstein DA, Curiel RE, DeKosky S, Bauer RM, Rosselli M, Guinjoan S, Adjouadi M, Penate A, Barker W, Goenaga S, Golde T, Greig-Custo M, Hanson KS, Li C, Lizarraga L, Marsiske M, Duara, R. Utilizing Semantic Intrusions to Identify Amyloid Positivity in Mild Cognitive Impairment. *Neurology*. 2018;91:e976-e984. doi.10.1212/WNL.0000000000006128.

Matias-Guiu JA, Cabrera-Martin MN, Curiel RE, Valles-Salgado M, Rognoni T, Moreno-Ramos T, Carreras JL, **Loewenstein DA**, Matias-Guiu J. Comparison between FCSRT and LASSI-L to detect early stage Alzheimer's Disease. *Journal of Alzheimer's Disease*. 2018;61(1):103-111.

McDermott M, Miller EC, **Rundek T**, Hurn PD, Bushnell CD. Preeclampsia: Association With Posterior Reversible Encephalopathy Syndrome and Stroke. *Stroke*. 2018;49(3):524-530.

Morris TP, Costa-Miserachs D, Rodriguez-Rajo P, Finestres J, Bernabeu M, **Gomes-Osman J**, Pascual-Leone A, Tormos-Muñoz JM. Feasibility of Aerobic Exercise in the Subacute Phase of Recovery From Traumatic Brain Injury: A Case Series. *Journal of Neurologic Physical Therapy*, 2018;268-275.

Mowrey WB, Lipton RB, Katz MJ, Ramratan WS, **Loewenstein DA**, Zimmerman ME, Buschke H. Memory Binding Test predicts incident dementia: Results from the Einstein Aging Study 2017. *Journal of Alzheimer's Disease*. 2018;62(1):293-304.

Nakanishi K, Jin Z, Homma S, Elkind MSV, **Rundek T**, Lee SC, Tugcu A, Yoshita M, DeCarli C, Wright CB, **Sacco RL**, Di Tullio MR. Association Between Heart Rate and Subclinical Cerebrovascular Disease in the Elderly. *Stroke*. 2018;49(2):319-324.

Oleson S, Eagan D, **Kaur S**, Hertzling WJ, Alkatan M, Davis JN, Tanaka H, Haley A. Apolipoprotein E genotype moderates the association between dietary polyunsaturated fat and brain function: an exploration of cerebral glutamate and cognitive performance. *Nutritional Neuroscience*. 2018;1-10.

Petrov ME, Weng J, Reid KJ, et al. (**Ramos AR**). Commuting and Sleep: Results From the Hispanic Community Health Study/Study of Latinos Sueno Ancillary Study. *Am J Prev Med*. 2018;54(3):e49-e57.

Ramos AR, Weng J, Wallace DM, et al. Sleep Patterns and Hypertension Using Actigraphy in the Hispanic Community Health Study/Study of Latinos. *Chest*. 2018;153(1):87-93.

Reid KJ, Weng J, et al. (**Ramos AR**). Impact of shift work schedules on actigraphy-based measures of sleep in Hispanic workers: results from the Hispanic Community Health Study/Study of Latinos ancillary Sueno study. *Sleep*. 2018;41(10).

Ricardo AC, Chen J, Singh M, et al. (**Ramos AR**). Sleep-Disordered Breathing and Prevalent Albuminuria in Hispanics/Latinos. *Kidney Int Rep*. 2018;3(6):1276-1284.

Rundek T, Hofman A, Mathiesen EB, Castelnuovo S, Landecho MF, Rosvall M, Gabriel R, de Luca N, Liu J, Baldassarre D, Kavousi M, de Groot E, Bots ML, Yanez DN, Thompson SG; PROG-IMT study group. Correction: Predictive value for cardiovascular events of common carotid intima media thickness and its rate of change in individuals at high cardiovascular risk - Results from the PROG-IMT collaboration. *PLoS One*. 2018 Sep 20;13(9):e0204633.

Shao Y, Jiang H, Wei Y, Shi Y, Shi C, Wright CB, **Sun X**, Vanner EA, Rodriguez AD, Lam BL, **Rundek T**, **Baumel BS**, Gameiro GR, **Dong C**, **Wang J**. Visualization of Focal Thinning of the Ganglion Cell-Inner Plexiform Layer in Patients with Mild Cognitive Impairment and Alzheimer's Disease. *J Alzheimers Dis*. 2018;64(4):1261-1273.

Wilson KE, Abulafia C, **Loewenstein DA**, Vigo DE, Sevlever G, Nemeroff CB, Villarreal MF, Guinjoan SM. Individual cognitive and depressive traits associated with maternal versus paternal family history of Late-onset Alzheimer's disease: Proactive semantic interference versus standard neuropsychological assessments. *Personalized Medicine in Psychiatry*. 2018;11-12:1-6.

Bacman SR, Kauppila JHK, Pereira CV, Nissanka N, Miranda M, **Pinto M**, Williams SL, Larsson NG, Stewart JB, **Moraes CT**. MitoTALEN reduces mutant mtDNA load and restores tRNA^{Ala} levels in a mouse model of heteroplasmic mtDNA mutation. *Nat Med*. 2018;Nov;24 [PMID: 30250143], [PMID: 30291358]

Capuani B, Pacifici F, **Della-Morte D**, Lauro D. Glucagon Like Peptide 1 and MicroRNA in Metabolic Diseases: Focusing on GLP1 Action on miRNAs. *Frontiers in Endocrinology*. 2018. (In Press)

Carmona-Gutierrez D, Bauer MA, Zimmermann A, Aguilera A, Austriaco N, Ayscough K, Balzan R, Bar-Nun S, **Barrientos A**, Belenky P et al. Guidelines and recommendations on yeast cell death nomenclature. *Microb Cell*. 2018;5(1):4-31.

Curcio F, Sasso G, Liguori I, Ferro G, Russo G, Cellurale M, **Della-Morte D**, Gargiulo G, Testa G, Cacciatore F, Bonaduce D, Abete P. The reverse metabolic syndrome in the elderly: Is it a "catabolic" syndrome? *Aging Clin Exp Res*. 2018;(30):547-554.

De Marchis ML, Guadagni F, Silvestris E, Lovero D, **Della-Morte D**, Ferroni P, Barbanti P, Palmirotta R. Genetic bases of the nutritional approach to migraine. *Crit Rev Food Sci Nutr*. 2018;1-13.

Ferroni P, Barbanti P, **Della-Morte D**, Palmirotta R, Jirillo E, Guadagni F. Redox Mechanisms in Migraine: Novel Therapeutics and Dietary Interventions. *Antioxid Redox Signal*. 2018;(28):1144-1183.

Guedes-Monteiro RF, Ferreira-Junior JR, Bleicher L, Nóbrega FG, **Barrientos A**, Barros MH. Mitochondrial ribosome bL34 mutants present diminished translation of cytochrome c oxidase subunits. *Cell Biol Int*. 2018;42(6):630-642.

Jackson CW, Escobar I, Xu J, **Perez-Pinzon MA**. Effects of ischemic preconditioning on mitochondrial and metabolic neuroprotection: 5' adenosine monophosphate-activated protein kinase and sirtuins. *Brain Circ*. 2018;4(2):54-61.

Jy W, **Rehni AK**, Bidot C Jr, Navarro-Quero H, Haase CR, Koch S, Ahn YS, **Dave KR**. Pharmacokinetics of Human Red Blood Cell Microparticles Prepared Using High-Pressure Extrusion Method. *Front Pharmacol*. 2018;9:599.

Kim H-J, **Barrientos A**. MTG1 Couples Mitoribosome Large Subunit Assembly with Inter-Subunit Bridge Formation. *Nucleic Acids Res*. 2018;46(16):8435-8453.

Klingbeil KD, Koch S, **Dave KR**. Potential link between post-acute ischemic stroke exposure to hypoglycemia and hemorrhagic transformation. *Int J Stroke*. 2018. (In Press)

Koronowski KB, **Khoury N**, Morris-Blanco KC, **Stradecki-Cohan HM**, Garrett TJ, **Perez-Pinzon MA**. Metabolomics Based Identification of SIRT5 and Protein Kinase C Epsilon Regulated Pathways in Brain. *Front Neurosci*. 2018;12:32.

Liguori I, Curcio F, Russo G, Cellurale M, Aran L, Bulli G, **Della-Morte D**, Gargiulo G, Testa G, Cacciatore F, Bonaduce D, Abete P. Risk of Malnutrition Evaluated by Mini Nutritional Assessment and Sarcopenia in Noninstitutionalized Elderly People. *Nutr Clin Pract*. 2018;(33):879-886.

Liguori I, Russo G, Aran L, Bulli G, Curcio F, **Della-Morte D**, Gargiulo G, Testa G, Cacciatore F, Bonaduce D, Abete P. Sarcopenia: assessment of disease burden and strategies to improve outcomes. *Clin Interv Aging*. 2018:913-927.

Liguori I, Russo G, Aran L, Bulli G, Curcio F, **Della-Morte D**, Gargiulo G, Testa G, Ungar A, Cacciatore F, Bonaduce D, Abete P. Acute care hospital at different levels of intensity: the role of Geriatrician. *Aging Clin Exp Res*. 2018;(7):703-712.

Liguori I, Russo G, Coscia V, Aran L, Bulli G, Curcio F, **Della-Morte D**, Gargiulo G, Testa G, Cacciatore F, Bonaduce D, Abete P. Orthostatic Hypotension in the Elderly: A Marker of Clinical Frailty? *J Am Med Dir Assoc*. 2018;779-785.

Liguori I, Russo G, Curcio F, Bulli G, Aran L, **Della-Morte D**, Gargiulo G, Testa G, Cacciatore F, Bonaduce D, Abete P. Oxidative stress, aging, and diseases. *Clin Interv Aging*. 2018;13:757-772.

Liguori I, Russo G, Curcio F, Sasso G, **Della-Morte D**, Gargiulo G, Pirozzi F, Cacciatore F, Bonaduce D, Abete P, Testa G. Depression and chronic heart failure in the elderly: an intriguing relationship. *J Geriatr Cardiol*. 2018;(15):451-459.

Lobo-Jarne T, Nývltová E, Pérez-Pérez R, Timón-Gómez A, Molinié T, Choi A, Mourier A, Fontanesi F, Ugalde C, **Barrientos A**. Human COX7A2L regulates the biogenetic rates of respiratory chain complex III and complex III-containing supercomplexes. *Cell Reports*. 2018;25(7):1786-1789.

Maiti P, Kim H-J, Tu Y-T, **Barrientos A**. Human GTPBP10 is essential for mitochondrial ribosome maturation. *Nucleic Acids Res*. 2018;46(21):11423-11437.

Micarelli A, Viziano A, **Della-Morte D**, Augimeri I, Alessandrini M. Degree of Functional Impairment Associated With Vestibular Hypofunction Among Older Adults With Cognitive Decline. *Otol Neurotol*. 2018;(39);e392-e400.

Narayanan SV, **Dave KR**, **Perez-Pinzon MA**. Ischemic Preconditioning Protects Astrocytes against Oxygen Glucose Deprivation Via the Nuclear Erythroid 2-Related Factor 2 Pathway. *Transl Stroke Res*. 2018;9(2):99-109.

Nissanka N, **Moraes CT**, **Pinto M**. Image-Based Analysis of Mitochondrial Area and Counting from Adult Mouse Dopaminergic Neurites. *Bio-protocol*. 2018;8(16): e2471. DOI: 10.21769/BioProtoc.2471.

Pacifici F, **Della-Morte D**, Capuani B, Pastore D, Bellia A, Sbraccia P, Di Daniele N, Lauro R, Lauro D. Peroxiredoxin6, a Multitask Antioxidant Enzyme Involved in the Pathophysiology of Chronic Non-Communicable Diseases. *Antioxid Redox Signal*. 2018.

Pacifici F, **Della-Morte D**, Capuani B, Piermarini F, Pastore D, Arriga R, Coppola A, Ciccocanti F, Donadel G, Fimia GM, **Rundek T**, **Barrientos A**, Bellia A, Orlandi A, Lauro D. Depletion of Peroxiredoxin6 Modulates Insulin Secretion by Impairing Mitochondrial Fate. *Metabolism*. Submitted 2018.

Pinto M, Nissanka N, **Moraes CT**. Lack of Parkin anticipates the phenotype and affects mitochondrial morphology and mtDNA levels in a mouse model of Parkinson's disease. *J Neurosci*. 2018 Jan 24. [PMID: 29222404]

Pinto M, Vempati UD, Diaz F, Peralta S, **Moraes CT**. Ablation of Cytochrome c in Adult Forebrain Neurons Impairs Oxidative Phosphorylation Without Detectable Apoptosis. *Mol Neurobiol*. 2018 Sep 6. [PMID: 30191381]

Raval AP**, Martinez CC, Mejias NH, de Rivero Vaccari JP. Sexual dimorphism in inflammasome-containing extracellular vesicles and the regulation of innate immunity in the brain of reproductive senescent females. *Neurochem Int*. 2018;S0197-0186(18)30536-9.

**Denotes corresponding author

Raval AP**, Schatz M, Bhattacharya P, **d'Adesky ND**, **Rundek T**, Dietrich WD, Bramlett HM**. Whole body vibration therapy after ischemia reduces brain damage in reproductively senescent female rats. *Int J Mol Sci*. 2018;19(9).

**Denotes corresponding author

Smith L, Chakraborty D, Bhattacharya P, Sarmah D, Koch S, **Dave KR**. Exposure to hypoglycemia and risk of stroke. *Ann N Y Acad Sci*. 2018;1431(1):25-34.

Viziano A, Micarelli A, Pasquantonio G, **Della-Morte D**, Alessandrini M. Perspectives on multisensory perception disruption in idiopathic environmental intolerance: a systematic review. *Int Arch Occup Environ Health*. 2018;(91):923-935.

Zeng R, Smith E, **Barrientos A**. Yeast Mitoribosome Large Subunit Assembly Proceeds by Hierarchical Incorporation of Protein Clusters and Modules on the Inner Membrane. *Cell Metab*. 2018;27(3):6

3. Publications (other)

Bacman SR, Williams SL, **Pinto M**, **Moraes CT**. *Methods in Enzymology, Mitochondrial Function*, Edited by Anne Murphy & David Chan (book chapter).

Banerjee N, **Getz S**, **Levin BE**. (2018). Neurosensory, neuropsychological and psychiatric comorbidities in mild TBI. In M. Hoffer & C. Balaban (Eds.), *Neurosensory Disorders in Mild Traumatic Brain Injury* 1st Edition. Cambridge, MA: Academic Press.

Della-Morte D. Interview for Italian scientific magazine *Oggiscienza*: “Aggiustare i mitocondri per curare malattie” July 10th 2017.

Gardener H, **Caunca MR**. Mediterranean Diet in Preventing Neurodegeneration. Invited Review for *Current Nutrition Reports*, 2018 Mar;7(1):10-20. PMID: 29892785.

Gomes-Osman J. What kinds of exercise are good for brain health? Harvard Health Publication Blog Post. <https://www.health.harvard.edu/blog/what-kinds-of-exercise-are-good-for-brain-health-2018050213762>. May 2018.

4. Presentations at Scientific Meetings

Loewenstein D. Presentation: Novel Cognitive Stress Test in Alzheimer's disease. Mt. Sinai MCI Symposium, January 2018.

Aldraiwiesh S, **Rice J, Gomes-Osman J.** Assessing the influence of cognitive training and physical exercise on mechanisms of plasticity and static balance in individuals post-stroke. Combined Sections Meeting American Physical Therapy Association. Poster February 21-24, 2018. New Orleans, LA.

Banerjee N, Hoffer M, Kiderman A, Hotz G, **Getz S, Levin BE.** Antisaccade abnormalities predict recovery on the Trail Making Test in mild TBI patients. Presented at the 3rd Joint Symposium of the International and National Neurotrauma Societies and AANS/CNS Section on Neurotrauma and Critical Care meeting, Aug 2018 Toronto, Ontario, Canada.

Banerjee N, Sun-Suslow N, Getz SJ, Sarno M, Bure-Reyes A, Pinjala M, Luca C, **Levin BE.** Age-related differences in the association between cardiometabolic risk factors and cognition in Parkinson's disease. *Journal of the International Neuropsychological Society*, 2018: 24 (1).

Barrientos A. sMitochondrial mechanisms of neurodegenerative disorders. Army Research Laboratory Symposium. Cocoa Beach, Florida, January 8-11, 2018.

Barrientos A. Assembly of Organellar Protein Complexes: Proteins, Lipids and Cofactors. Gordon Research Conference in Mitochondria and Chloroplasts. Introduction to session and Discussion Leader. Luca (Italy), July 8-13, 2018.

Barrientos A. Assembly of the cytochrome c oxidase Cu_B site in human COX1. Copper Meeting 2018. Bridging clinical and fundamental science. Sorrento (Italy), September 23-28, 2018.

Barrientos A. Mitochondrial biogenesis from yeast to human. A Symposium to Honor the Career of Alexander Tzagoloff. Columbia University. New York, October 5, 2018.

Brito, Y, CC Pedraza, AR Abreu, **AR Ramos.** Poster presentation: The Case for Spino-cerebellar Ataxia with Insomnia and Comorbid Obstructive Sleep Apnea. SLEEP41, A418-A418.

Cabral D, Ramon V, Teixeira O, **Rice J,** Oliveira A, **Gomes-Osman J.** An evidence-based health education program may improve cognition in sedentary older adults: an ongoing randomized controlled trial. University of Miami Neuroscience Day. Poster December 7th, 2018. Miami, FL.

Camargo C. Served on Advisory Board for NUTRICIA Advanced Medical Nutrition, "Patient-Centered Outcomes in Souvenaid Clinical Trials," Clinical Trials in Alzheimer's Disease 2018. Barcelona, Spain October 27th, 2018.

Capuani F, Pacifici D, Pastore S, Rea F, Piermarini A, Coppola R, Arriga G, Donadel A, Bellia D, **Della-Morte D**, Lauro D. L'inibizione di SIRT1 mediata dal miRNA543 attiva l'infiammazione nel diabete mellito di tipo 2 at 27th National Congress of the Italian Society of Diabetologia (SID) Rimini, May 16-19, 2018.

Caunca MR, Odden M, Glymour MM, Elfassy T, Kershaw K, Sidney S, Yaffe K, Launer L, Zeki Al Hazzouri A. Long Term Patterns of Neighborhood-Level Racial Segregation and Midlife Cognitive Performance. Oral presentation at the Society for Epidemiologic Research Annual Meeting, Baltimore, MD.

Caunca MR, Simonetto M, Alperin N, Elkind MSV, **Sacco RL**, Wright CB, **Rundek T**. Greater Body Mass Index is Associated with Smaller Cortical Thickness in the Alzheimer Disease-Signature Regions: The Northern Manhattan Study. Oral Data Blitz Presentation and Poster at the American Neurological Association Annual Meeting, Atlanta, GA.

Caunca MR, Simonetto M, Dong C, Gardener H, Cheung K, **Alperin N**, McLaughlin C, Elkind MSV, **Rundek T, Sacco RL**, Wright CB. Association of Systolic Blood Pressure Targets and Regional White Matter Lesion Load: the Northern Manhattan Study (NOMAS). Oral presentation at the American Academy of Neurology Annual Meeting, Los Angeles, CA.

Caunca MR, Simonetto M, Gardener H, Ng-Reyes M, Guerrero R, **Alperin N**, Lee SG, Elkind MSV, **Sacco RL**, Wright CB, **Rundek T**. Adiponectin and Components of Metabolic Syndrome are Associated with Cortical Thickness: the Northern Manhattan Study. Poster at International Stroke Conference, Los Angeles, CA.

Caunca MR, Simonetto M, Rice J, De Leon-Benedetti A, Hartley G, Czaja S. A Mobile-Friendly Website to Reduce Stroke Caregiver Burden: A Qualitative and Pilot Study. Poster at International Stroke Conference, Los Angeles, CA.

Cohan CH, Perez E, **Stradecki-Cohan HM**, Brusko D, Garvin AA, **Dave KR, Sacco RL, Perez-Pinzon MA**. Exercise improves motor recovery in aged animals but not young. Bugher Symposium organized by the American Heart Association, Los Angeles, California. January 2018. Abstract was not refereed.

Dave KR, Cohan CH, Youbi M, Ruiz A, **Saul I**, Furones C, Patel P, **Stradecki-Cohan HM**, Perez E, Brusko D, Garvin AA, **Raval A, Zhao W, Dong C, Sacco RL, Perez-Pinzon MA**. Physical exercise promotes post-stroke cognitive recovery in elderly animals. Bugher Symposium organized by the American Heart Association, Los Angeles, California. January 2018. Abstract was not refereed.

Haase CR, Jy W, **Rehni AK**, Bidot C Jr., Navarro-Quero H, Koch S, Ahn YS, **Dave KR**. Pharmacokinetics of human red blood cell microparticles intended for use as a hemostatic agent.

44th Annual Eastern-Atlantic Student Research Forum, held at the University of Miami, February 2018. Abstract was not refereed.

Kaur S, Banerjee N, Miranda M, Slugh M, Sun-Suslow N, McInerney K, Sun X, Ramos A, Rundek T, Sacco R, Levin B. Sleep quality, frailty and cognitive dysfunction in non-demented middle aged to older adults. To be presented at the 47th Annual meeting of the International Neuropsychological Society 2019, New York, New York.

Pacifici B, Capuani F, Piermarini D, Pastore R, Arriga R, Coppola A, Rea S, Donadel G, Bellia A, **Della-Morte D**, Lauro D. La Prdx6 previene la miopatia diabetica promuovendo il differenziamento delle cellule muscolari at 27th National Congress of the Italian Society of Diabetologia (SID) Rimini, May 16-19, 2018.

Pacifici B, Capuani F, Piermarini D, Pastore R, Arriga A, Coppola S, Rea S, Donadel A, Bellia A, **Della-Morte D**, Lauro D. Prdx6 prevents Diabetic Myopathy by improving skeletal muscle cells differentiation at 78th American Diabetes Association (ADA), Orlando, June 21-26, 2018.

Pacifici B, Capuani F, Piermarini D, Pastore R, Arriga R, Coppola A, Rea S, Donadel G, Bellia A, **Della-Morte D**, Lauro D. Prdx6 deletion increased the risk of Type 2 Diabetes-associated Sarcopenia by impairing skeletal muscle cells differentiation at 54th EASD Annual meeting, Berlin 1-5, October 2018.

Perez E, **Caunca M**, Montero D, Reyes-Iglesias Y. The Importance of Neurology as a Required Third-Year Clerkship: a Medical Student Survey. Poster at the American Academy of Neurology Annual Meeting, Los Angeles, CA.

Raval AP, Schatz M, Bhattacharya P, **d'Adesky N, Rundek T**, Dietrich WD, Bramlett HM. Whole body vibration after ischemia reduces inflammation in the brain of reproductively senescent female rats. International Stroke Conference held at Los Angeles, January 23rd 2018. (Refereed)

Raval A. Society for neuroscience (SFN) 2018 annual meeting and McKnight Brain Research Foundation 2018 Poster Reception. San Diego, California.

Rehni AK, Shukla V, Dave KR. Potential role of endoplasmic reticulum stress in mediating recurrent hypoglycemia-induced increase in ischemic brain damage in treated diabetic rats. 9th annual Postdoctoral research day, University of Miami Miller School of Medicine, March 2018.

Reyes-Iglesias Y, **Caunca M**, Ribot R. Changing the Image of Neurology. Poster at the American Academy of Neurology Annual Meeting, Los Angeles, CA.

Rice J, Cahalin L, Corp D, Swarowsky A, Levin B, Tatjana R, McInerney K, Gomes-Osman J. Timed Up-and-Go Performance and Dual-Task Effects are Correlated with Distinct Neuropsychological Measures of Executive Function in Healthy Older Adults. Evelyn F. McKnight Poster Reception at Society for Neuroscience Meeting. Poster November 5th, 2018. San Diego, CA.

Rice J, Corp D, Swarowsky A, Gomes-Osman J. Dual-task performance is related to a neurophysiological measure of plasticity in individuals with memory disorders. Evelyn F. McKnight Poster Reception at Society for Neuroscience Meeting. Poster November 5th, 2018. San Diego, CA.

Rice J, McInerney K, Levin B, Morris T, Cabral D, Rundek T, Gomes-Osman J. Effects of a 4-week Aerobic Exercise Intervention on TMS Neuroplasticity Measures and Cognition in Healthy Sedentary Adults: an Ongoing Pilot Study. Evelyn F. McKnight Poster Reception at Society for Neuroscience Meeting. Poster November 5th, 2018. San Diego, CA.

Sacco RL. Neurology Update & Stroke Intensive 2018, Stroke Prevention and Maintaining Brain Health, Miami, FL, January 18-20, 2018.

Sacco RL. 2018 Evelyn F. McKnight Brain Institute Inter-Institutional Meeting, Birmingham, AL, April 4 – 6, 2018.

Sacco RL. Hypertension, Small Vessel Disease and Cognition, The Heart & Brain Symposium, Chicago, IL, June 29, 2018.

Sacco RL. 16th Pan Arab Neurological Societies (PAUNS), Improving Acute Stroke Management, Amman, Jordan, September 20, 2018.

Sacco RL. 16th Pan Arab Union Neurological Societies Meeting, Preventing Stroke and Maintaining Brain Health, Amman, Jordan, September 20, 2018.

Sacco RL. 11th World Stroke Congress Stroke Congress, Life's Simple Seven Determinants of Stroke and Brain Health, Montreal, Canada, October 17, 2018.

Sacco RL. 42nd Mexican Academy of Neurology Annual Meeting 2018, Treatment of Carotid Stenosis in 2018, Merida, Yucatan, Mexico, November 7, 2018

Sacco RL. The Annual Israeli Neurological Association Meeting 2018, Neurology Challenges and Future Opportunities, Tel Aviv, Israel, December 11, 2018.

Sacco RL. The Annual Israeli Neurological Association Meeting 2018, Preventing Stroke and Promoting Brain Health, Tel Aviv, Israel, December 11, 2018.

Swarowsky A, **Rice J**, Aldraiwiesh S, **Gomes-Osman J.** An individualized locomotor training for freezing of gait in Parkinson's Disease augmented by transcranial direct current stimulation: a case report. Combined Sections Meeting American Physical Therapy Association. Poster February 21-24, 2018. New Orleans, LA.

Watanabe M, Bhattacharya P, Khan A, Hare JM, **Perez-Pinzon MA, Raval AP**, Yavagal DR. Multiple intra-arterial dosing of the mesenchymal stem cells reduces ischemic brain injury in a rat stroke model. International Stroke Conference held at Los Angeles, January 23rd 2018. (Refereed)

5. Publications at Public (Non-scientific) Meeting or Events

Buré-Reyes A, Fernández McInerney K, Miranda M, Sarno M. Workshop for the South Florida Hispanic Coalition on Aging “Normal and Abnormal Aging: The Need for Neuropsychological Assessment”, Trustbridge Health, Ft. Lauderdale, FL, August 2018.

Buré-Reyes A, Fernández McInerney K, Miranda M, Sarno M. Workshop for the South Florida Hispanic Coalition on Aging “Normal and Abnormal Aging: The Need for Neuropsychological Assessment”, University of Miami, Miami, FL, November 2018.

Camargo C. "Alzheimer's Disease vs. Senile Dementia," Invited Speaker Medical Education Speakers Network, North Shore Medical Center, Miami, FL. May 11, 2018.

Caunca M. Advanced Psychometric Methods Workshop for Cognitive Aging Research. August 2018, Tahoe, CA.

Caunca M. Freesurfer Workshop, October 2018, Boston, MA.

Caunca M. Epidemiology Journal Club, October 2018. LASSO Regression and Prediction Modeling using Biomarker Data.

Dave K. The McKnight brain research foundation, 10th inter-institutional meeting, University of Alabama at Birmingham April 2018.

Loewenstein D. A Novel Cognitive Test, Brain Biomarkers and Early Detection of Preclinical Alzheimer’s Disease. Deans Lecture for Weil Cornell Medical School, Manhattan, New York, March, 26, 2018.

Loewenstein D. A Novel Cognitive Test, Brain Biomarkers and Early Detection of Pre-Clinical Alzheimer’s Disease. Research. Seminar for Florida Atlantic University, Boca Raton, March, 30, 2018.

Loewenstein D. Lecture: Nurturing Your Brain in Middle Age and Beyond, Broward Women's Health Forum, October 17, 2018.

Getz S. Cognitive, Cultural and Affective Dimensions of Frailty: Low Emotional Reserve. Tenth McKnight Inter-Institutional Meeting, Birmingham, Alabama. April, 2018.

Getz S. (2018). Susceptibility to Deception: Decreasing Vulnerability in Age Related Memory Loss. Presentation at the University of Miami Evelyn F. McKnight Brain Institute Research Symposium, Miami, FL December.

Gomes-Osman J. Exercise for Brain Health: Plasticity, and the pursuit of Data-Driven, Dose-Specific Recommendations. Frontiers in Neuroscience Seminar Series, Neuroscience Graduate Program, Emory Laney Graduate School, Atlanta, GA, March 2018.

Gomes-Osman J. Exercise for Brain Health: Plasticity, and the pursuit of Data-Driven, Dose-Specific Recommendations. Massachusetts General Hospital Institute of Health Professions, Department of Physical Therapy, Boston, MA, April 2018.

Gomes-Osman J. Exercise for Brain Health: Neuroplasticity and the pursuit of data-driven, dose-specific recommendations. University of Miami Evelyn F. McKnight Research Symposium and Chair Installation. Miami, FL, October 31st, 2018.

JiangH. Retinal tissue hypoperfusion in late onset clinical Alzheimer's type dementia. Department of Ophthalmology, Sun Yat-sen University, Guangzhou, China. June 21, 2018.

Kaur S. Didactic titled "Using existing medical data collection systems for cardiovascular disease surveillance," University of Miami.

McInerney K. (2018). Cognitive, Cultural and Affective Dimensions of Frailty: Hispanic v. Non-Hispanic Outcomes. Tenth McKnight Inter-Institutional Meeting, Birmingham, Alabama.

Perez-Pinzon M, Dave K International Stroke Conference 2018 held at Los Angeles, California, January 2018.

Perez-Pinzon M, Dave K. 10th International Symposium on Neuroprotection Neurorepair 2018 held at Dresden, Germany October 2018.

Perez-Pinzon M, Dave K. The 5th International Symposium on Conditioning Medicine 2018 held at Beijing, China November 2018

Pinto M. Presenter at Neurology grand round: "Basic/Translational roundtable on Alzheimer's disease: MSCs for the treatment of Alzheimer's disease" Apr, 6th 2018.

Ramos AR. Vice Chair-Young Investigator Research Forum. American Academy of Sleep Medicine/National Institutes of Health. April 18-20th 2018. Bethesda, MD

Ramos AR. Sleep and cognitive impairment lecture. Baptist Health System Sleep Symposium. Miami, FL November 3rd, 2018, 0.25 CME.

Ramos AR. Sleep In Neurological Disorders. Advances in Sleep Research. UM-Dept. of Biochemistry. November 16th, 2018. Diplomat Hotel, Hollywood, FL .

Ramos AR. Sleep and Women's Health Conference. The NIH and its different institutes wanted to highlight the most important sleep science of the last 10 years emphasized in sleep and women's health. It was attended by close to 300 people at the NIH headquarters in Bethesda, Maryland and seen by close to 1300 people in the live webcast (link below). The video for Day 1 is up: <https://videocast.nih.gov/PastEvents.asp?c=1> I also got some media attention in their twitter account: https://twitter.com/nih_nhlbi/status/1052289630274560000 https://twitter.com/nih_nhlbi/status/1052227674805014529?s=20 and also provided two national telephone interviews (one for CNN Español) and one TV interview for Univision (link to follow). See attached emails with NIH staff requesting to complete these interviews.

Sacco RL. Preventing Stroke and Improving Brain Health, Neurology Grand Rounds, John Hopkins University, May 24, 2018.

Sacco RL. Preventing Stroke and Cognitive Decline, Neurology Grand Rounds, UT Southwestern Medical Center, December 5, 2018.

6. Awards (other)

6.1. Trainee Awards

Dr. Anita Seixas Dias Saporta is our second McKnight Fellow. She has experience in clinical and translational neuroscience research. Her previous research work includes brain neuroimaging from the neonatal period to adulthood and utilizing multiple imaging modalities to analyze brain function and structure (PET, MRI, DTI, MRS). She also has experience with large database management and development of clinical tools. Since her clinical training in child neurology in Rio de Janeiro, Brazil, she developed an increased interest in the normal and pathological development of the brain, behavior and cognition. She pursued research training in neuroimaging in reference centers including the PET Center at Wayne State University (Detroit, MI) and the Neonatal Brain Disorders Lab at UCSF (San Francisco, CA). Her current research interests include the neuroimaging and electrophysiology markers of epilepsy severity and of normal and pathological aging.

Since she joined us in June, Anita has been processing MRI scans of subjects enrolled in the McKnight Frailty Registry, which is going to be added to the registry dataset and will be available for further use in future projects of the multidisciplinary research group.

The MRI processing techniques she uses are described below:

Regional brain volumes: Regional analysis is being done on the 3D T1 MPRAGE images with FreeSurfer 5.3 (<http://surfer.nmr.mgh.harvard.edu>) (Soon, with Freesurfer 6.0 as well). This MRI software package is comprised of a suite of automated tools for segmentation, re-construction,

and derivation of regional volumes and surface-based rendering. The FreeSurfer pipeline will be applied to the MRI scans to produce 115 cortical and subcortical volumetric measures. These 115 regional volumes will be corrected for head size variation using FreeSurfer's estimate of total intracranial volume (TIV), which has been shown to be highly accurate in adults. Currently, the focus on studying the aging brain is on volumetric changes in bilateral hippocampal volumes as well as other structures affected early in those at AD risk (e.g., precuneus, entorhinal cortex, anterior cingulate and posterior cingulate) and volumetric changes in the ventricular spaces that have been shown to be early markers as well. Hippocampal volumes derived from FreeSurfer are comparable to manually traced regions of interest and provide a practical method for big data studies.

Regional cortical thicknesses: In addition to regional volumes, the FreeSurfer analysis also provides measurements of regional cortical thicknesses. This analysis provides the framework to study the relationship between the characteristics of cortical thinning and relate them to normal or abnormal aging changes, with or without cognitive decline.

Dr. Christian Camargo, formerly the McKnight Brain Institute Cognitive Fellow, was appointed Instructor, with the plan to be appointed Assistant Professor in Clinical Neurology in July 2019.

Dr. Sarah Getz received a UM Miller School of Medicine Medical Faculty Association travel award to present McKnight Frailty research at the 2018 Annual Meeting of the International Neuropsychological Society in Washington DC. She is mentored by Dr. Bonnie Levin, and has been appointed Instructor of Neuropsychology in the Department of Neurology at the University of Miami.

Dr. Marina Sarno who is mentored by Dr. Bonnie Levin has been appointed Instructor of Neuropsychology in the Department of Neurology at the University of Miami.

Dr. Annelly Buré-Reyes who is mentored by Dr. Bonnie Levin has been appointed Assistant Professor of Neurology in the Department of Neurology at the University of Miami.

Michelle Caunca, our McKnight MD/PhD student received the following awards and honors:

- The following grant went into effect in 2018: Ruth L. Kirschstein National Research Service Award (NRSA) Fellowship for Students at Institutions with NIH-Funded Institutional Pre-doctoral Dual-Degree Training Programs (F30)
- Delta Omega Honors Society
- PEO International Scholar Award Nominee
- Travel Award, American Neurological Association Annual Meeting
- Best Poster, 10th Annual Medical Scientist Training Program (MSTP) Student Symposium
- Medical Faculty Association Travel Award, University of Miami
- Young Investigator Scholarship, Annual Meeting, American Academy of Neurology (AAN)

Jing Xu (Graduate student in **Dr. Miguel Perez-Pinzon's** laboratory) received the American Heart Association (AHA) pre-doctoral fellowship award.

Ashish Rehni (Post-doc in **Dr. Kunjan Dave's** laboratory) received the American Heart Association (AHA) Post-doctoral fellowship award.

Andrea Ruetenik (Ph.D. Student in **Dr. Antonio Barrientos's** laboratory) has received *Huntington's Disease Human Biology Project Fellowship* from the Huntington's Disease Society of America on *The protective role of NAD salvage pathway proteins against mutant huntingtin toxicity*

6.2. Faculty Grants and Awards

Dr. Ralph Sacco is serving his second and last year as **President of the American Academy of Neurology**.

Dr. Ralph Sacco was **elected to the National Academy of Medicine**. (See **Section 22**)

Dr. Ralph Sacco is **PI for the NIH/NCRR/NIMHD UL1 (Clinical and Translational Science Award)** to facilitate translational research at the University of Miami which was awarded a five-year renewal.

Dr. Ralph Sacco is **Co-PI for the NIH/NINDS U10 (Miami Regional Coordinating Center for NINDS -StrokeNET)**, which was awarded a five-year renewal to: a) provide a robust and efficient infrastructure to implement high-quality research clinical trials that address acute stroke treatment, prevention and recovery; b) to leverage the internal and regional resources to enhance the Stroke Trials Network; and c) to train the next generation of stroke clinical and translational researchers.

Dr. Ralph Sacco and **Dr. Tatjana Rundek** are **Co-Investigators for the NIH/NINDS U10 (University of Miami: Network of Excellence in Neuroscience Clinical Trials -NEXT)**, which was awarded a 5-year renewal to (a) function effectively as a NEXT consortium trial site, (b) to enhance quality and efficiency of NEXT and other NINDS trial implementation at the University of Miami and (c) to leverage institutional strengths to enhance NEXT consortium activities.

Dr. Ralph Sacco is Co-Chair and Co-I for the NIH/NINDS U01 (NSTN National Clinical Coordinating Center, StrokeNET), which was awarded a 5-year renewal to coordinate NINDS-funded trials in stroke prevention, acute therapy, and recovery. He serves as the co-chair of the Stroke Prevention Committee.

Dr. Hong Jiang received the Dean's NIH Bridge program award for "Novel retinal microvascular biomarkers of vascular contribution to dementia."

Dr. Joyce Gomes-Osman was selected to participate in the prestigious Training for Grantsmanship in Rehabilitation Research (TIGRR) funded by the NIH/NICHHD and hosted by the Medical University of South Carolina, Charleston, SC.

Dr. David Della-Morte and Dr. Guadagni received a European Social Fund, under the Italian Ministries of Education, University and Research (PNR 2015-2020 ARS01_01163) PerMedNet award to study personalized medicine for innovative strategies in neuropsychiatric and vascular diseases.

Dr. David Della-Morte and Dr. Lauro and received a Rome Foundation award for Diabetes Mellitus, Regenerative and Reparative Processes, and Improvement of Pancreatic Beta Cell Function: Role of Bone Marrow-Mesenchymal Stem Cells, Micrnas, M2 Macrophages and Myeloid Derived Suppressor Cells.

Dr. David Della-Morte and Dr. Suhrud submitted an ITS proposal to study the role and the therapeutical approach for mitochondrial sirtuins in noise-induced hearing loss.

Dr. David Loewenstein (PI) has received funding from the National Institute on Aging (NIA) R01AG061106: for his research proposal: *A Novel Computerized Stress Designed for Clinical Trials in Early Alzheimer's: Relationship with Multimodal Imaging Biomarkers in Diverse Cultural Groups*.

Dr. David Loewenstein (PI) has received funding from the State of Florida #9AZ24: to study *Middle-aged Offspring of late Alzheimer's Probands: Novel Cognitive and Biomarker Assessment*.

Dr. David Loewenstein (PI) received funding from State of Florida Ed and Ethel Moore Grant #8AZ23 for the Program: *New Cognitive Stress Tests and Multimodal Imaging Diverse Ethnic/Cultural Groups*.

Dr. David Loewenstein (Co-Investigator) is included on an NIH/NIA grant: *Precision-Based Assessment for Detection of MCI in Older Adults*.

Dr. David Loewenstein (PI) received funding from the State of Florida Ed and Ethel Moore Grant # 7AZ18 Program: to research *Cognitive Stress Tests and Amyloid Load in Diverse Ethnic/Cultural Groups*.

Dr. David Loewenstein (PI) received funding from NIH/NIA for the research study: *Novel Detection of Early Cognitive and Functional Impairment in the Elderly grant*.

Dr. David Loewenstein (PI) received an R01 grant for the: *Non-Pharmacological Intervention for Patients with Alzheimer's Disease and Family Caregivers*.

Dr. David Loewenstein (PI of scientific project and Co-PI of the clinical core) received a grant from the Florida Alzheimer's Disease Research Center (ADRC) to explore novel cognitive measures/biomarkers for early detection of Preclinical Alzheimer's in English/Spanish speaking elderly.

Dr. David Loewenstein has been appointed Director of the Center for Cognitive Neuroscience and Aging, Department of Psychiatry & Behavioral Sciences.

Dr. David Loewenstein has been appointed as a Member of the University of Miami Scientific Advisory Board of the Evelyn F. McKnight Brain Institute, Department of Neurology.

Dr. David Loewenstein has been appointed Co-Director of the Integrating Special Populations Program-Older Adults at the UM Clinical and Translational Science Institute (CTSI).

Dr. David Loewenstein's paper published in *Neurology* was highlighted on the National Institute on Aging website showing that semantic intrusion on the LASSI-L could differentiate amnesic MCI patients with high and low amyloid loads significant implications for screening into novel clinical trials.

7. Faculty

Our MBI Faculty is categorized to those receiving direct support from the Institute (*Members*) and those with whom the Institute is collaborating across the University of Miami (*Collaborators*).

A Table with our McKnight Brain Institute Faculty and their biosketches are provided at the end of the report.

8. Trainees

A table with our trainees is provided at the end of the report.

9. Clinical/Translational Programs

9.1. Update on Existing Clinical Studies

9.1.1. Update on Population-Based Research

McKnight Brain Aging Registry (MBAR) - This study is a collaborative research project with our fellow McKnight Brain Institutes on those who are 85 years or older and have aged 'successfully'. Successful aging refers to physical, mental and social well being in older age. It incorporates cognitive (thinking abilities), physical and emotional areas and the way the aging process affects them. *(A detailed report on MBAR has been submitted to the Trustees by the Inter-Institutional MBAR investigators in a separate document).*

This year, the majority of research activity has been directed toward our ongoing recruitment. Substantial effort was made to increase the enrollment from 9 subjects to 35. We had the help of **Marti Flothmann** who was still responsible for another study but made tremendous efforts to help with MBAR recruitment as well as study coordination. **Dr. Bonnie Levin's** team of neuropsychologists, **Dr. Katalina McInerney**, **Dr. Marina Sarno** and **Dr. Sonya Kaur** worked an incredible amount of time administering and scoring assessments while fitting in the many clinical patients they see. Together with Dr. Rundek, **Dr. Christian Camargo** performed the neurology exams engaging each participant in meaningful conversation. **Dr. Noam Alperin** and **Sang Lee** made it possible to schedule and conduct several MRIs in a very short period of time. Additionally, a summer volunteer worked in the community to recruit study subjects. The group effort led by **Stacy Merritt** enabled our site to get our enrollment numbers on par with all sites. *Our main recruitment strategy* this year was to obtain a public list of registered English speaking voters over 84 in Miami-Dade County. About 600 envelopes were stuffed with flyers, hand stamped and mailed out. Several respondents were ineligible because they were not old enough

or were unable to have an MRI. Participants have truly enjoyed the study and being able to refer to themselves as ‘successful agers.’

Operationally, we had bi-weekly conference calls attended by Dr. Rundek, Dr. Levin, Dr. Alperin, Stacy Merritt and Dr. McInerney. These calls focused on resolving any logistical, procedural and data management issues that may have arisen. On alternative weeks, we held additional conference calls that were either focused on specific project-related discussions on neuroimaging and cognitive issues or were dedicated for our newly implemented MBAR Scientific Advisory Committee (SAC) call. The SAC consists of an eight-member committee of MBAR PIs and investigators, fully familiar with the MBAR cohort and data collection, with two representatives from each MBAR MBI participating site. The SAC calls provide for monthly meetings for discussions of broader issues related to the registry, including plans for new grant submissions, identifying priorities for data analyses and lead investigators for MBAR manuscripts, and plans for enhancing use and accessibility of the growing MBAR dataset. Dr. Rundek and Dr. Levin are our MBAR SAC members.

With our MBAR database infrastructure established, the REDCap dataset is now fully operational and actively being populated with data from each participant across all MBI sites. MRI data is uploaded from each site to the HiPerGator super-computer at UF, where it is pre-processed into a unified format enabling different imaging modalities to be more easily examined simultaneously. Cognitive and clinical data is uploaded to UM, where it is double entered into REDCap with ongoing reliability checks.

- **MBAR Neuroimaging Core Progress:** The neuroimaging protocol is now finalized and fully operational. MR standardization across all sites has been accomplished following standard procedures for the MRI protocols and order of administration. Neuroimaging data collection is well underway and imaging quality assurance across the sites is ongoing.

Dr. Noam Alperin has dedicated significant time in 2018 working on the neuroimaging core of the McKnight Brain Aging Registry (MBAR) study. During this period the recruitment of subjects for the MBAR study has grown substantially largely due to the dedication of our research team led by Stacy Merritt. A comprehensive MRI protocol and scans were successfully completed on 20 MBAR subjects.

Preliminary Analyses of blood flow scans Measurement of blood flow dynamics are unique for the MBAR study protocol. In a preliminary study testing the quality of the scans we tested the relationships between total cerebral blood flow (tCBF) and 1) Cognitive scores (MMSE and MoCA), and 2) Brain gray matter volume. The results are described in the figures below.

Figure 1: Scatter plot of the total CBF measurements vs MMSE (left) and MoCA (right). A strong and significant ($P=0.002$) correlation was found between tCBF and MoCA scores. No significant correlation was found with MMSE suggesting that MoCA provide a more sensitive and comprehensive measure of cognitive performance than MMSE.

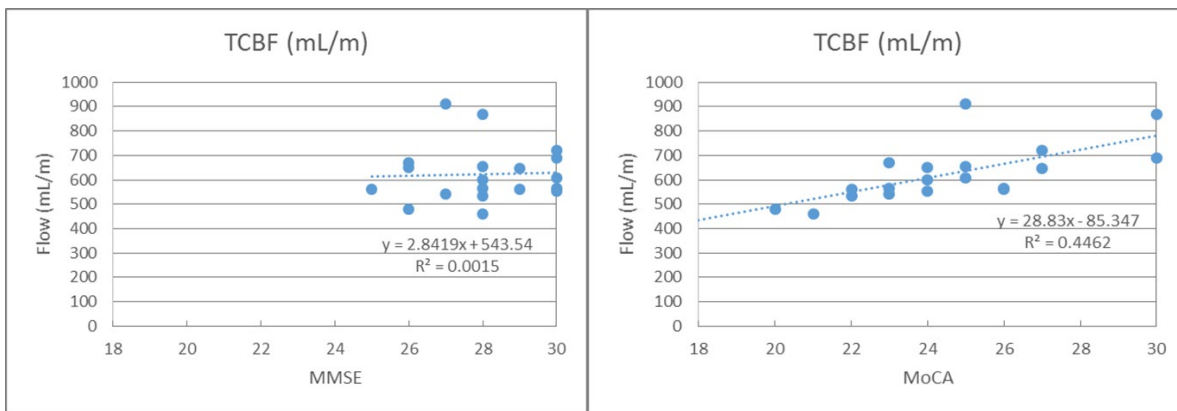
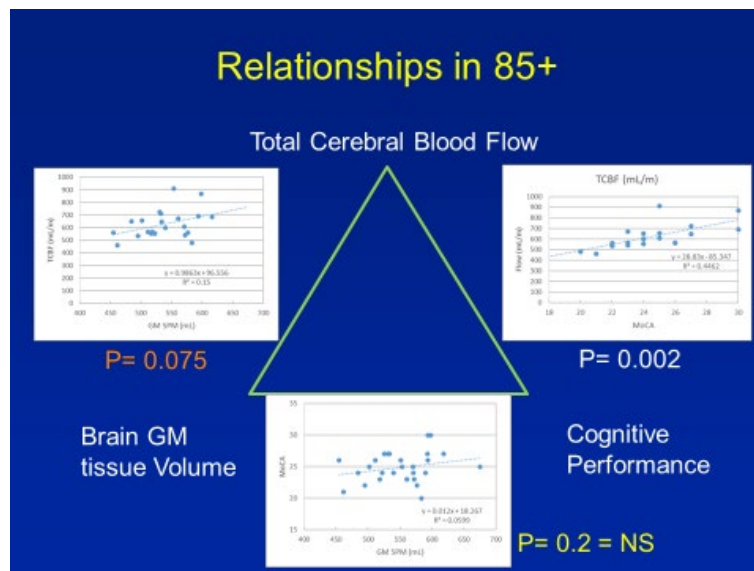


Figure 2: The inter-relationship between blood flow, cognitive performance, and GM brain volume. The initial results suggest that in cognitively normal elderly subjects the tCBF is more strongly correlated with cognitive performance than with GM brain volume. Thus tCBF may be a stronger predictor of cognitive performance than brain GM volume.



- MBAR Cognitive Core Progress:** The Cognitive Core has also integrated their conference calls into the regular weekly calls described above to facilitate group communication across the cores and MBI sites. Most discussions have focused on resolving any data entry and analytic questions, as well as occasional queries from the study coordinators regarding minor procedural and scoring questions. However, most of the focus has been on planning of the sequence of analyses to be conducted in the next year. There has also been ongoing discussion to consider adding a few additional cognitive measures or rating scales that might provide added value for the cognitive assessments. Dr. Bonnie Levin, Dr. Katalina McInerney and their UM team continued implementation of neuropsychological testing for the UM MBAR study as well as led the data analyses and organized the MBAR cognitive and behavioral database for all the McKnight sites. Dr. Levin works closely with Dr. McInerney and the other members of the Division of Neuropsychology in leading the data cleaning, monitoring for quality control and overseeing the MBAR site entries in order to prepare the data set for collaboration with our McKnight and MBAR collaborators.

McKnight Frailty Project - Under the supervision of **Drs. Katalina McInerney** and **Bonnie Levin**, the McKnight Frailty Project is unique to the University of Miami and includes clinic and community dwelling participants from diverse backgrounds ranging in age from 50 to 95+. The

battery has been validated in both English and Spanish and the database is well balanced in terms of an equal representation of Hispanic and Non-Hispanic males and females. The project data (demographic, medical, neuropsychological, imaging and psychosocial data) gathering phase is nearing completion. The frailty database has yielded 7 abstracts this year and we anticipate many more going forward, as well as peer-reviewed publications. The Frailty Project has been strengthened through collaborations with the Department of Psychology.

Dr. McInerney holds bi-weekly meetings with our MBI team of research assistants to address issues related to data management and quality control of the McKnight Frailty database. All neuropsychology Post-doctoral Fellows and graduate students are actively engaged in the project. Dr. Levin leads a weekly research rounds on the Frailty and Normative Aging Project, being driven from the McKnight Frailty Registry. This meeting focuses exclusively on research topics related to frailty and normative aging. Our database, which is now approaching 400 participants, has become for the first time, a wonderful resource for generating new hypotheses and preliminary data for grant applications regarding cognitive aging and functional ability for our MBI Trainees and faculty to propose. However, it requires continued quality control and maintenance. Therefore, we are still largely focused on data check and entry into the REDCap database, data management and monitoring quality control.

Uncovering Risk Profiles of Deception and Mitigating Susceptibility to Scamming in Midlife and Older Age: A Novel Intervention Tool - Drs. Bonnie Levin and Sarah Getz work with Drs. Ebner and Oliveriera (UF) and Grilli and Wilson (UA) on susceptibility to deception tools and the collection of pilot data. Our team has been meeting via monthly conference calls. The UM team has organized a battery to examine targeted domains and generate a more comprehensive understanding of susceptibility profiles. This battery assesses areas that have been shown to be highly relevant to scamming, and include measures of cognition (emphasizing memory and executive functioning and utilizing the NIH toolbox), mood and emotional wellbeing, and socio-affective functioning. Dr. Getz drafted the IRB protocol to carry out the Miami portion of the multisite collaboration with the Universities of Florida and Arizona. Data collected in this protocol will lay the foundation for a future R01 proposal in which we will study the efficacy of an online intervention tool in the real world and extend the investigation of cognitive and socio-affective risk profiles to neurobiological factors contributing to scam susceptibility in midlife and old age.

The Northern Manhattan Study (NOMAS) - Dr. Ralph Sacco is the Principal Investigator (Drs. Rundek, Levin and Sun are co-Investigators). Stroke Incidence and Risk Factors in a Tri-Ethnic Region, currently in its fourth year of funding for cycle 5, is a 26-year-old longitudinal study. Through the continued participation of the now aging NOMAS cohort, the project is addressing gaps in knowledge related to the risks and determinants of stroke, as well as cognitive impairment and dementia. In collaboration with Columbia University, the project is advancing research on: (1) specific neuro-immune and inflammation-related molecules and networks and their association with accelerated cognitive trajectories; (2) regional white matter volumes, lobar volumes, hippocampal volume, perivascular spaces, dolichoectasia, and collateral variants and their association with accelerated cognitive trajectories and dementia; (3) vascular risk factors, including immune biomarkers and networks and their significance as determinants of dementia; (4) individual vascular risk factors and global vascular risk scores and their ability to predict

trajectories of functional outcomes and quality of life independent of stroke; and (5) vascular risk factors and varying effects for specific ischemic stroke subtypes.

In this past year, this study has successfully accomplished obtaining data necessary to conduct various analyses to explore the association between cognitive trajectories and biomarkers/networks (assayed with neuro-immune and neuro-inflammatory biomarker panels). Approximately 200 more participants have provided a 3rd data point for cognitive trajectories by completing a 10-year follow-up neuropsychological evaluation this year. The same cohort (now reaching almost 400) has provided plasma samples and all baseline samples have been processed with the biomarker panels enabling the study team to conduct cross-sectional analysis to define the relationship between biomarkers and cognitive status at baseline.

The project has also begun to assemble a NOMAS dementia cohort. Through the dementia adjudication protocol, a data-driven algorithm validated this year, the dementia adjudication committee reviews cases that have not meet the algorithmic criteria to be categorized as “normal cognition”. Dementia adjudication includes the review of all available cognitive performance data via a centralized REDCap database application.

Using other available NOMAS data, multiple studies have been completed this year yielding at least 12 published manuscripts demonstrating the association between cerebrovascular disease and cognitive trajectories. We have recently reported on the association of brain arterial diameters with cognitive performance demonstrating that NOMAS participants with larger brain arterial diameters, particularly in arteries supplying domain-specific territories had greater cognitive decline. We studied the association of small and large vessel cerebrovascular disease and vascular cognitive impairment and found that white matter lesions are associated with a regional pattern of gray matter atrophy that is mitigated by blood pressure control, exacerbated by aging, and associated with cognitive performance. This study extends and support work from last year, in which explored the regional patterns of gray matter atrophy using a neuroimaging technique, which applies gray matter voxel-based morphometry with the scaled sub-profile model. We found that the pattern of reduced gray matter volume was associated with white matter lesion load in bilateral temporal-parietal regions with relative preservation of volume in the basal forebrain, thalami and cingulate cortex. This pattern was expressed most in those with uncontrolled hypertension and least in normotensives. Expression of this pattern was associated with worse performance in executive function and memory.

This year we have also accomplished a series of studies testing the effects of vascular risk factors and global vascular risk scores on trajectories of functional outcomes. We tested the hypothesis that white matter hyperintensity volume (WMHV) asymmetry may be an important predictor of long-term functional status. Greater WMHV asymmetry in the parietal lobes and temporal lobes was associated with lower overall function. Greater WMHV asymmetry in the parietal lobes was also independently associated with accelerated functional decline (Regional WMHV was also predictive of functional decline, with periventricular WMHV particularly associated with accelerated functional decline. In another analysis, we reported a strong and independent association between the subclinical markers pathology-informed subclinical brain infarct (PI-SBI) and WMHV and trajectories of patient-centered outcomes over time. Though PI-SBI was independently associated with steeper functional decline, over and above the decline due to aging, WMHV did not moderate the relationship between cognitive performance and function.

Our findings suggest that WMHV may function through mechanisms distinct from SBI to affect ongoing functional decline independently of processes that determine cognitive ability.

Other NOMAS studies this year have explored healthy behaviors, cardiovascular health, and cognitive aging. We reported a relationship between greater depressive symptoms and worse episodic memory, smaller cerebral volume, and silent infarcts. We have shown also that physical inactivity predicted slow gait speed, and that white matter hyperintensity volume particularly in the anterior cerebral regions was associated with lower mobility scores suggesting that prevention of subclinical cerebrovascular disease might be a potential target to prevent physical decline in the elderly. Our studies also show that having a greater number of ideal cardiovascular health factors is associated with a reduced burden of biomarkers of brain aging, including silent brain infarcts, white matter hyperintensity volume, and brain atrophy, which supports the American Heart Association's recommended use of the Life's Simple 7 metric in adulthood as an important predictor of optimal brain health.

Finally, this year we have initiated studies examining the associations between inflammatory biomarkers and long-term functional trajectories. Specifically, we focused on tumor necrosis factor (TNF) receptors, as the TNF pathway has been found to play a role in acute and chronic cerebrovascular disease. We found that higher TNFR1 levels were associated with lower baseline functional status, as well as accelerated decline over time. As data becomes available, we look forward to reporting on more studies exploring the relationship between biomarkers/networks assayed with neuro-immune and neuro-inflammatory biomarker panels and cognitive trajectories.

The University of Miami American Heart Association/Bugher Center of Excellence - Dr. Ralph Sacco is the Center Director and **Dr. Tatjana Rundek** is the Training Director. In its final year of funding, the project and nears completion of its complementary clinical and basic science research aimed to enhance scientific knowledge base on the recovery of brain health following stroke.

In the clinical arm of the project, Dr. Sebastian Koch leads the pilot randomized clinical trial designed to identify methods to improve cognitive recovery and quality of life after stroke through the exploration of the combined benefits of cognitive and physical exercise. The study team is currently finalizing analysis towards the study's primary outcome of safety and feasibility and will present the results at the 2019 International Stroke Conference in Hawaii. Preliminary results show that the Cognitive and Resistance Exercise Training protocol is feasible among stroke survivors. These promising feasibility results will provide needed preliminary data to propose a larger and more definitive study to improve functional and cognitive recovery after stroke.

Other preliminary study results address issues related to socioeconomic status and mental health as important contributors to physical well-being, quality of life, and cognition. Because all participants in the study underwent detailed psychosocial evaluation, the complex interactions of social and psychological factors on cognitive recovery was available for examination within the Bugher cohort, all of which had recently experienced a stroke. Our preliminary findings confirm the high prevalence of depression and cognitive impairment following stroke. At baseline the average Montreal Cognitive Assessment score was 20, significantly below the threshold of 26,

indicating a significant cognitive impairment. Depression is highly prevalent in our stroke subjects and particularly in women whose scores on depression (Clinical Epidemiological Scale-Depression) were significantly lower than in men. Our follow-up results demonstrate that both depression and cognition improved for the group as a whole over the course of the cognitive and physical exercise intervention. Interestingly, the improvement of mood in women was greater than in men.

While it may not be readily apparent, we are not aware of any adverse events related to depression. We have also not found depression to negatively influence adherence with the study intervention. However, a final more quantitative analysis may reveal a detrimental effect on compliance with the intense exercise and cognitive training intervention, as well as the effect of these interventions on stroke recovery. Only on rare occasions, we had to intervene and provide treatment and appropriate referrals for mental health management. Our careful attention to monitoring depression and cognition post stroke shows that brain and mental health remain a priority for our overall Bugher program. We hope that exercise and cognitive training may provide non-pharmacological means of treating neuropsychiatric complications that may hinder recovery from stroke.

The complimentary basic science project, led by Dr. Miguel Perez-Pinzon, aims to provide insight into cellular mechanisms underlying stroke-mediated damage and repair in an animal stroke model. Pre-clinical studies conducted in Dr. Perez-Pinzon's lab are intended to lay the foundation for future clinical trials. This year, the basic science project describes new results for work including female rats. Ongoing studies to increase the total study numbers have been conducted in both young and aged rats to determine how exercise intensity effects cognitive deficits following focal cerebral ischemia. It was found that moderate intensity physical exercise provided the most beneficial impact on cognitive recovery compared to other exercise intensities. Specifically, these experiments revealed not only that exercise at varying intensities post stroke is feasible in young and aged rats, but also that (moderate) exercise ameliorates cognitive deficits following a stroke in young rats, while in aged rats exercise reduced cognitive deficits following stroke. The results suggest that exercise improves plasticity following stroke in young and aged rats. The ongoing animal studies are also utilizing pharmacological agents with and without exercise that will provide preliminary pre-clinical data for other human intervention studies.

The University of Miami Stroke Prevention Intervention Research Program, Florida-Puerto Rico Collaboration to Reduce Stroke Disparities (FL-PR CReSD) - Dr. Ralph Sacco is the Principal Investigator. It is in its final year of NIH funding (through a No Cost Extension). The project has successfully addressed its aims to identify race-ethnic and sex disparities in acute stroke care and to inform hospital quality improvement. Our recent study, linking pre-hospital emergency service data with the FL-PR CReSD data reinforced the potential of our data to inform improvement of quality of care beyond the acute in-hospital phase. The study identified race-ethnic differences in the time to call 9-1-1 services following acute stroke onset suggesting the need to explore innovative strategies to improve public education regarding stroke symptoms and immediate 9-1-1 system activation. Another study published this year reflects post-hospital outcomes and compares benefits to hospital participation in quality improvement programs. The study showed that disparities in outcomes were less common in hospitals participating in the FL-PR CReSD than in hospitals that did not participate in any sort of quality improvement program. The results from

our study support the benefits of quality improvement programs, particularly those focusing on race/ethnic disparities. These observations also demonstrate the need to design and implement evidence-based interventions that continue beyond the acute hospitalization period in order to reduce disparities in longer term outcomes after stroke. Although NIH funding for the project is complete, the value of the project and the data compiled is recognized by its continuation through new funds described in the next section.

The Florida Stroke Registry - Dr. Ralph Sacco is the Principal Investigator. In 2018, the University of Miami, Department of Neurology, was awarded its second round of state appropriations funds to manage and maintain the Florida Stroke Registry (the Registry). Originating from the NIH funded Florida Puerto Rico Collaboration to Reduce Stroke Disparities (described above), the Registry currently consists of 80 participating Florida stroke center hospitals. Actively engaged in recruiting all Florida stroke center hospitals, approximating 160 stroke centers in total, the Registry aims to obtain a standardized and comprehensive dataset.

The Registry currently consists of at least 250,000 Florida stroke cases obtained since 2010 to current from the 80 participating Florida hospitals. Data is downloaded quarterly, thereby increasing the number of cases included in the Registry at every download. Analyses of the data offers hospital level reports that facilitate participating hospitals to track and measure their quality of stroke care performance. As a state registry, systems of care may be addressed and ultimately improved. Alternatively, the Regional Dashboards, provide a self-monitoring tool that improves the quality of care at a local level in collaboration with EMS. This reporting tool, which in this past year have been phased out of “pilot” to the “live” implementation stage, is now being actively used in two Florida counties (of the 65 in Florida). The Regional Dashboards allow participating hospitals to review their performance against nearby hospitals on measures specifically related to endovascular treatment, an increasingly utilized innovative and minimally invasive procedure. Though still very new, the Regional Dashboards are garnishing extensive attention statewide and even nationwide as a method to improve acute in-hospital care as well as potentially pre-hospital care.

The Transitions of Care Stroke Disparity Study (TCSD-S) - Drs. Ralph Sacco and Tatjana Rundek are Co-Investigators. This study aims to identify disparities in transitions of stroke care and key factors associated with effective transitions of care. In its second year of funding, the project has accomplished multiple operational milestones including the development of the TCSD-S follow-up protocol, accompanying Case Report Forms, Manual of Operations, and the final specification of Social Determinant of Health data elements to be captured for the project. After having successfully trained collaborating sites’ coordinators, enrollment has begun. Coordinators are now actively conducting TCSD-S structured telephone interviews to evaluate medication adherence, healthy lifestyle, utilization of rehabilitation interventions and medical follow-up 30 and 90 days after hospital discharge to home. Within this stage of the project, data is being collected to identify race-ethnic and sex disparities in hospital-to-home transition of stroke care and stroke outcomes. We look forward to reporting future analyses and results from this study which will help in the development of effective hospital-centered system level initiatives to reduce these disparities, improve stroke outcomes and reduce readmissions.

The University of Miami Clinical Translational Science Institute (UM CTSI) - Recently awarded a second competitive grant cycle, and directed by **Dr. Ralph Sacco**, the University of Miami Clinical and Translational Science Institute (Miami CTSI) is a university-wide institute dedicated to accelerating and transforming culturalized clinical and translational science. Serving as an indispensable resource for researchers and stakeholders, the Miami CTSI serves as the Miami Hub of the national Clinical and Translational Science Award consortium, which works to advance scientific discoveries into improved health care. Together with Hub partners that include the entire University of Miami as well as Jackson Memorial Hospital, the Miami VA, OneFlorida Clinical Research Consortium, Health Choice Network, and Health Council of South Florida, the Miami CTSI focuses on translational workforce and career development, research infrastructure, methods and processes, team science, and community engagement.

The Miami CTSI strategy of “culturalizing” health sciences acknowledges that the region is composed of more than 85% racial and ethnic minorities. Through Miami CTSI programs, the research workforce are exposed to cultural competency skills and tools allowing the development of adaptable study techniques to better suit the culture, language, and norms of diverse groups to ensure their active participation and engagement in research. These programs effectively extend research opportunities to South Florida’s diverse and underrepresented communities to assure integration of special and underserved populations.

In 2018, the Miami CTSI successfully competed and awarded 4 KL2 career development awards, 9 pilot project awards, began integrating partner data for research use, participated in network trial activities, completed community health worker training across Florida and in three other states, was recognized for excellence in team science by NCATS, implemented grant writing support, held workshops for junior faculty, clinical research professionals, and multidisciplinary teams on research processes, best practices, innovation and entrepreneurship, and much more.

Drs. Sarah Getz and **Bonnie Levin** developed and piloted an online tool to assess susceptibility to scamming in the elderly. This tool has been translated in to French and is uniquely tailored to detect individual differences in ability to differentiate scams from legitimate scenarios. This tool has also been adapted to pen and paper format for administration among vulnerable minority populations.

Drs. Christian Camargo and **Katalina McInerney** have been collaborating on the design of the Souvenaid study and will continue once the project is funded. See **Section 1.3.1.** for project details.

Drs. Christian Camargo and **Barry Baumel** have been working on a stem cell study with Alzheimer’s Disease. Alzheimer’s disease (AD) is the most common progressive neurodegenerative disease causing dementia in the elderly. Alzheimer’s disease is irreversible and, depending on its stage, can interfere mildly or severely with a patient’s everyday activities. The symptoms are caused by neurodegeneration characterized initially by synaptic impairment followed by neuronal loss. This is accompanied by extracellular amyloid plaques, intracellular neurofibrillary tangles, neuroinflammation (astrogliosis and microglial cell proliferation), and impaired adult neurogenesis. Mesenchymal stem cells directly affect the pathophysiology of Alzheimer’s disease by reducing amyloid beta plaque burden, regulating inflammation, and

promoting neuro-restoration by increasing neurogenesis. Based on the existing preclinical literature, we believe there is a mechanistic argument for the use of mesenchymal stem cells in Alzheimer's disease. Therefore, we will be conducting a Phase 1, open-label, single center investigation to demonstrate the safety of allogenic Mesenchymal Stem Cells in patients diagnosed with mild-to-moderate Alzheimer's disease.

Sponsored clinical trials related to cognitive outcomes and our MBI clinical translational program - **Dr. Katalina McInerney** and **Dr. Marina Sarno** have been working together with Dr. Barry Baumel (Interim Director of Neurocognitive Division) on a series of clinical trials that investigate treatment for memory loss that are listed below:

- **Dr. Katalina McInerney** and **Marina Sarno** are Sub-Investigators in *A Phase I, Prospective, Randomized, Double-Blinded, Placebo-controlled Trial to Evaluate the Safety and Potential Efficacy of Longeveron Allogeneic Human Mesenchymal Stem Cell (LMSC) Infusion Versus Placebo in Patients with Alzheimer's Disease*. PI: Bernard Baumel, M.D. **Sponsor: Longeveron LLC.**
- **Dr. Katalina McInerney** and **Marina Sarno** are Sub-Investigators in *A Phase 3 Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel- Group Study to Evaluate the Efficacy and Safety of Aducanumab (BIIB037) in Subjects with Early Alzheimer's Disease*. PI: Bernard Baumel, M.D. **Sponsor: Biogen MA Inc.**
- **Dr. McInerney** and **Marina Sarno** are Sub-Investigators in *A Randomized, Double-Blind, Placebo-Controlled and Delayed-Start Study of LY3314814 in Mild Alzheimer's disease Dementia (The DAYBREAK Study)*. PI: Bernard Baumel, M.D. **Sponsor: Eli Lilly and Company.**
- **Dr. Katalina McInerney** is a Sub-Investigator in *A Seamless Phase 2A-B Randomized Double-Blind Placebo-Controlled Trial to Evaluate the Efficacy and Safety of BHV-4157 in Patients with Mild to Moderate Alzheimer's Disease*. PI: Bernard Baumel, M.D. **Sponsor: Biohaven Pharmaceuticals Holding Company Limited.**

Dr. Noam Alperin has submitted manuscripts that are based on methodology he developed for regional quantitation of the white matter hyperintensities, which is a primary sign for a cerebral small vessel disease.

Dr. Joyce Gomes-Osman has been working to develop a precision medicine approach to the delineation of effective exercise dose to achieve maximal cognitive benefits for older adults. She continues to work very hard at different projects related to brain plasticity, cognitive health and walking function. Please see a summary below:

- The past year has been exciting and very productive for **Dr. Joyce Gomes-Osman**. She has continued to make progress on her University of Miami McKnight Pilot Grant. This project aims to examine the influence of a 4-week aerobic exercise regimen (moderate versus high intensity) on cognition and neuroplasticity, or the brain's ability to adapt to changes imposed by experience, environment and aging itself. The study is ongoing, with 15 individuals enrolled and 9 individuals having completed the study.

- On the national level, **Dr. Joyce Gomes-Osman** was selected from a competitive pool of investigators from around the country to participate in the prestigious Training for Grantsmanship in Rehabilitation Research (TIGRR), an initiative continuously funded by the NIH for 20 years that recognizes outstanding young investigators in the Rehabilitation Research Community with high promise for research success. She completed this training successfully and with positive feedback from national leaders in the field.
- **Dr. Joyce Gomes-Osman** has leveraged both, participation in TIGRR and the pilot data generated with the McKnight Pilot Grant, by securing funding for a Mentored Translational Research Scholars Program Awards (KL2) by the University of Miami Clinical and Translational Science Institute (CTSI). Dr. Tatjana Rundek is her primary mentor for this project, and Dr. David Loewenstein and Dr. Alvaro Pascual-Leone (Harvard) are her additional mentors. This proposal will examine the effects of an 8-week aerobic exercise intervention on cognition and brain plasticity, and additionally consider how genetic differences may modify the cognitive response to exercise.
- **Dr. Joyce Gomes-Osman** has recently published a large-scale systematic regression determining evidence-based recommendations of dose and type of exercise to promote cognitive gains in older adults. This manuscript was published in the high-impact journal *Neurology: Clinical Practice*, and featured in media releases in several major media outlets, including *TIME Magazine*, *Medscape*, *CBS News*, *The London Times*, and *The Boston Globe*, among others. Dr. Gomes-Osman asserts there's no question that exercise is good for the body, and there is growing evidence that staying physically active can help slow the normal declines in brain function that come with age.

Dr. Joyce Gomes-Osman led the research to find an exercise prescription for the brain. She and her colleagues performed meta-analyses from nearly 100 existing studies that connected exercise with more than 122 different tests of brain function. Based on data that included more than 11,000 older people, they found that people who exercised about 52 hours over a period of about six months showed the biggest improvements in various thinking and speed tests. On average, people exercised for about an hour, three times a week. And the effect applied to both people without cognitive decline as well as those with mild cognitive impairment or dementia. People in the study showed the strongest improvements in their ability to solve problems and process information. The effect was not as robust in memory tests, but Dr. Gomes-Osman notes that most complex brain functions, from reasoning and processing speed to recall, are related.

What surprised the researchers was that the only strong correlation between exercise and brain function occurred when they looked at the overall time people spent being physically active. They did not find associations between improvements in thinking and the frequency, intensity or length of time people exercised. That may further support the idea that for brain health, the overall and cumulative effect of physical activity is what's important. This suggests that exercise affects the brain in a variety of different ways, from preserving the brain's nerve network that starts to decline with age, to boosting the function of neurons and improving blood flow to brain cells, as well as promoting the production of growth factors to help cells involved in higher level thinking tasks.

- **Dr. Joyce Gomes-Osman** has published a systematic review in *Frontiers in Aging Neuroscience* about Non-invasive Brain Stimulation in the Aging Brain in collaboration with Dr. Adam Woods, from the Evelyn F. and William L. McKnight Brain Institute at the University of Florida. In addition, she has authored 2 additional peer-reviewed publications, and presented her preliminary work in 6 posters at national meetings.
- In addition to the studies above, **Dr. Joyce Gomes-Osman** has been collaborating with **Dr. Tatjana Rundek** and the remainder of the University of Miami Bugher team investigating brain plasticity changes in individuals post-stroke who are undergoing combined exercise and cognitive training, exercise in isolation or stretching exercises. All data has been collected and processed, and manuscript preparation is underway.
- Furthermore, **Dr. Joyce Gomes-Osman** has collaborated with Dr. Sara Czaja on an NIH-funded project by Dr. Sara Czaja that consists of proposing an app-based intervention study for older individuals. Dr. Gomes-Osman has worked to create the content of this app. Finally, Dr. Gomes-Osman is collaborating with the Alagoas State University for Health Sciences, in Brazil, and is overseeing a study to evaluate the influence of an exercise literacy workshop to improve engagement in physical activity and cognitive performance in older adults. Thirty participants have completed the study, and data analysis and manuscript preparation are underway.

Dr. Elizabeth Crocco participated in and published research on the development of a novel cognitive assessment and its relationship to biological markers in Alzheimer's Disease in Pre-MCI subjects.

Dr. Elizabeth Crocco has continued working on the following clinical trials that are sponsored by pharmaceutical companies aiming to be on the cusp of therapeutic breakthroughs:

- PI: *A randomized double-blind, placebo controlled, parallel group study to evaluate the efficacy and safety of CNP520 in participants at risk for the onset of clinical symptoms of Alzheimer's Disease.* **Sponsor: Novartis.**
- PI: *Randomized, Double-blind, Parallel-Group, Placebo-Controlled, Dose-ranging study of Piromelatine in Patients with Mild Dementia due to Alzheimer's Disease* **Sponsor: Neurim Pharmaceuticals.**
- PI: *A Randomized, Double-blind, Placebo-controlled, Two Cohort Parallel Group Study to Evaluate the Efficacy of CAD106 and CNP520 in Participants at Risk for the Onset of Clinical Symptoms of Alzheimer's Disease.* **Sponsor: Novartis.**
- PI: *A Phase 3, Multicenter, Long-term, Extension Study of the Safety and Efficacy of AVP-786 (deuterated [d6] dextromethorphan hydrobromide [d6-DM]/quinidine sulfate [Q]) for the Treatment of Agitation in Patients with Dementia of the Alzheimer's Type.* **Sponsor: Avanir Pharmaceuticals.**
- PI: *A Phase 3, multicenter, randomized, double-blind, placebo-controlled study to assess the efficacy, safety, and tolerability of AVP-786 (deuterated [d6]-dextromethorphan hydrobromide [d6-DM]/quinidine sulfate [Q]) for the treatment of agitation in patients with dementia of the Alzheimer's type.* **Sponsor: Avanir Pharmaceuticals.**

- Co-Investigator: *A Phase III, Randomized, Placebo-Controlled, Parallel-Group, Double-Blind Clinical Trial to Study the Efficacy and Safety of MK-8931 (SCH 900931) in Subjects with Amnesic Mild Cognitive Impairment Due to Alzheimer's Disease (Prodromal AD)* **Sponsor: Merk & Co.**

Dr. David Loewenstein (Co-Director, Data Core and Biostatistician) will continue his work with the Center on Research and Education for Aging and Technology Enhancement (CREATE IV) grant which is a multidisciplinary research project aimed at understanding how age-related changes in function impact a person's ability to interact successfully with technical systems.

Dr. David Della-Morte and his team continued research on the association between different phenotypes of atherosclerosis and risk for cerebrovascular disease and neurodegeneration. Using data from an elderly multi-ethnic cohort from the Northern Manhattan Study (NOMAS), along with colleagues from the Departments of Neurology at the UM and Columbia University, he demonstrated a significant association between larger carotid intima media thickness and greater burden of cerebral white matter lesions independently of demographics and traditional vascular risk factors. Brain white matter hyperintensities (WMH) have been associated with increased risk of cognitive decline and dementia, therefore the results of this study may lead to a strategy to using ultrasound markers in order to prevent neurodegenerative diseases.

Also, by using the NOMAS dataset in another study, Dr. Della Morte investigated the associations between the different phenotypes of atherosclerosis: carotid plaque (CP), carotid intima media thickness (cIMT), and stiffness (STIFF), which may provide insight into the mechanisms to the increased risk of cardiovascular disease. He demonstrated that an increase in STIFF was associated with an increase in cIMT and carotid artery dilatation with greater plaque burden. Increased cIMT and plaque burden represent vascular remodeling that likely results from the two different age-related mechanisms, one that includes diffuse wall thickening (cIMT) with STIFF and another that incorporates focal atherosclerosis (plaque) with luminal dilatation. Understanding these phenomena may further elucidate the age-related mechanisms that underlie age-related cognitive decline.

Neighborhood Greenness and Alzheimer's Disease in 249,405 U.S. Medicare Beneficiaries - We established a new collaboration with **Scott Brown, PhD**, a Research Associate Professor in the Department of Public Health Sciences at the University of Miami Miller School of Medicine. He is an expert in the impacts of neighborhood built (physical) and social environments on residents' health and well-being across the lifespan. His research seeks to understand environmental policies and strategies that promote brain health for the most vulnerable residents (i.e., elders; the poor), particularly those at risk for physical inactivity, social isolation and behavioral health problems.

The overarching goal of Dr. Brown's research is to inform policies pertaining to the built environment to enhance health in the most underserved populations and communities. Most recently, he collaborated with **Dr. Rundek** and conducted investigations linking higher levels of neighborhood greenness (e.g., tree canopy; parks) to lower risk for Alzheimer's disease.

The results of this research were presented on at the ‘Developing Topics’ poster session of the Alzheimer’s Association International Conference (AAIC) in Chicago, July 2018.

The results showed the following:

In a large CMS database, 5.5% (n=13,685) of Medicare beneficiaries had a diagnosis of Alzheimer’s disease. *Higher levels of neighborhood greenness were significantly associated with lower odds of Alzheimer’s disease, even after adjusting for individual age, gender, race/ethnicity, and neighborhood income. These results showed that neighborhood greenness might reduce risk of Alzheimer’s disease among older adults. Environmental improvements, such as increasing trees and vegetation in neighborhoods – even to moderate levels — may be important modifiable factors for reducing Alzheimer’s disease and improving mental and general health in older populations. Dr. Brown together with Dr. Rundek just obtained funding from the FL DOH to conduct similar research in South Florida and extend these findings to MCI and other cognitive impairments in Medicare beneficiaries over the age of 65.*



9.1.2. Update on Basic and Translational Science Research

Post-cerebral Ischemia Cognitive Impairment Research Program - Patients that have experienced cerebral ischemia suffer long-term disability, affecting both motor and cognitive function. The laboratory run by **Drs. Kunjan Dave** and **Miguel Perez-Pinzon** has been investigating strategies to improve post-cerebral ischemia cognitive impairments. As mentioned in earlier reports, they demonstrated that cerebral ischemia (both focal cerebral ischemia/stroke and global cerebral ischemia) impairs cognitive function, and moderate intensity physical exercise provides a beneficial impact on cognitive recovery in young and middle-aged male rats. In an earlier report they evaluated the effect of physical exercise on post-stroke cognitive function in reproductively senescent female rats. These results are now under peer-review in a manuscript submitted for publication in the journal *Stroke*.

Because it may be difficult for ailing elderly cerebral ischemia patients to adhere to a chronic physical exercise regimen, **Drs. Dave** and **Perez-Pinzon** are presently evaluating the impact of synergistic effects of sub-threshold intensity physical exercise and resveratrol (a well-established neuroprotective agent) treatment on post-stroke cognitive function in middle-aged rats. For this study, male rats were subjected to 90 minutes of transient middle cerebral artery occlusion (MCAO). Following 3-4 days of recovery post-stroke, rats were exposed to physical exercise (9 m / min on a treadmill) and / or resveratrol treatment (50 mg / kg / day) for five consecutive days. Cognitive outcomes were evaluated 22 days post-stroke using a contextual fear-conditioning test. They observed that the differences in percent freezing on day 2 from day 1 of contextual fear conditioning in rats belonging to MCAO + sham exercise + vehicle (DMSO), MCAO + sham exercise + resveratrol, MCAO + exercise + vehicle DMSO, and MCAO + exercise + resveratrol were 19, 25, 18, and 30%. None of the differences were statistically significant. As mentioned above, they intentionally used a sub-threshold exercise intensity (intensity that did not demonstrate

improvement in cognitive outcomes post-stroke) in this present study. The results indicate a trend, although statistically non-significant, that exercise and resveratrol treatment has a synergistic effect on cognitive outcomes post-stroke.

As mentioned in an earlier report, most ischemic injury research focuses on gray matter injury despite 30% of strokes resulting in just subcortical white matter injury (WMI). Additionally, 90% of individuals older than 65 develop white matter hyper-intensities, a marker of ischemic WMI. The goal of this study was to characterize a model of WMI in young (3 months) and aged rats (12–18 months), using microinjections of the nitric oxide synthase inhibitor N5-(1-iminoethyl)-L-ornithine, dihydrochloride (L-NIO), and evaluate the impact of physical exercise on motor and cognitive outcomes post-white matter stroke. This year, [Drs. Dave](#) and [Perez-Pinzon](#) completed those studies and are now preparing a manuscript.

[Dr. Ami Raval](#) has continued her research to determine if whole body vibration improves stroke outcome in nicotine-exposed rats. Her research reveals that post-stroke physical exercise reduces ischemic brain damage and improves cognition in reproductively senescent female rats. Another finding thus far is that Nicotine alters brain energy metabolism and exacerbates ischemic injury and alters cognition in female rats.

[Dr. Antoni Barrientos'](#) laboratory has made major advances in three lines of research focusing on defining mechanisms of neuroprotection against human neurodegenerative proteinopathies, with a focus on Huntington's disease (HD). Research: Major advances on the role of (1) NAD enzymes as neuroprotective chaperones, (2) several new encephalocardiomyopathy mitochondrial assembly factors, and (3) discovery of several GTPases required for the biosynthesis of mitochondrial ribosomes.

(1) Catalytically inactive forms of NAD⁺ salvage pathway proteins retain protective activity against 103Q toxicity in yeast

Previously, [Dr. Barrientos](#) observed that multiple proteins that belong to the yeast NAD⁺ salvage pathway were able to protect against the growth deficit that occurs with 103Q mutant huntingtin expression in a yeast model of Huntington's disease. Furthermore, upon deletion of one of the essential genes of the yeast NAD⁺ salvage pathway, NPT1, they saw that the overexpression of the other NAD⁺ salvage pathway proteins maintained their ability to protect against 103Q expression, indicating that a functional NAD⁺ salvage pathway was unnecessary for protection by these NAD⁺ salvage pathway proteins (REF). To further study what aspects of these NAD⁺ salvage pathway proteins are required to confer protection against 103Q toxicity, they mutated the catalytic core of each of the NAD⁺ salvage pathway proteins as reported on to disrupt their catalytic activity. Then they performed serial dilution tests alongside yeast cells overexpressing the wild-type NAD⁺ salvage pathway proteins to see whether disruption of catalytic function impaired the ability of the NAD⁺ salvage pathway proteins to protect against 103Q toxicity.

Furthermore, his lab collected cell extracts from these yeast strains, ran the extracts on SDS-PAGE gels, and probed with antibodies that detect the 103Q mutant huntingtin fragment Figure. In cells expressing 103Q alone, over time, large oligomers form that are unable to enter the gel at all, seen by antibody binding within the wells of the stacking gel. However, in cells expressing either wild-type yeast NAD⁺ salvage pathway proteins or their catalytically inactive forms these

large oligomers are not seen, and instead, an increasing amount of 103Q degradation products are seen over time, supporting the hypothesis that the overexpression of these proteins confer protection through the clearance of toxic mutant huntingtin oligomers. Previously, unique 103Q degradation patterns were observed for each NAD⁺ salvage pathway protein. Importantly, it was observed that the same unique patterns for each protein in his preliminary studies, and furthermore observed that each catalytically inactive NAD⁺ salvage pathway protein displayed a visually identical degradation pattern as its wild-type counterpart. The finding that these degradation patterns are unique between proteins but identical for wild-type proteins and their catalytically inactive forms provides further evidence that the protective activities of these proteins is not disturbed by the mutations that render them catalytically inactive.

(2) NAD⁺ salvage pathway proteins display chaperone activity in vitro

To test their hypothesis that NAD⁺ salvage pathway proteins function as molecular chaperones, they performed in vitro chaperone assays of wild-type and catalytically inactive yeast NAD⁺ salvage pathway proteins purified from *E. coli* to determine whether these proteins have innate chaperone activity. All four wild-type yeast NAD⁺ salvage pathway proteins, as well as the catalytically inactive displayed significant chaperone activity, as seen through the ability of increasing concentrations of these proteins to inhibit the aggregation of citrate synthase, as compared to citrate synthase alone and lysozyme control.

(3) The proteasome, mitophagy, or yeast chaperone proteins Hsp42 or Ssa1 are not required for protection by NAD⁺ salvage pathway proteins

To elucidate the degradation pathways involved in degrading and clearing mutant huntingtin oligomers in cells when NAD⁺ salvage pathway proteins are overexpressed, [Dr. Barrientos](#) first tested whether protection by NAD⁺ salvage pathway proteins could be abolished or diminished by inhibiting the proteasome with MG132. While 10μM MG132 has previously been used in other studies to inhibit the proteasome in plated yeast, they further verified that the proteasome was fully inhibited by also treating cells with 50μM MG132, the concentration usually used to inhibit the proteasome in yeast cells growing in culture. Neither concentration of MG132 had any effect on the protection from 103Q toxicity by any of the NAD⁺ salvage pathway proteins, indicating that the proteasome is not required for this protection.

[Dr. Barrientos](#) further tested whether the inhibition of mitophagy could affect mutant huntingtin toxicity suppression by the NAD⁺ salvage pathway proteins through the knockout of the essential mitophagy protein Atg32. For most of the NAD⁺ salvage pathway proteins tested, the knockout of mitophagy function appears to lead to increased protection against 103Q toxicity. While this may seem counterintuitive, in research they've already published, they previously found that interventions that increase mitochondrial biogenesis also protects against 103Q mutant huntingtin toxicity. Thus, this data further supports their previous research and hypothesis that having elevated levels of mitochondria, even if they are only partially functional, helps protects cells against death. Furthermore, since the absence of mitophagy can further protect cells against 103Q toxicity in the presence of NAD⁺ salvage pathway proteins, they can conclude that the protection by these two mechanisms can be additive, and therefore that these two forms of protection are conferred through separate and independent mechanisms.

Furthermore, [Dr. Barrientos](#) tested whether knockout of two yeast chaperone proteins that have known interactions with mutant huntingtin proteins were essential for protection by NAD⁺

salvage pathway proteins. These proteins, Hsp42 and Ssa1 have both been found to influence the formation and clearance of mutant huntingtin aggregates. However, knockout of either Hsp42 or Ssa1 did not have a clear effect on the protection by NAD⁺ salvage pathway proteins, indicating that NAD⁺ proteins may confer protection through a pathway that does not require Hsp42 or Ssa1, or that NAD⁺ salvage pathway proteins and their catalytic mutant forms, when overexpressed, may be able to substitute for the roles that Hsp42 or Ssa1 normally play.

Dr. Milena Pinto has been expanding her knowledge and research in the study of the role of mitochondria in neurodegenerative diseases. Neuronal OXPHOS deficiency, in fact, has been associated with a variety of late-onset progressive neurodegenerative diseases. She induces mitochondrial defects in different neuronal subpopulations, mimicking the mitochondrial function decline that occurs naturally with aging. In the work published this year, she induced OXPHOS deficiency in adult neurons by knocking out Cytochrome c (Cyt c). Cyt c is a heme-containing mitochondrial protein, with critical functions in both respiration and apoptosis. Consistent with these vital functions, somatic Cyt c mouse knockout is embryonic lethal. In order to investigate the sensitivity of postnatal neurons to Cyt c depletion, she developed a neuron-specific conditional knockout model. Neuron-specific Cyt c KO mouse (nCytcKO) was created by crossing the floxed Cyt c mouse with a CamKII α -cre transgenic mouse, which deletes the floxed alleles postnatally. nCytcKO mice were normal at birth but developed an abnormal phenotype with weight loss, tremor, decreased sensorimotor coordination and sudden death between 12 and 16 weeks. Histological analysis did not show major neuronal degeneration. Analyses of oxidative phosphorylation showed a specific reduction in complex IV levels. Markers of oxidative stress were also increased. This novel model showed that neuronal complex IV is destabilized in the absence of Cyt c. It also showed that ablation of Cyt c in neurons leads to severe behavioral abnormalities and premature death without detectable neuronal loss, suggesting that neurons have the potential to survive for extended periods of time without a functional OXPHOS.

Dr. Pinto's manuscript describing this model was published in *Molecular Neurobiology* in August of 2018. Even though her main line of research is focused on neurodegenerative disorders, her contribution has also been essential in other fields where mitochondrial dysfunctions play an important role, like aging, age-related cachexia, and mitochondrial diseases (Leber's hereditary optic neuropathy plus dystonia), as shown in 2018 publications in *Nature Medicine*.

Dr. Pinto also collaborated on a long-term project that has a strong potential to be translated into clinical practice. Mutations in the mitochondrial DNA (mtDNA) are responsible for several metabolic disorders, commonly involving the muscle and the central nervous system. Because of the critical role of mtDNA in oxidative phosphorylation, the majority of pathogenic mtDNA mutations are heteroplasmic, co-existing with wild-type molecules. Using a mouse model with a heteroplasmic mtDNA mutation, she developed a mitochondrial-targeted TALENs that can reduce the mutant mtDNA load in muscle and heart. The molecular defect, namely a decrease in transfer RNAAla levels, was restored by the treatment.

9.2. Future Research Plans

9.2.1. Upcoming Population-Based Research

During this year **Dr. Noam Alperin** together with **Dr. Tatjana Rundek** submitted an R01 application to the NIH entitled *Quantitative MRI method for mapping cerebral perfusion regulation: Application to aging*. The grant was not funded- but the plans were made for its submission in the upcoming year.

In this proposal, the effect of reduction in total blood flow to the brain on regional blood perfusion will be investigated and whether the reduced perfusion in a certain brain region correlates with the brain volume loss at the same region, due to chronic low blood perfusion due to aging. We hypothesize that more perfusion protected brain regions demonstrate a smaller rate of volume loss. In this proposal we also plan to develop and validate a novel MRI method to map the cerebral perfusion regulation at different levels of blood supply under stable conditions. We term this method regional perfusion regulation (RPR) as it provides a rate of regional change in perfusion (e.g. hippocampus, amygdala) with respect to changes in total cerebral blood flow. This method is expected to be reproducible in healthy adults. This novel method combines two standard MRI techniques, CBF (cerebral volumetric blood flow) that measures the volumes of blood entering the brain by velocity encoding and ASL (arterial spin labeling) that measures regional perfusion across the brain. The feasibility of this method has been established and preliminary results clearly demonstrate regional reproducible heterogeneity of perfusion regulation. If successful, the RPR will be an important and helpful brain imaging biomarker of perfusion deficits predictive of structural age-related brain changes and age-related cognitive performance and decline.

Drs. Katalina McInerney and **Bonnie Levin** will continue to collect data for the McKnight Frailty Project. Posters, abstracts and manuscripts will be submitted based on the array of data and will highlight novel findings from the data analysis. Currently, there are 4 manuscripts under review. The Frailty database will serve as an important resource for pilot data.

Drs. Sarah Getz and **Bonnie Levin** are developing innovative questionnaires that will be validated among community participants and those at especially high risk of being scammed.

Dr. Alberto Ramos has submitted a large application to the NIH/NIA titled *Sleep in Neurocognitive Aging and Alzheimer's Research* (SANAR). The long-term goal of this research is to improve the sleep health disparities that contribute to ADRD in disparity populations, particularly in Latinos. Therefore, the study aims to quantify the contributions of sleep disorders and disturbances to silent cerebrovascular injury and brain atrophy obtained with magnetic resonance imaging. In addition, SANAR will evaluate the effect of sleep on nocturnal blood pressure using ambulatory blood pressure monitoring in a large and diverse sample of Latinos from the Hispanic Community Health Study/Study of Latinos (HCHS/SOL). The main hypothesis is that overnight hypoxemia in sleep apnea, insomnia, extreme sleep duration and/or disruption of sleep micro-architecture (arousals and reduced sleep spindles and slow wave sleep) contribute to neurocognitive deficits

through cerebrovascular disease, effects partially mediated by elevated nocturnal blood pressure.

Dr. Christian Camargo will primarily focus on the implementation of the REACTION grant once the AAN/MBRF funding is obtained and the award is executed. In addition he will work on developing a collaborative paradigm for evaluating more novel pharmacological interventions (e.g., HDAC inhibitors) for cognitive aging treatment. He will continue designing and seek funding for the study *A Role for Evaluating PET-Amyloid Status (AREPAS)* as part of the Key Hallmarks of Amyloid Tracer as an Ideal Biomarker Study (KHATIB).

Dr. David Loewenstein will be working on his new research project *Life Molecular Imaging – PI-2620 (TAU Imaging)*, which uses the first brain agent to be used at a Florida university for amyloid and tau imaging for at risk elders in prediction of future memory decline.

9.2.2. Upcoming Basic and Translational Science Research

Drs. Kunjan Dave and **Miguel Perez-Pinzon** will focus in 2019 on evaluating mechanisms by which physical exercise improves post-cerebral ischemic cognitive function. They will also evaluate mechanisms by which exposure of insulin-treated diabetic rats to recurrent hypoglycemia leads to cognitive impairment.

Dr. Ami Raval plans to investigate the effects of whole body vibration on stroke outcome in aged rats of both sexes. Secondly, she will conduct research on the effects of post-stroke physical exercise on post-stroke cognition in aged female rats.

Dr. Antoni Barrientos will continue working on the following research in 2019 (**Section 9.1**) Catalytically inactive forms of NAD⁺ salvage pathway proteins retain protective activity against 103Q toxicity in yeast. AND Line 2 - NAD⁺ salvage pathway proteins display chaperone activity in vitro.

In 2017 **Dr. Milena Pinto** started collaborating with Dr. Barry Baumel on the use of mesenchymal stem cells (MSCs) in the treatment of Alzheimer's disease. In recent years, the use of stem cells to reverse neurodegeneration has raised hopes toward a long-lasting treatment. In particular, mesenchymal stem cells are an attractive therapeutic possibility, due to their ease of isolation, low immunogenicity, and their ability to target multiple pathways involved in neuronal regeneration. The long-term goal of this project is to characterize the neuroprotective function of MSCs in a mouse model of Alzheimer's disease. The achievement of this goal will give them the possibility to build a "basic science" platform based on animal models at the University of Miami that can be translated clinically. To achieve the goals of this study they used the following approach: they extracted and expanded MSCs from a healthy mouse donor, injected the cells into a mouse model of AD and followed the progression of the pathology in presence or absence of MSCs. In 2018, Dr. Pinto completed most of the experiments planned and started a new session of treatments. This research will have a strong and lasting impact on our understanding of the use of MSCs as a new neuroprotective agent. Because neurodegeneration is the cause of

several progressive diseases she also started a new project that involves the use of MSCs in the treatment of frontotemporal dementia. Using the same approach utilized for the study of Alzheimer's Disease, she will inject two mouse models of fronto-temporal dementia (FTD) with MSCs and follow the evolution of their pathology.

9.2.3. Upcoming Education Program

Dr. Xiaoyan Sun, our McKnight Education Director, will continue our current educational programs and will focus on enhancing the learning of cognitive neuroscience in 2019.

We will continue:

- Seminar series, journal clubs, joint scientific lecture series
- Community education events and programs
- Cross-disciplinary mentorship in collaboration with the MD, MD/PhD, PIBS and MS programs
- Grant and manuscript writing classes (through UM CTSI under the directorship of Dr. Sacco and MS in Clinical Translational Investigations under the directorship of Dr. Rundek)
- CTSI classes (clinical trials, study designs, biostatistics)
- Formal MS degree in Clinical Translational Investigations
- Structured Neurocognitive Training program – McKnight Fellowship in cognitive aging

We plan to focus on learning about normal brain changes in aging by strengthening our collaborative relationships to attend and learn about seminars across departments and disciplines.

We are planning to provide diverse lectures and seminars to enhance learning of normal aging and disease process.

- Collaborative lectures between the McKnight Brain Institute and the Department of Geriatrics
- Collaborative lectures between the McKnight Brain Institute and the Brain Endowment Bank
- Collaborative seminar series between the McKnight Brain Institute and the Department of Psychology

We aim to strengthen our community education and outreach programs by working with local community leaders to enhance relationships in the community for purposes of disseminating information on brain health in aging to include normal changes in cognition and memory. We are planning to build on our established network in the Miami area which includes assisted living facilities, community and senior centers, churches and more, by expanding outreach through lectures and presentations. Dr. Camargo and Dr. Sun together with Stacy Merritt will lead these activities.

10. Technology Transfer

N/A

11. Budget

This is included at the end of the report in the *Financial and Budget Sheets* Section.

12. Educational Programs Focusing on Age-Related Memory Loss

Dr. Xiaoyan Sun continues in her role as the MBI Education Director.

The Education and Training Core of the McKnight Brain Institute at the University of Miami is committed to:

- Providing education on normal cognitive aging and memory related disorders to our medical students, graduate students, neurology residents, faculty and staff;
- Fostering collaborative educational efforts between faculty and staff at the McKnight Brain Institute and Center for Cognitive Neuroscience and Aging, Departments of Psychology and Psychiatry and the Brain Endowment Bank for promoting learning and research collaboration in the studies of cognitive aging and;
- Developing community education and outreach programs focusing on the aging population and brain health.

Our McKnight Education and Training Core consists of *McKnight Grand Rounds* (**Table 1**) weekly *Research Lab Meetings*, monthly *Research Seminars* (**Table 2**) and *Journal Clubs* (**Table 3**) and coordination of a *McKnight Brain Institute Scientific Lecture Series* with other Centers, Institutes, collaborators and partners.

Table 1. 2018 Evelyn F. McKnight Brain Institute Grand Rounds Speakers

Speaker	Visiting From	Date	Title
Eric M. Reiman, MD	Banner Alzheimer's Institute	January 31 st	<i>Brain Imaging in the Preclinical Study and Prevention of Alzheimer's Disease</i>
Ron C. Petersen, MD, PhD	Mayo Clinic College of Medicine, Rochester, MN	March 9 th	<i>How Much Forgetfulness is Too Much?"</i>
Richard Wurtman, MD	MIT Department of Brain and Cognitive Sciences	March 16 th	<i>Preservation of Cognition and Memory</i>
Howard J. Federoff, MD, PhD	University of California at Irvine	December 14 th	<i>The Human Peripheral Metabolome, Cognitive Function and Dementia</i>

Table 2. 2018 Evelyn F. McKnight Brain Institute Research Seminars

Speaker	Area of Expertise	Date	Title
William Hu, MD	Neurology	January 3 rd	<i>Biomarkers for Alzheimer's and Related Diseases: Diagnosis, Mechanisms, and Machine Learning</i>
Christian Camargo, MD	Neurology	January 31 st	<i>Defining Optimal Brain Health in Adults A Presidential Advisory From the American Heart Association/ American Stroke Association</i>
Katalina McInerney, PhD	Neuropsychology	February 23 rd	<i>Cognitive, Cultural and Affective Dimensions of Frailty</i>
Sarah Getz, PhD	Neuropsychology	February 23 rd	<i>The Relationship Between Fatigue and Executive Function in Aging Adults</i>

Alberto Ramos, MD	Neurology	March 14 th	<i>Sleep and Neurocognitive Aging in Population Based Studies</i>
Kunjan Dave, PhD	Neuroscience	March 14 th	<i>Post-Stroke Physical Exercise Improves Cognitive Outcomes in Young and Elderly Animals</i>
Bonnie Levin, PhD	Neuropsychology	March 21 st	<i>McKnight Brain Aging Registry I: Clinical Update</i>
Noam Alperin, MD	Radiology	May 30 th	<i>Findings of Interest on MRI Cases in the McKnight Frailty Database</i>
Christian Camargo, MD	Neurology	June 13 th	<i>Souvenaid: Designing Clinical Trials to Investigate the Treatment of Cognitive Decline Through the Synaptic Repair Hypothesis</i>
Alberto Ramos, MD	Neurology	August 8 th	<i>Update on the Latest Findings in Sleep Research</i>
Roger McIntosh, PhD	Psychology	August 29 th	<i>Update on Brain-Connectivity in fMRIs</i>
Judith Lobo	Psychology	September 19 th	<i>Age-related Changes in Functional Brain Connectivity</i>
Roger McIntosh, PhD	Psychology	October 24 th	<i>State Functional Brain Connectivity: A Potential Biomarker of Risk For Age-Related Cognitive Decline</i>
Sonya Kaur, PhD	Neuropsychology	October 24 th	<i>Sleep Quality Mediates the Relationship Between Cognitive Dysfunction and Frailty in Non-demented Older Adults</i>
Sarah Getz, PhD	Neuropsychology	October 24 th	<i>Susceptibility to Deception: Decreasing Vulnerability in Age-Related Memory Loss</i>
Ashish K. Rehni, PhD	Neuroscience	October 24 th	<i>Exposure to Recurrent Hypoglycemia Modulates Endoplasmic Reticulum Stress in Hippocampus of Insulin-treated Diabetic Rats</i>
Joyce Gomes-Osman, PT, PhD	Physical Therapy and Neurology	October 26 th	<i>Exercise for Brain Health: Neuroplasticity and the Pursuit of Data-driven, Dose-specific Recommendations</i>
Nikhil Banerjee	Neuropsychology	October 26 th	<i>Subjective Fatigue and Cognition in Non-demented Older Adults</i>

Christian Camargo, MD	Neurology	November 28 th	<i>Updates on Clinical Trials from the Clinical Trials in Alzheimer's Disease (CTAD) Conference</i>
Che Liu	Radiology	December 19 th	<i>Introduction to Resting State Functional Connectivity Data Analyses: Preliminary Results of the McKnight Brain Aging Registry Study (MBAR) Study</i>

Table 3. 2018 Evelyn F. McKnight Brain Institute Journal Clubs

Speaker	Area of Expertise	Date	Title
Christian Camargo, MD	Neurology	February 28 th	<i>Mechanisms, Clinical Significance, and Prevention of Cognitive Impairment in Patients With Atrial Fibrillation</i>
Sonya Kaur, PhD	Neuropsychology	March 28 th	<i>Estimating Total Cerebral Microinfarct Burden From Diffusion-Weighted Imaging Part 1</i>
Sonya Kaur, PhD	Neuropsychology	April 11 th	<i>Estimating Total Cerebral Microinfarct Burden From Diffusion-Weighted Imaging Part 2</i>
Anita Seixas Dias Saporta, MD	Neurology & Imaging	April 18 th	<i>Neuroimaging in Dementia</i>
Anita Seixas Dias Saporta, MD	Neurology & Imaging	May 23 rd	<i>Role of Neuroimaging as a Biomarker for Neurodegenerative Diseases</i>
Marialaura Simonetta, MD	Neurology	May 30 th	<i>MD on Microinfarcts are Common and Strongly Related to Dementia in the Oldest-old: The 90+ Study</i>

Structured Educational Activities at Different Levels

The McKnight Brain Institute's goal for trainee education is to facilitate the learning of cognitive neuroscience at different levels for our students. The McKnight Brain Institute has participated in teaching at medical and graduate schools at the University of Miami. We have organized research seminars, journal clubs and 4 special McKnight Grand Rounds speakers.

Medical and Graduate Student Education

Drs. Sacco, Rundek and Sun teach a neuroscience course of MD and MD/MPH students in the spring of each year. Dr. Sun taught MD/PhD students for a neurology case review class this October. Dr. Levin taught students in the University of Miami's Department of Psychology. Dr. Rundek organizes and teaches students in the Master Degree program through the Clinical Translational Science Institute (CTSI). Dr. Levin mentors a neuropsychology PhD student. Dr. Rundek mentors 3 MD/PhD students, 2 MD/MPH students and 2 MD students.

Post-doctoral Education

Dr. Levin has 5 Post-doctoral neuropsychology Fellows she mentors and trains. Dr. Sun has accepted students for clinical shadowing programs and is involved in mentoring the cognitive neurology Fellows in clinic. Dr. Rundek mentors KL2 and AAN research and career development awardees.

Neurology Resident Education

Our neurology residents are required to have a 2-week clinical rotation in the memory disorders clinic. The 3rd and 4th year neurology residents spend two weeks with the faculty of the memory disorders division. This rotation helps the residents understand memory-related disorders. Residents learn a systemic approach to diagnosis and treatment of patients with memory related disorders. Residents have opportunities to participate in research seminars and journal clubs at the McKnight Brain Institute. The residents have the opportunity to observe neuropsychological testing and discuss the neuropsychological test battery with our neuropsychologists. We also have an organized lecture series. Our cognitive neurology and geriatric psychiatry faculty give lectures to the neurology residents about diagnosis and management of memory related disorders during cognitive neurology month. Dr. Sun and Dr. Rundek give lectures providing an overview of dementia and cognitive decline to neurology and psychiatry residents every year.

Faculty and Staff Education

We have regular research seminars and journal clubs in which trainees, members and collaborators from the McKnight Brain Institute present their research findings and discuss the relevant papers focused on cognition in aging.

McKnight Grand Rounds

We scheduled joint Grand Rounds with the McKnight Brain Institute and the Center for Cognitive Neuroscience and with the UM Department of Psychiatry. In January, Dr. Eric M. Reiman from the Banner Alzheimer's Institute was invited to present at Grand Rounds. The title of his presentation was "Brain Imaging in the Preclinical Study and Prevention of Alzheimer's Disease." In early March, Dr. Richard Wurtman from MIT, gave a talk on "Preservation of Cognition and Memory." Also in March, Dr. Ron Petersen from the Mayo Clinic College of Medicine, Rochester, MN gave a presentation on "How Much Forgetfulness is Too Much?" In December, Dr. Howard Federoff from the University of California at Irvine gave a lecture on "The Human Peripheral Metabolome, Cognitive Function and Dementia" (See Table 1). We conducted 2-day visits with these distinguished MBI guest speakers and arranged for individual meetings with our collaborators, faculty and trainees. We also asked for their advice and suggestions regarding our MBI mission and vision and recruitment of new faculty and trainees. We may extend our Scientific Advisory Board by including some of the external members (after conducting our Phase II Strategic Plan).

McKnight Fellowship Program

Dr. Christian Camargo completed his McKnight Fellowship in cognitive neurology in June of 2018 and was recruited as faculty in the Department of Neurology. He continues to be an integral Collaborator with the McKnight Brain Institute. Dr. Anita Seixas Dias Saporta is the new McKnight Fellow beginning July of 2018. We also plan to enroll one MD/PhD student to join and formally work in our MBI on a research project and a PhD thesis. This work usually takes 3-4 years.

Mentorship Development

The mentorship development program is an important part of the McKnight Brain Institute's education core. We are committed to helping our junior faculty and trainees develop their research and grant writing skills and their careers in cognitive aging. Dr. Rundek is a nationally recognized mentor and educator and mentors junior faculty as well as trainees in our Department, institution and nationally. Our McKnight Members and Collaborators also mentor trainees.

Community Outreach Program

Through our McKnight education program we are committed to supporting the local community by participating in community health forums via lectures, presentations and media programs. Below is a list of education and outreach done in 2018.

- January 3, 2018, Dr. Camargo was interviewed on "The Effect of Exercise on Brain Activity and Work Productivity" on The Brian Mudd Show, News Radio 610 WIOD, Miami, FL.
- Dr. Sun was interviewed by Neurology Today, the news publication for neurologists from the American Academy of Neurology on her paper published in Neurology, "Neurogranin as a Predictor of Memory and Executive Function Decline in MCI patients."

- April 24, 2018, our Director of Research and Administration, Stacy Merritt gave a presentation at the Pine Crest Community Center on "The Aging Brain and Research" in Pine Crest, FL.
- May 11, 2018, Dr. Camargo gave a lecture at North Shore Medical Center at the Medical Education Speakers Network on "Alzheimer's Disease vs. Senile Dementia" in Miami, FL.
- June 27, 2018, Dr. Sun was on a panel at the Chamber of Commerce Alzheimer's Support Panel, Question and Answer Session: "Discerning between normal brain changes in aging and Alzheimer's" in Coral Gables, FL.
- October 23, 2018, Dr. Camargo was interviewed for the Health News|University of Miami Hospitals and Clinics, University of Miami Health News, on "It's Not Always Dementia. Here's What to Know."
- November 13, 2018, the article "Study Aims to Find Key to Brain Health for 'Super' Aging Seniors" was circulated through the University of Miami Communications network to educate the community on the importance of our research on healthy aging.
- November 27, 2018, Dr. Camargo was interviewed on the radio show Sundial airing on WLRN 91.3 FM, the local National Public Radio (NPR) affiliate. The topic was "Alzheimer's Disease Prevention through the study of 'Successful Agers.'"
- December 20, 2018, Dr. McInerney, Stacy Merritt and a study participant from the McKnight Brain Aging Registry (MBAR) study were filmed for a television segment on the local ABC television affiliate WPLG, Miami, FL. The segment title is "Why Do Some People Age Better Than Others?"

12.1. General Education Program

Dr. Ralph Sacco delivered a UHealth-sponsored lecture to about 100 community residents in Coral Gables at the Lennar Building on Treating Stroke and Preventing Cognitive Decline.

Dr. Bonnie Levin's Post-doctoral Fellow, **Dr. Annelly Buré** has been providing educational information on aging and memory loss to the Spanish speaking community via a radio segment that caters to Hispanic/Latino older adults titled *Para Mayores* on La Poderosa 670 AM in Miami, FL. During her interview she discusses issues related to normal cognitive aging and informs the public about research studies and clinical services offered by our department.

Dr. Levin serves on the board of Circle of Friends for Human Rights Watch, with a specific focus on elder abuse.

Dr. Elizabeth Crocco has been conducting the following trainings and lectures for Community and Caregivers:

- Alzheimer's Disease Initiative (ADI) Caregiver Training Seminars in Dementia Miami-Dade County, FL
- Alzheimer's Disease Initiative (ADI) Caregiving Training Program in Dementia in Monroe County
- ADI Respite Care and Day Care Centers in the Florida Keys

- Development and coordination of an annual 4-hour state-mandated training to caregivers, Alzheimer’s Disease Initiative (ADI) respite and Day Care professionals and para professionals for CEUs (continuing education credits) accreditation provided in both English and Spanish in South FL
- Development and coordination of an annual 4 hour state-mandated dementia training to caregivers in Respite and Day Care Centers in Monroe County, FL
- Presentation on *Memory: What Are You Going To Do?* at the University of Miami-Newman Alumni Center in Coral Gables, FL
- Presentation on *Focus On Caregiving* at the Mount Sinai Medical Center, Wien Center for Alzheimer’s Disease & Memory Disorders in Miami Beach, FL

Dr. David Loewenstein provides education and outreach on aging and memory loss for the East Ridge Retirement Village Outreach Program and the Unidad Outreach Program in Miami, FL.

12.2. Education of Trainees: Undergraduate, Medical and Doctoral Students, Post-Doctoral Students, Residents and Fellows

Dr. Ralph Sacco provides mentorship to faculty, Fellows and students listed below.

- Charles Cohan, PhD is a Fellow who receives funding from an AHA BUGHER Stroke Center of Excellence grant.
- Marialaura Simonetto, MD is a Fellow who receives funding from an AHA BUGHER Stroke Center of Excellence grant.
- Erika Marulanda-Londono, MD receives funding from StrokeNet.
- Nicole Sur, MD receives funding from StrokeNet.
- Michelle Caunca, our formal McKnight MD/PhD candidate, receives funding from an F30 grant.
- Sofia Oluwole is an MD/PhD candidate who receives funding from the research program NOMAS as well as from the Florida Department of Health (DOH).
- Brett Doliner is an MD student who graduates in 2019.

Dr. Ralph Sacco was invited to speak at the Grand Rounds Programs at Johns Hopkins and UT Southwestern Medical Center on Brain Health.

Dr. Tatjana Rundek is the formal mentor to Dr. Joyce Gomes-Osman on her research proposal for a KL2 Career Development Award. Dr. Rundek’s expertise, knowledge and mentoring skills proved instrumental in the process and to the success of Dr. Gomes-Osman being awarded the grant.

Dr. Tatjana Rundek encouraged **Dr. Christian Camargo** our former McKnight Cognitive Fellow, to apply for the grant award offered by the American Academy of Neurology (AAN) and McKnight Brain Research Foundation (MBRF) “*AAN McKnight Clinical Translational Research Scholarship in Cognitive Aging and Age-Related Memory Loss*”. Under the mentorship of Dr. Rundek they spent six months working on the submission titled *Reducing the Effects of Aging on Cognition with*

Therapeutic Intervention of an Oral Nutrient: The REACTION Study. She guided him along the path to further his career while fulfilling his research aspirations. Drs. Bonnie Levin and Katalina McInerney co-mentored him on the neuropsychological design of this research. The AAN/MBRF awardees have not been officially announced but Dr. Camargo has received provisional award approval (pending submission of the proposal revision according to the reviewers' recommendation; deadline for submission of these revisions is Jan 18, 2019).

Dr. Tatjana Rundek is the Director of a Master of Science degree in Clinical Translational Investigations at the UM Miller School of Medicine. She has been teaching 2 classes: One is on team science in the fall and another is an introduction to scientific writing and grant writing course in the spring. Our McKnight trainees are encouraged to attend these classes on Tuesday and Wednesday afternoons, from 4-6 pm during the semesters. The classes are given in our Clinical Research Building.

Dr. Tatjana Rundek also leads our Neurology Resident and Fellow Research program with a number of weekly research activities and journal clubs that our McKnight trainees can attend.

Dr. Tatjana Rundek is a Training Director of our American Heart Association (AHA) Stroke Bugher Center of Excellence and Training Director of the NIH-StrokeNet and NeuroNext. Each of these programs has active research activities and career advancement on-line seminars and courses. Dr. Rundek keeps our McKnight trainees informed of these activities and provides them with the opportunities to join, participate and network with these project group members and their trainees. Her mentees have received training awards (NIH F30 and F31, AHA, ANA, KL2 and other awards).

Schoninger Neuropsychology Program

The Division of Neuropsychology directed by **Dr. Bonnie Levin**, has six faculty, five Post-doctoral Fellows, three students and one volunteer research assistant. Each member of the Division devotes varying degrees of effort to McKnight related clinical and research activities. The Schoninger Neuropsychology Program was first established in 2007 as a result of the Schoninger family vision and provides funding for the McKnight/Schoninger Neuropsychology Program. The program is dedicated to understanding age-related memory loss and provides extensive clinical training to graduate students and Fellows in the evaluation of patients presenting with memory complaints. In this setting, Fellows are trained in the administration, scoring and interpretation of neurocognitive measures and work directly with their supervisor to arrive at a differential diagnosis. Supervision sessions involving Schoninger clinic referrals specifically focus on the exact nature of the memory complaint as well as the etiological basis and possible interventions and treatment for memory loss. In addition, Fellows are trained to carry out an extensive interview that includes a careful history examining a wide range of factors associated with memory loss in normal cognitive aging, including sleep hygiene, nutritional/dietary patterns, activity and exercise regimens, toxic exposures, and a careful exploration of other possible neurologic contributors (e.g., cardiometabolic disorders and other vascular conditions).

All Schoninger trainees participate in the McKnight Journal Club, neuropsychology rounds, case conferences and neurology and psychiatry grand rounds. They are also involved in the training of undergraduate and graduate level neuropsychology students. Fellows receive a minimum of one hour of individual clinical supervision and 2 hours of group supervision per week. They work closely with Dr. Rundek and other disciplines in the departments (e.g., neurologists, neurosurgeons, social workers, physical therapists, neurology residents) to provide our patients with well-rounded, multidisciplinary care. Collaboration with other disciplines spans clinical and research activities, enriching the training and mentorship of our Fellows.

Dr. Joyce Gomes-Osman has been mentoring two PhD Students from the Department of Physical Therapy at the University of Miami Miller School of Medicine (**Jordyn Rice**, DPT, **Danylo Cabral**, PT), who have now been fully trained in data collection procedures involving non-invasive brain stimulation, functional walking and cognitive function testing. In addition, during this year she has mentored two post-baccalaureate students who are supporting these efforts and learning about the exciting studies being carried out in her lab.

Dr. Joyce Gomes-Osman taught a 3-credit graduate level class to physical therapy students - Neuroscience II 641. In this class, students learn about clinical neurophysiology and functional performance in the healthy nervous system and in neurologic conditions.

Dr. Alberto Ramos Chaired the *Young Investigator Research Program* for the American Academy of Sleep Medicine.

Dr. Kunjan Dave and **Dr. Miguel Perez-Pinzon** mentor and train 2 Postdoctoral Fellows and 1 MD/PhD student in their lab.

Dr. Christian Camargo trained neurology residents through the University of Miami, Miller School of Medicine neurology residency program.

Dr. Loewenstein together with Dr. Rundek co-mentors:
Michelle Rae Caunca, MD/PhD candidate; and
Joyce Gomes Osman, Ph.D. – KL2 Award

Dr. Loewenstein also mentors a PhD student and is on 2 graduate students' dissertation committees.

Dr. Elizabeth Crocco led the following general education programs:

- *Geriatric Psychiatry Lecture Series*
- JMH General Psychiatry Residency Training Program
- Develop and implement comprehensive geriatric specialty lectures in all 4 years of general psychiatric residency training. Topics include: normal aging, late-life schizophrenia, late-life depression, ECT, bereavement, neurodegenerative disorders, Alzheimer's, Vascular, Lewy body disease, caregiving issues
- *Weekly Case Conference*
- Jackson Memorial Hospital Geriatric Psychiatry Training Program

- Coordination and supervision of all geriatric psychiatry fellows' weekly presentations of patients' case histories, including biological, psychological and sociological data and formulates an integrated treatment plan
- *Weekly Journal Club*
- Jackson Memorial Hospital Geriatric Psychiatry Residency Training Program.
- Weekly coordination and supervision of all geriatric psychiatry fellows with the objective of critical evaluation of peer-reviewed, original research articles and application of this knowledge to the care of their geriatric patients
- *Geriatric Psychiatry Seminar*
- Jackson Memorial Hospital Geriatric Psychiatry Residency Training Program.
- Development and implementation on a weekly basis of a core curriculum-focused conference that covers knowledge and skill in areas that are necessary to the successful completion of the geriatric psychiatry training program and commonly seen diagnoses in geriatric psychiatry
- *Doctoring II: Dementia Small Groups*
- UM Miller School of Medicine Students
- Leads small groups of 20-25 medical students in diagnosis and evaluation of cognitive disorders

13. Collaborative Activities with other McKnight Brain Institutes, Institutions and Research programs

McKnight Brain Aging Registry (MBAR) [Dr. Tatjana Rundek](#), the PI for the MBAR study together with other leaders at the University of Miami [Dr. Bonnie Levin](#) and [Dr. Noam Alperin](#), collaborates with all 3 other McKnight Brain Institutes. See [Section 9.1](#) for more information on MBAR.

The McKnight Brain Institutes Inter-Institutional McKnight Brain Aging Registry (MBAR) Grant Initiative The MBI sites are in the process of developing a proposal to the NIA that will expand on findings from our MBAR study. Following discussions with and recommendations from the NIA program, the MBAR PIs have been working to establish access to PET imaging and neuropathology follow-up across MBI sites to enhance this proposal effort. We are working to develop this initiative into an NIA grant submission for the coming year under the leadership of Dr. Gene Alexander and the MBAR Executive Committee (Drs. Gene Alexander, Ron Cohen, Kristina Visscher, Virginia Bradley Grissom, Bonnie Levin and Tatjana Rundek).

The MBRF Cognitive Aging and Memory Intervention Core - The second call for pilot-study applications has been announced. The project must include collaboration among two or more McKnight Brain Institute sites on a pilot-study that researches interventions to reduce age-related memory loss and cognitive decline. The goal is to facilitate grant submissions for extramural funding sources for multi MBI site cognitive aging and memory intervention trials.

U19 Application with the McKnight Brain Institute at the University of Arizona

A collaborative grant project is currently in progress with the University of Arizona MBI under the leadership of Dr. Carol Barnes. She leads a large U19 application to the NIA (deadline: Jan 25, 2019) to investigate main drivers of cognitive aging across the lifespan: *Precision Aging Network (PAN): Closing the Gap Between Cognitive Healthspan and Human Lifespan*. Dr. Rundek and Dr. Levin will lead the Miami Clinical Project (*In-depth Profiles of Resilience and Risk*) and serve on the PAN Executive committee.

14. Collaborative Activities With Non McKnight Brain Institutes, Institutions and Research Programs

Dr. Tatjana Rundek's grant submission to the Florida Department of Health (DOH) through the Ed and Ethel Moore Alzheimer's Disease Research Program was funded. This will be a collaborative program between the University of Miami, Mount Sinai Medical Center in Miami Beach, the University of Florida, Florida International University and Florida Atlantic University.

The overarching *goal* of this proposal is to determine the impact of novel brain vascular imaging phenotypes (VIPs) and modifiable vascular comorbidities on cognitive and neurodegenerative profile typical of the Alzheimer's Disease (AD) phenotype. Brain small vessel disease is the most prevalent cause of progressive cognitive impairment in the elderly. MRI studies have shown the high prevalence of covert small-vessel disease in the elderly and population-autopsy series have verified the high frequency of the coexistence of vascular pathology with AD pathology. The need for quantitative evaluations of the impact of brain vascular phenotypes on cognitive and neurodegenerative changes related to AD pathology is evident. To achieve our goal we would leverage reach and in-depth brain magnetic resonance (MR) imaging, clinical and neurocognitive data from the NIH-funded *1Florida Alzheimer Disease Research Center (1FL ADRC)*, which enrolled a diverse population of South Florida with a large representation of Hispanics/Latinos.

Our proposed research is of particular importance for the Hispanic/Latino population of South Florida, which is the largest and fastest growing ethnic minority in the US. Hispanics/Latinos have a disproportionately high burden of vascular risk factors and comorbidities and they are largely underrepresented in AD research. Moreover, vascular comorbidities are modifiable and preventable. The results from the proposed investigations will uniquely position our team to start closing the gap in our understanding of the mechanisms by which vascular phenotype contributes to AD pathology and to inform future strategies to reduce AD risk specifically tailored to high vascular-AD risk populations.

Dr. Ralph Sacco and **Dr. Tatjana Rundek** have active research programs with the NOMAS team at Columbia University in NY. They also have an active genetic research program as a part of the Family Study with **Dr. Susan Blanton** and **Dr. Liyong Wang** from the Miami Hussman Institute for Human Genomics.

Dr. Ralph Sacco and **Dr. Tatjana Rundek** participate and collaborate with the Hispanic Community Health Study- Study of Latinos (HCHS/SOL) with the Miami Site PI, Dr. Neil Schneiderman. They are also involved with Dr. Schneiderman's T32, one of the longest standing T32 training programs on cardiovascular risk funded by the NHLBI.

Dr. Tajana Rundek actively participates in research on brain hemodynamics in aging with the Einstein Aging Study (EAS) in the Bronx.

15. Briefly Describe Plans for Future Research and/or Clinical Initiatives

We are excited to execute and implement our future plans for the UM Evelyn F. McKnight Brain Institute in 2019. Here is an overview of what we plan to focus on:

Dr. Rundek and Dr. Sacco together with the MBI Scientific Advisory Board will move forward with **Phase II of the McKnight Brain Institute Strategic Plan** in 2019 to further the mission of our McKnight Brain Institute.

The next phase of Strategic Planning will include the development of our strategic goals along with tactics, measurable outcomes and timelines. We will build upon the team vision to develop a unified framework of cognitive aging and brain health utilizing our wealth of inter-disciplinary and multi-departmental knowledge and resources. We will prepare the MBI Strategic Plan document, share it with our team members, collaborators and broader community to present its goals and start its implementation. We plan for these activities to take significant time and effort in the next progress year. The conclusion of our Strategic Plan will also determine most of our activities in 2019.

Dr. Rundek and Dr. Loewenstein will begin working on the newly funded award from the Florida Department of Health (DOH) for the research project *Brain Vascular Imaging Phenotypes (VIP) and cognitive and neurodegenerative profile (or the VIP study)*. A description of the project can be found in **Section 14**.

Dr. Rundek and Dr. Loewenstein will collaborate on the competitive renewal of the 1FL ADRC (newly named ADC) with the University of Florida (PI: Todd Golde). They will participate in the 1FL ADC Clinical Core, Recruitment Core and co-direct Educational/Training Core in conjunction.

Dr. Rundek and Dr. Levin will collaborate on the submission of the U19 Application with the McKnight Brain Institute at the University of Arizona (PI: Carol Barnes). A description of the project can be found in **Section 13**.

Within our population-based prospective cohort, **NOMAS (Section 9.1.1)**, upcoming work in 2019 will focus on expanding recent studies on the role of the immune mechanisms in vascular cognitive impairment and dementia. Through the use of a highly multiplexed method for profiling innate and adaptive immunity pathways, we will enhance our efforts to explore inflammation networks in cerebrovascular disease as determinants of cognitive trajectories and functional decline.

We will expand our collaborative relationship with the University of Miami's newly established **Center for Cognitive Neuroscience and Aging** under the leadership of Dr. David Loewenstein. This will include partnering with his team of scientists on grant and research opportunities and creating a joint seminar series of prestigious speakers on topics relevant to our mission on aging and brain health.

Dr. Bonnie Levin, together with her neuropsychology team will continue leading the McKnight Frailty Project. Along with Dr. Sarah Getz, Dr. Levin will validate newly developed innovative questionnaires for scamming among community participants and those at especially high risk of being scammed. Posters, abstracts and manuscripts will be submitted based on their data and will highlight novel findings from the data analysis.

Dr. Sarah Getz under the mentorship of Dr. Levin is planning to apply for a CTSI pilot grant to examine scam detection and prevention among the vulnerable elderly. Without an effective 'primary elder financial fraud and scams intervention', the magnitude of this burgeoning public health crisis will likely increase twofold in the next 20 to 30 years in line with the ever growing elderly population. Minorities and those with lower SES and education are at the greatest risk. The proposed research will be highly innovative because it represents a substantive departure from the status quo by specifically targeting vulnerable minority populations with a behavioral science based primary intervention, and by assessing scam detection abilities pre and post intervention.

Dr. Bonnie Levin will continue working in collaboration with faculty in other Departments at UM including Ophthalmology, Medicine and Otolaryngology on NIH grants examining topics related to early biomarkers of cognitive change in normal aging and those presenting with memory complaints.

Dr. Christian Camargo will work on developing a collaborative paradigm for evaluating more novel pharmacological interventions (e.g., HDAC inhibitors) for cognitive aging treatment. He will be implementing the study *A Role for Evaluating PET-Amyloid Status (AREPAS)* as part of the Key Hallmarks of Amyloid Tracer as an Ideal Biomarker Study (KHATIB).

The UM McKnight Brain Institute MBI is one of the organizers and sponsor of ***the 13th International Conference on Cerebral Vascular Biology, Miami, June 2019***.

Dr. Sacco will be one of the keynote speakers and **Dr. Rundek** will moderate a session on the aging brain and age-related memory loss.

Dr. Vladimir Hachinski, MD, a renowned cognitive neurologist from London, Ontario, Canada, will be our MBI guest speaker at the conference.

CEREBRAL VASCULAR BIOLOGY
13TH INTERNATIONAL CONFERENCE
CVB2019
MIAMI
June 25th – 28th
www.cvb2019.com

THE EVELYN F. MCKNIGHT BRAIN INSTITUTE
UNIVERSITY OF MIAMI
Preserving memory, enhancing life

FIU | **Herbert Wertheim College of Medicine**
FLORIDA INTERNATIONAL UNIVERSITY & UNIVERSITY OF MIAMI

THE MIAMI PROJECT TO CURE PARALYSIS

Biogen

BMB DEPARTMENT

Keynote speaker:
Dr. Ralph L Sacco
Expanding the neuroscience frontier of brain health

Session 5. (T Rundek, Moderator)
Cerebrovascular pathology of the aging brain, age-related memory loss and cognitive decline

Dr. Vladimir Hachinski
VCI: Can we prevent some types of dementias beginning now?

Dr. Sun will lead the plans for our Educational Program in 2019 for our neurology residents, faculty and staff as well as our McKnight Brain Institute trainees, members and collaborators.

Dr. Sun will begin the process of implementing a **brain cutting class**, which will be instrumental to our neurology residents and McKnight Brain Institute trainees, members and collaborators in identifying the characteristics of normal aging brains versus those with pathological, and especially neurodegenerative conditions.

The Educational Program will also seek to enhance our community education and outreach via a structured lecture series. We want to reach more aging communities to teach about the significance of maintaining brain health through the aging process. We also plan to identify and collaborate with other partners with already strong community outreach and education programs (e.g., Center for Cognitive Neuroscience and Aging, All of Us, and others).

In June of 2019, **Dr. Ron Lazar**, the Director of the University of Alabama at Birmingham Evelyn F. McKnight Brain Institute, will be our MBI special Grand Rounds invited guest speaker.

Additional research endeavors for next year include:

Dr. Alberto Ramos will delve into the NIH/NIA funded project titled *Sleep in Neurocognitive Aging and Alzheimer's Research (SANAR)*. The long-term goal of this research is to improve the sleep health disparities that contribute to ADRD in disparity populations, particularly in Latinos.

Dr. David Della-Morte will work on the newly awarded project *Diabetes Mellitus, Regenerative and Reparative Processes, and Improvement of Pancreatic Beta Cell Function: Role of Bone Marrow-Mesenchymal Stem Cells, Micrnas, M2 Macrophages and Myeloid Derived Suppressor Cells*.

Dr. Kunjan Dave and **Dr. Miguel Perez-Pinzon** will focus in 2019 on evaluating mechanisms by which physical exercise improves post-cerebral ischemic cognitive function. They will also evaluate mechanisms by which exposure of insulin-treated diabetic rats to recurrent hypoglycemia leads to cognitive impairment.

Dr. Ami Raval plans to investigate the effects of whole body vibration on stroke outcomes in aged rats of both sexes. Secondly, she will conduct research on the effects of post-stroke physical exercise on post-stroke cognition in aged female rats.

Dr. Antoni Barrientos will continue working on the following research in 2019: (1) Catalytically inactive forms of NAD⁺ salvage pathway proteins retain protective activity against 103Q toxicity in yeast; and (2) NAD⁺ salvage pathway proteins display chaperone activity in vitro.

Dr. Milena Pinto will continue her collaboration with Dr. Barry Baumel on the use of mesenchymal stem cells (MSCs) in the treatment of Alzheimer's disease.

And finally, **Susan Fox-Rosellini** will increase her role at the UM MBI, starting in February of 2019. She will be responsible for managing and updating the MBI marketing, communications and social media platforms to include our website, collateral and social media serving as the MBI representative to the McKnight Communications Working Group. She will help with our Phase II Strategic Planning and the preparation of our Strategic Plan Document. She will also oversee the financials and operations, including the planning of the 11th Annual Inter-institutional Meeting in 2020, and annual reporting to the MBRF.

16. If applicable, please provide endowment investment results for the report period.

This is included at the end of the report in the *Financial and Budget Sheets* Section.

17. Were any funds used for a Prohibited Purpose during the report period?

No funds were used for prohibited purposes.

18. Do you recommend any modification to the Purpose or mandates in the Gift Agreement?

No.

19. Did all activities during the report period further the Purpose?

Yes.

20. Please describe any negative events (loss of personnel, space, budget, etc.) that occurred during the report period and the possible impact on carrying out the Gift Agreement.

None.

21. Please provide any general comments or thoughts not covered elsewhere – a response is not required. Please respond only if you would like to add something not otherwise covered elsewhere.

N/A

22. What do you consider your most important scientific achievements this year?

We are pleased with the UM MBI's grant awards, accomplishments and achievements in 2018. Our most important attainments are listed below.

We are most excited about our trainees' success and accomplishments:

Dr. Joyce Gomes-Osman's KL2 award is an important accomplishment that will further the mission of our McKnight Brain Institute. McKnight leadership at the University of Miami is proud that a McKnight Brain Institute Member has secured a Career Development Award. The successful completion of the research and training that comprise this grant will allow her to approach her long-term goal of developing exercise interventions that can be individually tailored to promote cognitive brain health in aging adults, which will be the focus of a future R proposal.

Dr. Christian Camargo has been provisionally awarded the AAN McKnight Clinical Translational Research Scholarship in Cognitive Aging and Age-Related Memory Loss, for the project *Reducing the Effects of Aging on Cognition with Therapeutic Intervention of an Oral Nutrient: The REACTION Study*. Pending the result of his submission to the reviewers' responses by January 18th, he will receive 2 years of funding. This will allow him dedicated research time and a tremendous opportunity to advance his career in cognition and memory in aging.

The appointment of the **Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging** to **Dr. Tatjana Rundek** is a truly honorable achievement. The University of Miami is grateful to the McKnight Brain Aging Foundation for the Chair award and the opportunity to fulfill the mission of learning about the role of aging in memory.

Dr. Rundek's Florida Department of Health (DOH) Ed and Ethel Moore Alzheimer's Disease Research Program **grant received funding**.

The work and effort of **Dr. Levin's team on MBAR and McKnight Frailty Registry; her post-doctoral Fellows and graduate students working together with Stacy Merritt, Research and Administration Director**, has populated and expanded REDCap to include a large demographic and medical data base of almost 400 subjects. This provided the framework for seven conference presentations or posters. Currently, there are 4 manuscripts based on this database under review.

The award for the research project collaboration with the McKnight Brain Institutes at the Universities of Florida and Arizona **Uncovering Risk Profiles of Deception and Mitigating Susceptibility to Scamming in Midlife and Older Age: A Novel Intervention Tool** was awarded by the McKnight Brain Research Foundation through its Inter-Institutional Cognitive Aging and Memory Interventional Core.

Lastly, a truly significant scientific achievement to report in 2018 is **Dr. Ralph Sacco's nomination to the prestigious National Academy of Medicine (NAM)**.

The National Academy of Medicine, established in 1970 as the Institute of Medicine, is an independent organization of eminent professionals from diverse fields including health and medicine; the natural, social and behavioral sciences; and beyond. It serves alongside the National Academy of Sciences and the National Academy of Engineering as an adviser to the nation and the international community. Through its domestic and global initiatives, the NAM works to address critical issues in health, medicine and related policy and inspires positive action across sectors.

The NAM announced Dr. Ralph Sacco as one of the 75 new members and 10 international members at its annual meeting on October 15, 2018. Membership in the NAM is considered one of the highest honors in the fields of health and medicine and recognizes individuals who have demonstrated outstanding professional achievements and commitment to service. The Academy nominated him as a result of his “instrumental involvement in policies promoting ideal cardiovascular health, brain health, stroke prevention, and non-communicable disease targets”. He is humbled and proud to know that his clinical research has had an impact on the practice of medicine nationwide. The award encourages him to fortify his dedication towards new discoveries that advance the field and to disseminate those findings. It is an honor and privilege for him to join past honorees from UM and serve on the NAM recommendation panels that have had a tremendous impact on health care, education and public health. He is proud to share the extraordinary honor with the entire University of Miami community. Particularly, he shares this great honor with the incredibly talented people he’s had the great fortune to work with in the past as well as today. This achievement recognizes the success of team-based research which has been a cornerstone of our McKnight Institute. He is motivated and energized by this important scientific achievement, and looks forward to another successful and productive year for the McKnight Institute. The press release is included below.

PRESS RELEASE

Top UM Neurologist Dr. Ralph Sacco Elected to Prestigious National Academy of Medicine

A luminary stroke neurologist and researcher, **Ralph L. Sacco, M.D., MS**, professor and chair of neurology and the Olemberg Family Chair of Neurological Disorders at the University of Miami Miller School of Medicine, has been elected to the prestigious National Academy of Medicine (NAM).

This extraordinary honor reflects the height of professional achievement and commitment to service in health and medicine. Dr. Sacco received the honor “for his instrumental involvement in policies promoting ideal cardiovascular health, brain health, stroke prevention, and non-communicable disease targets,” according to the Academy.

University of Miami President Julio Frenk, himself a member of the National Academy of Medicine, said, “This is an extraordinary honor, not only for Dr. Sacco, but our entire University community. It speaks to the excellence of Ralph’s clinical research and its impact on the practice of medicine nationwide. His dedication to making new discoveries that advance the field and disseminating those findings in a meaningful way are the hallmark of his stellar career.” Membership in the NAM is considered one of the highest honors in the fields of health and medicine and



recognizes individuals who have demonstrated outstanding professional achievements and commitment to service. The NAM announced the names of the 75 new members and 10 international members publicly at its annual meeting, held on October 15.

“I am very grateful to the members of the National Academy of Medicine for electing me,” said Dr. Sacco, an internationally renowned stroke neurologist and prolific researcher who serves as president of the American Academy of Neurology. He is also executive director of the Miller School’s Evelyn McKnight Brain Institute, director of UM’s Clinical & Translational Science Institute, and senior associate dean of Clinical & Translational Science. “It is an honor and privilege to join past honorees from UM and serve on the NAM recommendation panels that have had a tremendous impact on health care, education, and public health.”

Edward Abraham, M.D., executive vice president and CEO of UHealth, called Dr. Sacco “a luminary in his field. He is not only an outstanding clinician, but also an exceptional researcher who has leveraged team science to help us more clearly understand the impact of genetics, disparities, epidemiology, and prevention of stroke, which is a leading cause of disability. We congratulate him on this honor.”

Dr. Sacco serves as a professor of neurology, public health sciences, human genetics, and neurological surgery at the Miller School. He has published extensively in the areas of stroke prevention, treatment, risk factors, outcomes, disparities, and genetics. He is also chief of the neurology service at UM/Jackson Memorial Hospital.

“It means a great deal to me to have my team-based research in the fields of stroke epidemiology, prevention, genetics, and health care disparities recognized by the NAM,” said Dr. Sacco. “It is all about teamwork, and I am so grateful to the incredibly talented people I’ve had the great fortune of working with for many years.”

As a leading author of numerous evidence-based neurological and cardiac guidelines, Dr. Sacco has received many awards, including the World Stroke Organization Global Stroke Leadership Award, the Javits Award in Neuroscience from the National Institute of Neurological Disorders and Stroke, the William M. Feinberg Award for Excellence in Clinical Stroke from the American Heart Association (AHA), and the AHA Gold Heart Award. In addition, in 2010, Dr. Sacco was the first neurologist to serve as the national president of the AHA.

“Ralph is an exemplary clinical leader and researcher,” said Henri R. Ford, M.D., MHA, dean and chief academic officer of the Miller School of Medicine. “This honor recognizes his ability to lead teams in the pursuit of evidence-based science that can change the practice of medicine. Time and again, he has demonstrated new ways of approaching the prevention and treatment of stroke and advanced our knowledge on a broad scale. Our patients and students are all beneficiaries of his brilliance.”

Dr. Sacco is the principal investigator of the Northern Manhattan Study; the Florida-Puerto Rico Collaboration to Reduce Stroke Disparities; and American Stroke Association-Bugher Foundation Centers of Excellence in Stroke Collaborative Research. He is also co-investigator of multiple National Institutes of Health grants.

Besides President Frenk, Dr. Sacco joins four other University of Miami faculty as Academy members: former UM president and professor Donna E. Shalala; Margaret Pericak-Vance, Ph.D., the Dr. John T. Macdonald Foundation Professor of Human Genomics and director of the John P. Hussman Institute for Human Genomics; Diana D. Cardenas, M.D., MHA, professor emeritus; and Mary Bartlett Bunge, Ph.D., professor emeritus.

The **National Academy of Medicine**, established in 1970 as the Institute of Medicine, is an independent organization of eminent professionals from diverse fields including health and medicine; the natural, social, and behavioral sciences; and beyond. It serves alongside the National Academy of Sciences and the National Academy of Engineering as an adviser to the nation and the international community. Through its domestic and global initiatives, the NAM works to address critical issues in health, medicine, and related policy and inspire positive action across sectors. The NAM collaborates closely with its peer academies and other divisions within the National Academies of Sciences, Engineering, and Medicine.

23. Signature, date, and title of person submitting the report

Tatjana Rundek

January 15, 2019

Tatjana Rundek, M.D., Ph.D.
Scientific Director
Evelyn F. McKnight Brain Institute

Date



FACULTY AND TRAINEES



Faculty (Members)

Name	Center Role	Area of Expertise
Noam Alperin, PhD	Member	Radiology, Physics (MRI)
Kunjan R. Dave, PhD	Member	Neurobiology, Basic Science
David Della Morte, MD, PhD	Member	Neurology
Joyce Gomes-Osman, PhD, PT	Member	Physical Therapy, Neurology
Hong Jiang, MD, PhD	Member	Neuro-ophthalmology, Neurology
Bonnie Levin, PhD	Cognitive Core Director, Scientific Advisory Board Member	Neuropsychology
Tatjana Rundek, MD, PhD	Scientific Director, Scientific Advisory Board Member	Neurology, Epidemiology
Ralph L. Sacco, MD, MS	Executive Director, Scientific Advisory Board Member	Neurology, Epidemiology, Genetics
Xiaoyan Sun, MD, PhD	Educational Director, Scientific Advisory Board Member	Neuroscience, Biochemistry

Faculty (Collaborators)

Name	Center Role	Area of Expertise
Antoni Barrientos, PhD	Collaborator	Neuroscience, Genetics
Susan Blanton, PhD	Collaborator	Genetics
Scott Brown, PhD	Collaborator	Public Health
Christian Camargo, MD	Collaborator	Neurology
Elizabeth Crocco, MD	Collaborator	Psychiatry
Chuanhui Dong, PhD	Collaborator	Epidemiology, Biostatistics
Hannah Gardener, ScD	Collaborator	Epidemiology
David Loewenstein, PhD	Collaborator, Scientific Advisory Board Member	Neuropsychology
Katalina McInerney, PhD	Collaborator	Neuropsychology
Roger McIntosh, PhD	Collaborator	Psychology
Teshame Monteith, MD	Collaborator	Headache Science
Carlos Moraes, PhD	Collaborator	Neuroscience
Miguel Perez-Pinzon, PhD	Collaborator, Scientific Advisory Board Member	Neuroscience
Milena Pinto, PhD	Collaborator	Neuroscience
Alberto Ramos, MD	Collaborator	Neurology, Sleep Medicine
Ami P. Raval, PhD	Collaborator	Neuroscience, Epidemiology
Jianhua Wang, MD, PhD	Collaborator	Neuro-ophthalmology, Neurology

Trainees

Name	Center Role	Area of Expertise
Shatha Aldraiwiesh, PT	PhD Student	Physical Therapy
Nikhil Sebastian Banerjee	Graduate Practicum Student	Neuropsychology
Myriam Bourens, PhD	Associate Research Scientist	Neuroscience
Jabari-Ture Ghingo Brooks	Post-Bac Student	Neuroscience
Kyle Andrade-Bucknor	Undergrad Student	Pre-Med
Annelly Buré-Reyes, PhD*	Postdoctoral Fellow	Neuropsychology
Danylo Cabral, BS, PT	PhD Student	Physical Therapy/Cognition
Nicholas Cassidy	Undergrad Student	Neurology
Michelle Caunca, MD/PhD Student	Formal McKnight Trainee	Neurology
Austin Choi	PhD Student	Neurobiology
Charles Cohan, PhD	Postdoctoral Fellow	Neurology
Crizia Crespo, PhD	Postdoctoral Fellow	Neuropsychology
Samuel Del'Olio, BS	PhD Student	Pharmacology
Brett Doliner	MD Student	Neurology
Carolina Flores	Post-Bac Student	Physical Therapy
Wendy Gaztanaga	Trainee	Neuropsychology
Sarah Getz, PhD*	Postdoctoral Fellow	Neuropsychology
Alison Headley, MD	Resident	Neurology
Jason Hokenson	Undergrad Student	Physical Therapy
Sonya Kaur, PhD	Postdoctoral Fellow	Neuropsychology
Nathalie Khoury, BS	PhD Student	Neuroscience
Hyun-Jun Kim	PhD Student	Neuroscience
Kevin Koronowski, BS	MD/PhD Student	Neuroscience

Jonathan Landman, MD	Research Assistant	Neurology
Cril Larhssen	Undergrad Student	Physical Therapy
Diego Lasso	Undergrad Student	Biology
Suzanne Lippman	MD Student	Neurology
Priyanka Maiti, PhD	Post-Doctoral Trainee	Cell Biology
Ava Marsh	Undergrad Student	Biology
Michelle Miranda, PhD	Postdoctoral Fellow	Neuropsychology
Eva Nyvltova, PhD	Post-Doctoral Trainee	Biochemistry
Sofia Oluwole	MD/PhD Student	Neurology
Sabrina Pastore	Undergrad Student	Physical Therapy
Pujan Patel	Undergrad Student	Neuropsychology
Sonia Patel	Undergrad Student	Neuroscience
Maya Pinjala	Graduate Practicum Student	Neuropsychology
Andy Hinojo-Perez	Undergrad Student	Biology
Adele Raymo	Undergrad Student	Physical Therapy
Ashish Rehni, PhD	Postdoctoral Fellow	Neuroscience
Jordyn Rice, PT, DPT	DPT, PhD Student	Physical Therapy/Cognition
Joshua D. Rooks	Postdoctoral Fellow	Neuropsychology
Andrea L. Ruetenik	PhD Student	Neuroscience
Anita Seitas Dias Saporta, MD	McKnight Fellow	Neurology, Imaging
Sharnikha Saravanan	Undergrad Student	Neuroscience
Kasra Sarhadi	MD/MPH Student	Physical Therapy/Cognition
Marina Sarno, PhD*	Postdoctoral Fellow	Neuropsychology
Marc Schatz	MD Student	Neurology
Vibha Shukla, PhD	Postdoctoral Fellow	Neurology
Nikhil Sikha	Undergrad Student	Biology
Marialaura Simonetto, MD	Fellow	Neurology

Mitchell Slugh, PhD	Postdoctoral Fellow	Neuropsychology
Hesley Solano	Undergrad Student	Neuroscience
Chantel Sorochuk	Graduate Practicum Student	Neuropsychology
Courtney Sparger	Undergrad Student	Neuroscience
Holly Stradecki, MS	MD/PhD Student	Neuroscience
Ni (Sunny) Sun-Suslow	Graduate Practicum Student	Neuropsychology
Alba Timon, PhD	Postdoctoral Trainee	Biotechnology
Kristopher Wolford, MPH	Undergrad Student	Public Health
Jing Xu, BS	PhD Student	Neuroscience
Michelle Zambik	Post-Bac Student	Physical Therapy, Cognition
Rui Zeng	PhD Student	Neuroscience
Hui Zhong, BS	PhD Student	Biochemistry

*Became University of Miami Department of Neurology Faculty this year.

FINANCIAL AND BUDGET SHEETS



Evelyn F. McKnight Brain Institute's Endowments
at the Miller School of Medicine
Market Value Analysis
05/31/2018

2002 Gift & Match

McKnight Contribution	\$5,000,000
UM Match	5,050,913
Transfers from Other University Funds	1,362,153
Investment Return	6,358,326
Distributions for Spending	(5,568,164)
05/31/18 Endowment Balance	<u>\$12,203,228</u>
Unmatched Balance	<u>\$0</u>

2014 Gift & Match

McKnight Contribution	\$2,000,000
UM Match	2,000,000
Transfers from Other University Funds	0
Investment Return	871,009
Distributions for Spending	(388,336)
05/31/18 Endowment Balance	<u>\$4,482,673</u>
McKnight Foundation Pledge Balance	<u>\$0</u>

University of Miami – All Managed Assets
Performance Periods Ending: May 31, 2018

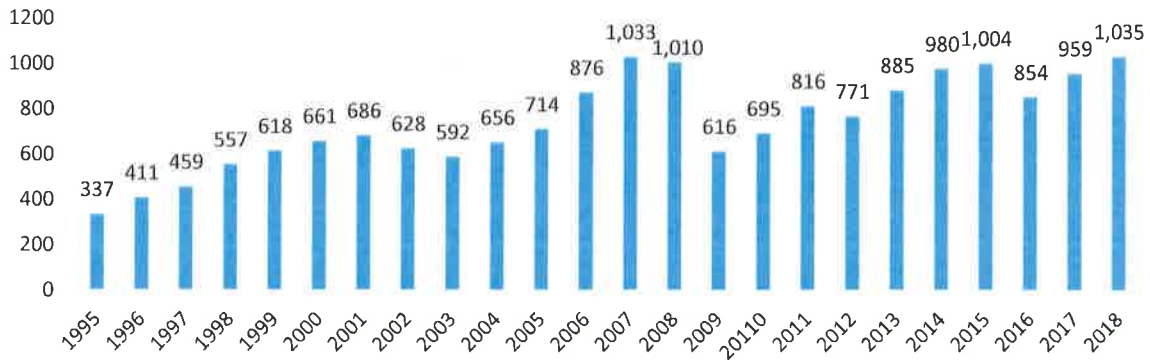
Total Returns (Periods Greater Than 1 Year are Annualized)						
Growth Pool	Inception	1 Year (%)	3 Year (%)	5 Year (%)	7 Year (%)	10 Year (%)
Growth Pool Total Composite*	12/31/1990		9.4	5.9	6.8	5.0
Growth Pool Market Benchmark**	12/31/1990		9.7	6.7	7.8	5.3
Value (+/-)			-0.3	-0.8	-1.0	-0.3

15 Year Growth Pool Risk/Return as of May 31, 2018		
Growth Pool	15 Year Return	15 Year Standard Deviation
Growth Pool Total Composite	6.9	9.4
Growth Pool Market Benchmark	7.0	10.5

*Net of fee returns

** A weighted average return derived by applying the target policy weights of each asset class to the performance of the asset class benchmarks

Growth of Assets (\$ Millions)



University of Miami Manager Structure – Market Values and Allocations

As of May 31, 2018

Manager	Asset Class	Market Value (\$)	Growth Pool
			% of Total Fund
Vanguard Institutional Index (10/31/14)	US Large Cap Core Equity	154,184,203	14.9%
Adage Capital Mgmt (6/30/04)	US Large Cap Core Equity	85,059,745	8.2%
Columbia Dividend Income (2/2/17)	US Large Cap Core Equity	17,188,516	1.7%
Loomis Large Cap Growth (2/2/17)	US Large Cap Growth Equity	19,455,745	1.9%
MFS Large Cap Value (2/2/17)	US Large Cap Value Equity	16,268,461	1.6%
GAMCO Investors (01/01/91)	US Midcap Value Equity	22,863,283	2.2%
Janus Enterprise Mid Cap Growth (2/2/17)	US Midcap Growth Equity	17,087,285	1.7%
Vanguard Mid Cap (2/2/17)	US Midcap Core Equity	25,867,908	2.5%
Apex Capital (2/2/17)	US Small Cap Growth Equity	21,230,713	2.1%
Hillcrest (2/2/17)	US Small Cap Value Equity	18,348,185	1.8%
Vanguard Small Cap (2/2/17)	US Small Cap Equity	21,115,085	2.0%
Silchester International (6/30/05)	Non-US DM/EM Value Equity	65,936,890	6.4%
Vanguard Developed Markets (2/2/17)	Non-US DM Core Equity	62,611,249	6.1%
Schroders International Growth (2/2/17)	Non-US DM Core Equity	26,782,120	2.6%
Delaware Emerging Markets Fund (2/2/17)	Non-US EM Equity	11,165,522	1.1%
Vanguard FTSE Emerging Markets (2/2/17)	Non-US EM Equity	49,812,740	4.8%
WGI Emerging Markets (10/31/08)	Non-US EM Equity	30,198,398	2.9%
Highclere Emerging Markets SMD (7/31/14)	Non-US EM Equity	17,489,850	1.7%
Davidson Kempner (10/01/93)	Event Arbitrage	24,091,070	2.3%
Watershed Capital (1/01/08)	Event Arbitrage	328,483	0.0%
Regiment Capital (6/30/07)	High Yield Bonds	1,050,775	0.1%
Viking Global Equities III (11/30/10)	Equity Long/Short	21,911,080	2.1%
Renaissance Institutional (8/31/17)	Equity Long/Short	21,163,585	2.0%
Glenview Capital Management (2/01/06)	Equity Long/Short	247,654	0.0%
AQR Delta XN Offshore (1/31/17)	Multi-Strategy	17,240,837	1.7%
AQR Risk Parity (2/21/17)	Multi-Strategy	55,917,292	5.4%
AQR Style Premia (12/14/16)	Multi-Strategy	18,672,159	1.8%

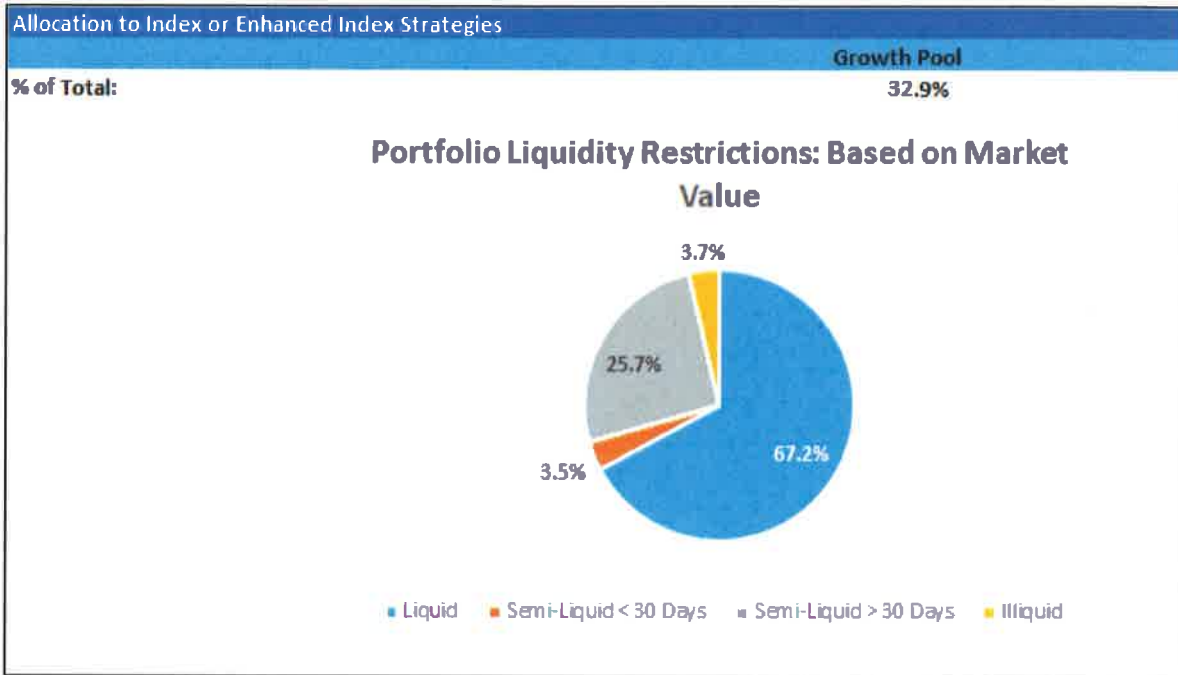
University of Miami Manager Structure – Market Values and Allocations (continued)

As of May 31, 2018

TIFF Partners IV (01/31/01)	Private Equity	1,632,860	0.2%
TIFF Partners V (04/30/04)	Private Equity	278,369	0.0%
TIFF Partners 2006 (04/30/06)	Private Equity	746,594	0.1%
TIFF Partners 2007 (01/31/07)	Private Equity	2,003,620	0.2%
TIFF Partners 2008 (01/31/08)	Private Equity	7,954,995	0.8%
OCM Principal Opportunities IV (12/31/06)	Private Equity	324,992	0.0%
Denham Commodity Fund V (6/30/08)	Private Equity	1,889,214	0.2%
Clayton, Dubilier & Rice Fund IX (5/31/2014)	Private Equity	7,758,507	0.7%
Carlyle Strategic IV (11/30/16)	Private Equity	1,516,083	0.1%
KKR Americas XII (9/30/16)	Private Equity	1,379,709	0.1%
HIG Advantage Buyout (4/30/18)	Private Equity	30,477	0.0%
WCP Real Estate Strategies Fund (7/31/06)	Private Real Assets	246,285	0.0%
Parmenter Realty Fund III (04/30/06)	Private Real Assets	1	0.0%
WCP Real Estate Fund I (7/31/06)	Private Real Assets	1,348,803	0.1%
WCP Real Estate Fund II (11/30/08)	Private Real Assets	4,590	0.0%
Metropolitan Real Estate Fund (9/30/06)	Private Real Assets	370,667	0.0%
SRI Nine REIT (3/31/08)	Private Real Assets	1,057,264	0.1%
LBA Realty IV (10/31/09)	Private Real Assets	1,658,351	0.2%
Warburg Energy (5/31/14)	Private Real Assets	6,083,678	0.6%
Vanguard Total Bond Fd (10/30/14)	Aggregate Bonds	26,140,060	2.5%
Guggenheim US Bank Loans (2/2/17)	Bank Loans	54,854,648	5.3%
PIMCO Income Fund (7/24/17)	Aggregate Bonds	25,585,800	2.5%
Lord Abbett Limited Maturity (2/2/17)	Short Duration Bonds	17,575,392	1.7%
Prudential US High Yield (2/2/17)	High Yield Bonds	18,565,870	1.8%
Cash		12,234,838	1.2%
Total Managed Assets		1,034,530,500	100.0%

University of Miami Manager Structure – Market Values and Allocations (continued)

As of May 31, 2018



University of Miami – Growth Pool
Inception to Date Performance vs. Relevant Benchmark(s)
Periods Ending - May 31, 2018

Net of Fees

Total Returns (%) - Annualized if Greater than 1 Year			
Large/Mid/All Cap Equity	ROR	Value Added (+/-)	Years
Vanguard Institutional Index (10/31/14)	10.54	-0.75	3.6
S&P 500	11.29		3.6
Adage Capital Mgmt (6/30/04)	11.56	2.77	13.9
S&P 500	8.79		13.9
GAMCO Investors (01/01/91)	12.38	1.76	27.4
Russell 3000 Value	10.62		27.4
Columbia Dividend Income (2/2/17)	13.36	5.38	1.3
Russell 1000 Value	7.98		1.3
Loomis Large Cap Growth (2/2/17)	24.92	0.52	1.3
Russell 1000 Growth	24.40		1.3
MFS Large Cap Value (2/2/17)	8.71	0.73	1.3
Russell 1000 Value	7.98		1.3
Janus Enterprise Mid Cap Growth (2/2/17)	22.95	3.01	1.3
Russell Midcap Growth	19.94		1.3
Vanguard Mid Cap (2/2/17)	13.02	-0.12	1.3
CRSP MidCap Index	13.14		1.3
Small Cap Equity			
Apex Capital (2/2/17)	15.72	-7.10	1.3
Russell 2000 Growth	22.82		1.3
Hillcrest (2/2/17)	3.64	-6.91	1.3
Russell 2000 Value	10.55		1.3
Vanguard Small Cap (2/2/17)	15.25	0.21	1.3
CRSP US Small Cap TR Index	15.04		1.3
Developed International Equity			
Silchester International (6/30/05)	8.84	4.51	12.9
MSCI EAFE Value ND	4.33		12.9
Vanguard Developed Markets (10/31/2014)	5.97	-0.40	3.6
FTSE Dev All Cap ex US	6.37		3.6
Schroders International Growth (2/2/17)	16.03	1.74	1.3
MSCI EAFE ND	14.29		1.3

University of Miami – Growth Pool

Inception to Date Performance vs. Relevant Benchmark(s) (continued)

Periods Ending - May 31, 2018

Net of Fees

Emerging Markets			
Delaware Emerging Markets Fund (2/2/17)	17.72	-1.31	1.3
MSCI Emerging Markets ND	19.03		1.3
Vanguard FTSE Emerging Markets (2/2/17)	15.18	-3.85	1.3
MSCI Emerging Markets ND	19.03		1.3
WGI Emerging Markets (10/31/08)	12.04	7.99	9.6
MSCI Emerging Markets ND	4.05		9.6
Highclere Emerging Markets SMID (7/31/14)	0.38	-6.85	3.8
CG S&P EPAC BTWN 2B&10B USD net	7.23		3.8
Credit Strategies			
Davidson Kempner (10/01/93)	8.95	-0.31	24.7
HFR Event-Driven	9.26		24.7
Equity Long/Short			
Viking Global Equities III (11/30/10)	10.20	0.20	7.5
MSCI World Index	10.00		7.5
Renaissance Institutional (8/31/17)	5.82	-2.07	0.8
MSCI ACWI ND	7.89		0.8
Multi-Strategy			
AQR Delta XN Offshore (1/31/17)	-3.05	-8.96	1.3
HFRI Fund of Funds Composite	5.91		1.3
AQR Risk Parity (2/21/17)	7.36		1.3
60 MSCI AC WORLD/40 BB Barclays U.S. Aggregate	8.40		1.3
AQR Style Premia (12/14/16)	4.54	3.49	1.4
ICE ML 3M US Treasury Bill	1.05		1.4
Fixed Income			
Vanguard Total Bond Fd (10/30/14)	1.53	-0.37	3.6
BB Barclays U.S. Aggregate	1.9		3.6
Pimco Income Fund (7/24/17)	1.86	2.67	0.8
BB Barclays U.S. Aggregate	-0.81		0.8
Guggenheim US Bank Loans (2/2/17)	3.52	-0.75	1.3
S&P/LSTA Leveraged Loan Index	4.27		1.3
Lord Abbett Limited Maturity (2/2/17)	0.33	0.06	1.3
BB Barclays U.S. Corporate 1-3 Year	0.27		1.3
Prudential US High Yield (2/2/17)	4.59	0.46	1.3
BB Barclays U.S. Corporate High Yield	4.13		1.3

McKnight - FY19 Budget For Annual Report
June 1, 2018 - May 31, 2019

	Budget as submitted to McKnight	Actual as of December 31, 2018	Projected at Year End (May 2019)
Revenue	732,597.06	425,552.45	732,597.06
Personnel			
Faculty			
<i>Role in Project</i>	<i>Effort</i>		
Tatjana Rundek, MD	Scientific Director	30%	
Ralph Sacco, MD	Executive Director	5%	
Xiaoyan Sun, MD	Educational Director	25%	
Bonnie Levin, PhD	Neuropsychology	20%	
Kunjan Dave, PhD	Neurology - Basic Science	6%	
Noam Alperin, MD	Radiology	10%	
Jiang Hong, MD	Neurologist	5%	
Christian Camargo, MD	Neurology	5%	
David Della Morte, MD PhD	Neurology (part time)	90%	
Subtotal Faculty Salary and CFB	298,266.61	215,243.85	332,752.53
Staff			
<i>Role in Project</i>	<i>Effort</i>		
Stacy Merritt	McKnight Project Manager	75%	
Digna Cabral - Main	Neurology	7%	
Marti Flothmann (starting April 2019)	Clinical Research Coordinator	80%	
Isabel Saul	Research Support Specialist-Basic Science	15%	
Anita Saporta	Post Doc Associate	7%	
Susan Fox Rosellini (starting Jan 2019)	Neurology	75%	
Marina Lucia Sarno	Neuropsychology	25%	
Joshua Daniel Rooks	Neuropsychology	30%	
Annelly Bure-Reyes	Neuropsychology	25%	
Sarah J Getz	Neuropsychology	25%	
Michelle Miranda	Neuropsychology	30%	
Mitchell R Slugh	Neuropsychology	30%	
Sonya Sarjit Kaur	Neuropsychology	30%	
Subtotal Staff and CFB	354,389.69	169,826.57	319,903.76
Total Personnel	652,656.30	385,070.42	652,656.30
Non Personnel Expenses			
Communications	2,000.00	1,297.80	2,224.80
Internal UM Services Provided/Animal purchasing/Supplies/Chemicals	17000	2578.97	17000
Conference,Registration,Dues,Memberships,Travel,Postage,Freight,Printing,Publishing, etc.	35,940.76	13,375.26	35,940.76
Two Pilot awards	20,000.00	20,000.00	20,000.00
Other	5,000.00	3,230.00	4,775.20
Total Non Personnel Expenses	79,940.76	40,482.03	79,940.76
Grand Total Expenses	732,597.06	425,552.45	732,597.06

University of Miami FY20 - Budget Proposal
June 1, 2019 - May 31, 2020

			Budget
			Summary
Revenue (based on FY19 endowment)			708,327.00
Personnel			
Faculty	Role in Project	Effort	
Tatjana Rundek, MD	Scientific Director	30%	
Ralph Sacco, MD	Executive Director	5%	
Xiaojan Sun, MD	Educational Director	20%	
TBA Cognitive Chief	Research for Age-related Cognitive Disorder	20%	
Bonnie Levin, PhD	Neuropsychology	20%	
Kunjan Dave	Neurology - Basic Science	5%	
Chuanhui Dong, PhD	Neurology -Statistician	5%	
Noam Alperin, MD	Radiology	10%	
Jiang Hong, MD	Neurologist	5%	
Subtotal Faculty Salary and CFB			252,593.67
Staff (2% increase added)	Role in Project	Effort	
Stacy Merritt	McKnight Project Manager	100%	
Sang Lee	Radiology	10%	
Digna Cabral	Neurology	7%	
Marti Flothmann	Clinical Research Coordinator	70%	
MD-PhD Student	MD/PhD Student - Neuro	100%	
TBA volunteer	Bugher volunteer	50%	
Isabel Saul	Research Support Specialist-Basic Science	15%	
Anita Saporta	Post Doctoral Associate	50%	
Susan Fox Rosellini	Neurology	75%	
NeuroPsych Post Doc TBA 1	Neuropsychology	100%	
NeuroPsych Post Doc TBA 2	Neuropsychology	25%	
NeuroPsych Post Doc TBA 3	Neuropsychology	25%	
NeuroPsych Post Doc TBA 4	Neuropsychology	25%	
NeuroPsych Post Doc TBA 5	Neuropsychology	25%	
Subtotal Staff and CFB			377,215.86
Total Personnel			629,809.53
Non Personnel Expenses			
Communications			2,500.00
Internal UM Services Provided/Animal purchasing/Supplies/Chemicals			6,000.00
Conference,Registration,Dues,Memberships,Travel,Postage,Freight,Printing,Publishing,Speakers,etc.			38,844.97
Two Pilot awards			15,000.00
Other			5,000.00
Total Non Personnel Expenses			67,344.97
Grand Total Expenses			697,154.50

Stroke Incidence and Risk Factors in a Tri-ethnic Region

Source: NIH, NINDS (R01 NS029993)

Principal Investigator: **Ralph Sacco**

2018 Budget: \$1,731,055

University of Miami ASA/Bugher Foundation Center for Excellence in Stroke Collaborative Research

Source: American Heart Association Bugher Foundation

Principal Investigator: **Ralph Sacco**

2018 Budget: \$604,000

Miami Clinical and Translational Science Institute

Source: NIH//NCRR/NIMHD

Principal Investigator: **Ralph Sacco**

2018 Budget: \$4,304,587

Family Study of Stroke Risk and Carotid Atherosclerosis

Source: NIH/NINDS R01 NS040807

Principal Investigators: **Tatjana Rundek**

2018 Budget: \$632,874

Disparities in Transition of Care after Acute Stroke Hospitalization: The Transition of Care Stroke Disparity Study (TCSD-S)

Source: NIN/NIHHD MD R01MD012467

Principal Investigators: **Ralph Sacco, Tatjana Rundek,** and Jose Romano

2018 Budget: \$724,673

Disparities in Care Delivery in Patients with Atrial Fibrillation: FLiPER-AF Study

Source: ARISTA-USA CV185-564, Pfizer/BMS

Principal Investigators: **Tatjana Rundek**

2018 Budget: \$199,428

University of Miami Memory Disorder Clinic

Source: State of Florida, Division of Elder Affairs

Co-Investigator: **Xiaoyan Sun**

2018 Budget: \$222,801

The Effects of Cannabinoids on TBI

Source: Scythian Biosciences

Co-Investigator: **Bonnie Levin**

2018 Budget: \$867,351

Red Blood Cell Microparticles (RMPs) to Reduce Bleeding Following Hemorrhagic Stroke

Source: NIH, NINDS (R2121 NS094896)

Principal Investigator: **Kunjan Dave**

2018 Budget: \$412,594

Ischemic Preconditioning: Mechanisms of Neuroprotection

Source: NIH, NINDS (R01NS034773)

Principal Investigator: **Miguel Perez-Pinzon**

2018 Budget: \$335,781

Ischemic Preconditioning: Mechanisms of Neuroprotection/Diversity Supplement

Source: NIH, NINDS (R01NS034773-18S1)

Principal Investigator: **Miguel Perez-Pinzon**

2018 Budget: \$70,167

Decellularized Extracellular Matrix Biomaterials as Therapy to Ameliorate Cerebral Ischemia Damage

Source: NIH, NINDS (R21 NS098896)

Principal Investigator: **Miguel Perez-Pinzon**

2018 Budget: \$163,438

Metabolic Master Regulators for Ischemic Neuroprotection

Source: NIH/NINDS

Site Principal Investigator: **Miguel Perez-Pinzon**

2018 Budget: \$335,781

Neuroprotective mechanisms regulating Nmnats by PKCε preconditioning

Source: AHA, Greater Southeast Affiliate Winter 2018 Predoctoral Fellowship (19PRE34400074)

Principal Investigator: **Jing Xu** (PhD student in **Perez-Pinzon** lab)

2018 Budget: \$26,844

ORCATECH Collaborative Aging (in Place) Research Using Technology CART

Source: NIH/NIA (1U2CAG054397-03)

Site PI: **David Loewenstein**

2018 Budget: \$61,942

A non-pharmacological intervention for patients with Alzheimer's disease and family caregivers

Source: NIH/NIA (1 R01 AG054009)

Principal Investigator: **David Loewenstein**

2018 Budget: \$395,951

A Personalized Health Behavior System to Promote Health and Well-Being in Older Adults

Source: NIH (1 R01 AG053163)

Principal Investigator: **David Jimenez**

2018 Budget: \$316,599

Center for Research and Education for Aging and Technology Enhancement (CREATE IV)

Source: NIA/NIH (5P01AG0172)

Principal Investigator: **David Loewenstein/Joseph Sharit**

2018 Budget: \$748,929

Novel Detection of Early Cognitive and Functional Impairment in the Elderly

Co-Investigator: **David Loewenstein**

Source: NIH (1R01AG047649)

2018 Budget: \$535,901

A Tailored Technology Intervention for Diverse Family Caregivers of AD Patients

Source: NINR/NIH (1R01NR014434)

Principal Investigator: **David Loewenstein**

2018 Budget: N/A (NCE)

The Role of Retinal Microvascular Impairment on Neurodegeneration

Source: National Multiple Sclerosis Society

Principal Investigator: **Hong Jiang**

2018 Budget: N/A (NCE)

Imaging of Conjunctival Microvasculature During Contact Lens Wear

Source: Johnson and Johnson contact lens study

Principal Investigator: **Hong Jiang**

2018 Budget: N/A (NCE)

Exploring Sleep in Neurocognitive Aging and Alzheimer's Research (eSANAR)

Source: NIH/NIA (1R21AG056952)

Principal Investigator: **Alberto Ramos**

2018 Budget: \$196,211

Elucidating the link between sleep apnea and dementia using multimodal MRI and cognitive testing.

Source: Scientific Advisory Committee Pilot Study Award, Miller School of Medicine, University of Miami

Principal Investigator: **Alberto Ramos**

2018 Budget: \$42,847

Arrhythmia Detection In Obstructive Sleep apnea (ADIOS)

Source: Boehringer Ingelheim

Principal Investigator: **Seemant Chaturvedi/Alberto Ramos**

2018 Budget: \$47,142

***NEW SCIENTIFIC
ADVISORY BOARD
MEMBERS
BIOSKETCHES***



BIOGRAPHICAL SKETCH
DO NOT EXCEED FIVE PAGES.

NAME: Carrasquillo, Olveen

eRA COMMONS USER NAME (credential, e.g., agency login): Carraso

POSITION TITLE: Professor of Medicine & Public Health Sciences

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Sophie Davis School of Biomed/City College, NY	B.S	06/1989	Bio-Medicine
New York University School of Medicine, NY, NY	M.D.	06/1991	Medicine
Columbia University, NY	Residency	06/1994	Internal Medicine
Harvard School of Public Health, Boston, MA	MPH	05/1997	Clinical Effectiveness
Cambridge Hospital / Harvard Medical School, MA	Fellowship	05/1997	NRSA Research Fellowship

A. Personal Statement

I am pleased to serve as a consultant on this project whose objective is to determine the efficacy of two approaches to improving Physical Activity in Latino adults with one or more CVD risk factors, a culturally and individually tailored App and motivational interviewing (MI). As Division Chief of General Internal Medicine, I oversee a clinical, teaching and research enterprise of 51 full time faculty including clinical operations that involve over 130,000 annual patient visits. As a researcher, my interests have long been in minority health and health disparities with a focus on community based research. I have over twenty years of experience leading NIH funded clinical and community based research projects and to date I have been awarded over \$60 million of external support for my research projects as PI, Multiple PI and Core lead of program project or center grants. At present most of my work involves community based RCTs in various disease areas including diabetes, heart disease, stroke, HIV, and cancer. As examples, were two RCTs among Latinos diabetics testing multi-modal Community Health Worker Interventions to improve blood pressure, cholesterol and glycemic control. I also have extensive experience mentoring junior faculty and trainees in these areas. In addition, I am also involved in several regional research consortia including the One Florida Clinical Research Consortia partially sponsored by PCORNet (all Florida academic health centers), Center on Precision Medicine and Disparities (Vanderbilt, Morehouse, UM, I direct the consortium Core), the Florida-Puerto Rico Stroke Collaboration, and most recently the South East Enrollment Center for the Precision Medicine Health Provider Organization (UM, UF, Emory, Morehouse). My combined experience as clinician, director of several large primary care practices, successfully conducting several large RCTs among under-served populations, and role in various regional networks are important strengths I bring to this project. Recent publications highlighting these include:

Recent publications highlighting my work in HPV self-sampling include:

1. **Carrasquillo O**, Lebron C, Alonzo Y, Li H, Chang A, Kenya S. A Randomized Trial of a Community Health Worker Intervention among Latinos with Poorly Controlled Diabetes: The Miami Healthy Heart Initiative. JAMA Int Med 2017;77(7):948-954 PMID: 28459925
2. **Carrasquillo O**, Young B, Dang S, Fontan O, Ferras N, Romano JG, Dong C, Kenya S. Hispanic Secondary Stroke Prevention Initiative Design: Study Protocol and Rationale for a Randomized Controlled Trial. JMIR research protocols. 2018;7(10):e11083.
3. Chang A, Patberg E, Cueto V, Li H, Singh B, Kenya S, Alonzo Y, **Carrasquillo O**. Community Health Workers, Access to Care, and Service Utilization among Florida Latinos: A Randomized Controlled Trial. Am

J Public Health. 2018 Sep;108(9):1249-1251. doi: 10.2105/AJPH.2018.304542. Epub 2018 Jul 19. PMID:30024805

4. Palmas W, Findley SE, Mejia M, Batista M, Teresi J, Kong J, Silver S, Fleck EM, Luchsinger JA, **Carrasquillo O**. Results of the Northern Manhattan Diabetes Community Outreach Project: A Randomized Trial Studying a Community Health Worker Intervention to Improve Diabetes Care in Hispanic Adults. *Diabetes Care*. 2014 Feb 4. PMID: 24496805
5. Palacio AM, Uribe C, Hazel-Fernandez L, Li H, Tamariz LJ, Garay SD, Carrasquillo O. Can phone-based motivational interviewing improve medication adherence to antiplatelet medications after a coronary stent among racial minorities? A randomized trial. *J Gen Intern Med*. 2015 Apr;30(4):469-75. PMID: 25500787

B. Positions and Honors

Positions and Employment

1991-1994 Residency in Internal Medicine, Columbia-Presbyterian Hospital, New York, NY.

1994-1995 Instructor in Clinical Medicine, Columbia University College of Physicians and Surgeons, NY

1995-1997 Clinical Fellow, Harvard Gen. Medicine Fellowship and Faculty Develop. Program, Boston, MA

1997-2009 Assistant → Associate Prof. of Medicine, Health Policy & Community Partnerships, Columbia University

Associate Professor (tenure) → Professor of Medicine & Public Health, University of Miami, School of Medicine

2009- Chief, Division of General Medicine, University of Miami Miller School of Medicine

2015- Division Head, Health Services Research & Policy, Department Public Health Sciences, Miller School of Medicine

2015- Interim Division Head, Division of Geriatrics and Palliative Medicine

Other Experience and Professional Memberships

1995- Society Gen Int. Medicine, abstract/workshop/section chairs, past president Mid Atlantic Chapter

1998-2005 National Hispanic Medical Association, National Advisory Committee

1999-2009 Co-Director then Director, General Medicine Fellowship Program, Columbia University

2002-2005 HRSA Study Sections- Faculty Dev. Prim Care/ Acad. Units Prim Care

2003-2009 Director, Columbia University Center of Excellence for Health Disparities Research

2003- NIMHD/ NIH Project Export, R01, LRP, Various Special Emphasis Panel Study Sections

2004- Hispanic Health Professions Serving Schools Adv, (Columbia U. rep 04-09), U Miami rep (2010-)

2004-2015 AHRQ, Health Services Research Study Section (04-09) then various special emphasis panels

2008, 09, 17 NCCR/NCATS Various Special Emphasis Panels including RCMI and CTSA Study Sections

2008-2013 Advisory Committee on Minority Health (ACMH), Department Health and Human Services

2009- Deputy Editor, *Journal Of General Internal Medicine*

2012- Advisory Board, Miami-Dade Area Health Education Center

2014- Board of Directors, Health Council of South Florida

2014- Editor, *Journal General Internal Medicine Suppl. Issue, Patient Centered Medical Home (VA)*

2015- Dissemination and Implementation Study Section (DIRH), NIH (6 year appt)

Honors

1989 Summa Cum Laude, City College

1999 Robert Wood Johnson Generalist Physician Faculty Scholar

2002 Society Of General Internal Medicine, President Mid. Atlantic Chapter

2003 Distinguished Alumni, Sophie Davis School of Bio-Medical Education

2006 Clinician-Investigator of the Year, Mid-Atlantic Chapter Society General Internal Medicine

2007 Helen Rodriguez-Trias Advocacy Award, NYU School of Medicine

2012 Herbert Nickens Award (Minority Advocacy) Society General Internal Medicine

2014 Top 50 Diverse Executive Leaders, DiversityMBA Magazine.

C. Contribution to Science

1. As a junior faculty, my early research focused on access to care by minorities and focused primarily around issues related to health insurance status. My work was one of the first to describe in detail the health insurance crisis among Latino populations. Examples of this work include:
 - a. **Carrasquillo O**, Carrasquillo A, Shea S. Health insurance coverage of immigrants living in the United States: Differences by citizenship status and country of origin. *Am J Public Health* 2000;90:917-923.
 - b. **Carrasquillo O**, Himmelstein DU, Woolhandler S, Bor D. Private employer's role in providing health insurance: A reappraisal. *N Engl J Med* 1999;340:109-114
 - c. **Carrasquillo O**, Brennan TA, Orav EJ, Burstin HR. The impact of language barriers on patient satisfaction. *J Gen Int Med* 1999;14:82-87.
 - d. Shah. S, **Carrasquillo O**. Twelve Year Trends in Latino Health Insurance Coverage: Analysis by Latino Sub-group and Immigration Status. *Health Affairs* 2006;25:1612-19.
2. Aside from CVD I have also led RCTs in other areas.
 - a. **Carrasquillo O**, Carrasquillo O, Seay J, Amofah A, Pierre L, Alonzo Y, McCann S, Gonzalez M, Trevil D, Koru-Sengul T, Kobetz E. HPV Self-Sampling for Cervical Cancer Screening Among Ethnic Minority Women in South Florida: a Randomized Trial. *J Gen Intern Med*. 2018 Mar 28. doi: 10.1007/s11606-018-4404-z
 - b. Kobetz E, Seay J, Koru-Sengul T, Bispo JB, Trevil D, Gonzalez M, Brickman A, **Carrasquillo O**. A randomized trial of mailed HPV self-sampling for cervical cancer screening among ethnic minority women in South Florida. *Cancer Causes Control*. 2018 Jul 11. doi: 10.1007/s10552-018-1055-7.
 - c. Kenya S, Jones J, Arheart K, Chida N, Baer R, Powell A, Symes S, Hunte T, Monroe A, Kobetz E. **Carrasquillo O**. Using Community Health Workers to Improve Clinical Outcomes among People Living with HIV: A Randomized Controlled Trial. *AIDS Behav*. 2013 Nov;17(9):2927-34
3. My more recent work also includes being part of large research networks and partnerships:
 - a. Shenkman E, Hurt M, Hogan W, **Carrasquillo O**, Smith S, Brickman A, Nelson D. OneFlorida Clinical Research Consortium: Linking a Clinical and Translational Science Institute With a Community-Based Distributive Medical Education Model. *Acad Med*. 2018 Mar;93(3):451-455. doi: 10.1097/ACM.0000000000002029. PMID: 29045273
 - b. Sacco RL, Gardener H, Wang K, Dong C, Ciliberti-Vargas MA, Gutierrez CM, Asdaghi N, Burgin WS, **Carrasquillo O**, Garcia-Rivera EJ, Nobo U, Oluwole S, Rose DZ, Waters MF, Zevallos JC, Robichaux M, Waddy SP, Romano JG, Rundek T. Racial-Ethnic Disparities in Acute Stroke Care in the Florida-Puerto Rico Collaboration to Reduce Stroke Disparities Study. FL-PR CRESD Investigators and Collaborators. *J Am Heart Assoc*. 2017 Feb 14;6(2). PMID: 28196814

Complete List of Published Work at NCBI MyBibliography:

<http://www.ncbi.nlm.nih.gov/sites/myncbi/olveen.carrasquillo.1/bibliography/46374829/public/?sort=date&direction=ascending>

D. Active Research Support

U01 MD010614 (Carrasquillo PI) 05/19/16 – 12/31/20
NIH/NIMHD Increasing Uptake of Evidence Based Screening Services through a CHW =program:
This study will test a CHW-led multi-modality strategy towards the early detection and/or prevention of Human Immunodeficiency Virus (HIV); Hepatitis C Virus (HCV); colorectal cancer (CRC) and cervical cancer.

R01 MD009164 Carrasquillo (PI) 07/14/14-03/31/19
NCMHD (NIH), Hispanic Secondary Stroke Prevention Initiative
The major goal of this RCT project is to reduce the risk for a recurrent stroke among Latinos at high risk for a second and potentially much debilitating stroke.

Grant # 7239-UMiami Carrasquillo (PI) 10/01/17-09/30/19
PCORI (Eugene Washington Engagement Award Program)
National Partnership Training CHWs in PCOR

1OT2OD025285 Carrasquillo (PI, mult. PI) 8/26/17-5/31/23
SouthEast Enrollment Center (SEEC)
NIH Office of the Director.
The Goal of this project is to lead a consortium involving Emory, Morehouse, University of Florida and UM towards serving as an enrollment site for the SouthEast US as part of the ALL of US/ Precision Medicine Initiative.

U54 RR031279-01A1 (Sacco PI) 04/01/12-03/31/22
NCATS Miami Clinical Translation Science Institute
The overall theme of the Miami CTSI is "Culturalized Health Sciences for the health of South Florida" with an emphasis on health disparities and health issues that disproportionately impact minorities
Role: Co-Director of Community Engagement and Diversity Core

U54 MD010722 (PIs Wilkins, Cox, Lima, Weiss) 05/19/16 – 03/31/21
NIH/NIHMD Center of Excellence in Precision Medicine and Population Health
The major goals of this application is to provide a diverse group of researchers with the infrastructure and resources to develop collaborative research teams with the aims to develop novel methods and translate precision medicine discoveries to improve health outcomes of racial and ethnic minorities, specifically among African Americans and Latinos. Role: Consortium Core PI

R01 CA183612 (Kobetz PI) 05/14/14-04/30/18
NCI Addressing Cervical Cancer Disparities in South Florida
The major goal of this project is to address cervical cancer disparities affecting racial/ethnic minorities, recent immigrants and low-income individuals, through a Community-based Participatory Research.
Role: Investigator

1600463062 (Shenkman, PI) 10/01/16 – 09/30/22
PCORI/PCORNet The OneFlorida Clinical Research Consortium
The major goals of this project are to create a learning network for the state, in which lessons from research and care in diverse clinical settings are systematically captured and translated back into improved health, health care and health policy for Floridians.
Role: Co-Director, Community Engagement

Recently Completed Research Support

Grant # D55HP23209 Carrasquillo (PI) 10/01/11-09/30/16
HRSA Primary Care Research Faculty Development Program
Primary care research fellowship program

Grant # 2BT02 Carrasquillo (PI) 07/01/11-6/30/15
Florida Dept Health (Bank Head Coley), Team Science PO1 Like Grant
South Florida Center for Reducing Colorectal Cancer Disparities Team Science grant
Includes 3 sub-projects admin core and community engagement Core.

Grant # R01 HL083857 Carrasquillo (PI) 09/01/08-06/30/14
NHLBI (NIH), Miami Healthy Heart Initiative
RCT of 400 diabetics patients looking at impact of Community Health Workers on diabetes outcomes.

KB16 (Shenkamn PI, Univ FI) 07/30/14-06/30/17
FL Dept of Health: BankHead Program OneFlorida CCA: Smoking Cessation Trail
The goal of this project is to focus on enhancing the infrastructure available to conduct tobacco- related cancer and CVD pragmatic clinical trials in primary care settings and increase physician capacity to follow evidence-based guidelines for tobacco screening and brief interventions.
Role: UM site PI

U54 CA153705 Carrasquillo (PI, mult) 09/01/10-08/30/17
NCI / South Florida Center to Reduce Cancer Disparities
NCI Community Networks Program: NCI Center Grant
Establishes a Center for cancer health disparities research, training and community outreach

Grant #2219-UMiami Carrasquillo (PI) 10/01/15-09/30/17
PCORI (Eugene Washington Engagement Award Program)
State-wide Partnership for Training Community Health
Workers in PCOR

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors. Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: David Loewenstein, PhD, ABPP/CN

eRA COMMONS USER NAME (credential, e.g., agency login): DLOEWENSTEIN

POSITION TITLE: Professor of Psychiatry and Behavioral Sciences and Director of Neuropsychology

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	Completion Date MM/YYYY	FIELD OF STUDY
University of South Florida	B.A.	04/1981	Psychology
University of South Florida	M.S.	04/1983	Psychology
Florida State University	Ph.D.	09/1986	Clinical Psychology
University of Washington School of Medicine	Internship	08/1986	Clinical Psychology

A. Personal Statement

I am a board certified neuropsychologist who has been Principal Investigator on a number of NIH studies investigating novel cognitive and functional measures for the early detection of Alzheimer’s disease (AD) and other cognitive disorders of aging as well as intervention studies involving the effects of cognitive and exercise in older adults with mild cognitive impairment (MCI). I am widely published in the identification of early stage MCI and am Co-Leader of the Clinical Core for the 1Florida, Alzheimer’s Disease Research Center (ADRC) as well Director of Scientific Project 2. I previously served as Director of Research for the Wien Center for Alzheimer’s Disease and Memory Disorders at Mount Sinai Medical Center and currently am Principal investigator of a large NIH longitudinal study on novel cognitive and biomarkers for MCI and early Alzheimer’s Disease. I have been leader of Biostatistics Cores for a number of NIH funded program project grants.

B. Positions and Honors

- 1986-1992 Research Assistant Professor, Department of Psychiatry, University of Miami School of Medicine, Miami, FL
- 1986-2010 Director of Cognitive/Neuropsychological Laboratory and Psychological Services, Wien Center for Alzheimer's Disease and Related Disorders, Mount Sinai Medical Center, Miami Beach FL.
- 1990-Present Director of Psychological Services and Neuropsychological Laboratories. Department of Psychiatry, Mount Sinai Medical Center, an affiliated Program of Mount Sinai and University of Miami, School of Medicine.
- 1992- 2002 Associate Professor, Department of Psychiatry, University of Miami School of Medicine, Miami, FL
- 2001-2010 Director of Research, Wien Center for Alzheimer’s Disease and Memory Disorders, Mount Sinai Medical Center.
- 2002- Present Professor of Psychiatry and Behavioral Sciences, University of Miami School of Medicine.
- 2010-Present Director of Neuropsychology, Department of Psychiatry and Behavioral Sciences

Other Experience and Professional Memberships

Adult Psychopathology and Disorders of Aging (Regular Study Section Member 2010-2014); Associate Editor, Journal of Alzheimer's Disease
Triage Editor, American Journal of Geriatric Psychiatry; Member Institute of Medicine Subcommittee for Determining Functional Capacity and the Need for Representative Payees (2015); American Psychological Association (Division 40: Neuropsychology; Division 20: Aging; National Academy of Neuropsychology)

C. Contributions to Science (167 Peer Reviewed Journal Articles)

1. Development of tests for early detection of neurodegenerative diseases. I am the author of 167 peer-review referenced journal articles and book chapters, and have been a funded NIH Principal investigator on a number of longitudinal studies investigating detection of Preclinical Alzheimer's Disease, assessment of MCI and PreMCI states, development of novel cognitive stress tests for the early detection of neurodegenerative disease, development of objective functional assessment measures, relating neuroimaging findings (e.g., MRI, amyloid PET) to cognitive function both cross-sectionally and longitudinally. Our focus has been on four major areas as outlined below.

First, my team and I have pioneered tests that employ proactive and retroactive semantic interference Tests (SIT: Loewenstein et al 2004:2007); Loewenstein, Acevedo Scales of Semantic Interference Test (LASSI-L: Crocco et al.,2014; Curiel et al., 2013) and the newly developed Miami Test of Semantic Interference and Learning (MITSI-L: Curiel et al., 2016), we have also explored the relationship between these novel measures and have their relationship with neuroimaging measures in older adults with MCI and PreMCI.

A. Loewenstein DA, Acevedo A, Luis CA, Crum T, Barker WW, Duara R. (2004) Semantic interference deficits and the detection of mild Alzheimer's Disease and mild cognitive impairment without dementia. *Journal of the International Neuropsychological Society*, 1, 91-100.

B. Crocco E, Curiel RE, Acevedo A, Czaja SJ, Loewenstein DA. (2014). An Evaluation of Deficits in Semantic Cuing, Proactive and Retroactive Interferences as Early Features of Alzheimer's Disease. *The American Journal of Geriatric Psychiatry*, 22(9), 889-897.

C. Loewenstein DA, Greig MT, Curiel R, Wicklund M, Rodriguez R, Rosado M, Hidalgo J, Barker WW, DuaraR. (2015). Proactive Semantic Interference Is Associated With Total and Regional Abnormal amyloid Load in Non-Demented Community-Dwelling Elders: A Preliminary Study. *The American Journal of Geriatric Psychiatry*, 23(12), 1276-1279.

D. Loewenstein DA, Curiel RE, Greig MT, Bauer RM, Rosado M, Bowers D, Wicklund M, Crocco E, Pontecorvo M, Joshi AD, Rodriguez R. (2016). A Novel Cognitive Test for the Detection of Preclinical Alzheimer's Disease: Discriminative Properties and Relation to Amyloid Load. *The American Journal of Geriatric Psychiatry*, 24(10), 804-813.

E. Curiel RE, Crocco E, Rosado M, Duara R, Greig MT, Raffo A, Loewenstein DA. (2016). A Brief Computerized Paired Associate Test for the Detection of Mild Cognitive Impairment (MCI) in Community-Dwelling Older Adults. *Journal of Alzheimer's Disease*, 54(2), 793-799.

F. Loewenstein DA, Curiel RE, Wright C, Sun X, Alperin N, Crocco E, Czaja SJ, Raffo A, Penate A, Melo J, Capp K, Gamez M, Duara R. (2017). Recovery from Proactive Semantic Interference in Mild Cognitive Impairment and Normal Aging: Relationship to Atrophy in Brain Regions Vulnerable to Alzheimer's Disease. *Journal of Alzheimer's Disease*, 56(3), 1119-1126. doi: 10.3233/JAD-160881.

G. Loewenstein DA, Curiel R, Duara R, Buschke H. (2017). Novel cognitive paradigms for the detection of

2. Cross-Cultural Assessment and translation of neuropsychological measures. Another focus of research is cross-cultural fair neuropsychological assessment and vast experience with translation, back-translation and committee translation of neuropsychological measures. I have vast experience in training psychometrics in community based epidemiological studies so that neuropsychological testing can be done in home-based settings.

A. **Loewenstein DA**, Duara RD, Barker WW, Argüelles T. (1993). A comparative analysis of neuropsychological test performance of Spanish-speaking and English-speaking patients with AD. *Journal of Gerontology*, 48: 142-149.

B. **Loewenstein DA**, Argüelles T, Argüelles S. (1994). Potential cultural bias in the neuropsychological assessment of the older adult. *Journal of Clinical and Experimental Neuropsychology*, 16: 623- 629.

C. **Loewenstein DA**, Rubert M, Argüelles T, Duara R. (1995). Neuropsychological test performance and the prediction of functional capacities among Spanish-speaking and English-speaking patients with dementia. *Archives of Clinical Neuropsychology*, 10(2): 75-88.

D. Acevedo A, **Loewenstein DA**, Agron J, Duara R. (2007) Influence of Socio-Demographic Variables on Neuropsychological Test Performance in Spanish-Speaking Older Adults. *Journal of Clinical and Experimental Neuropsychology*, 29(5) 363-368.

E. Matías-Guiu JA, Curiel RE, Rognoni T, Valles-Salgado M, Fernández-Matarrubia M, Hariramani R, Fernández-Castro A, Moreno-Ramos T, **Loewenstein DA**, Matías-Guiu J. (2016). Validation of the Spanish Version of the LASSI-L for Diagnosing Mild Cognitive Impairment and Alzheimer's Disease. *Journal of Alzheimer's Disease*, 56(2), 733-742.

F. Matias-Guiu JA, Cabrera-Martín MN, Curiel RE, Valles-Salgado M, Rognoni T, Moreno-Ramos T, Carreras, JL, **Loewenstein DA**, Matias-Guiu J. Comparison between FCSRT and LASSI-L to detect early stage Alzheimer's disease. *J Alzheimers Dis* 2017. doi: 10.3233/JAD-170604

3. Development of functional assessment for dementia. Third, my team also developed the first behaviorally-based functional assessment instrument for early dementia (The Direct Assessment of Functional Status: DAFS, Loewenstein et al., 1989), which has been translated into eight different languages, and has been used worldwide and was the basis for the current performance –based functional tests in schizophrenia such as the UPSA. My colleague, Dr. Sara Czaja and I, have also developed other functional measures as well as cognitive and functional training paradigms.

A. **Loewenstein DA**, Amigo EA, Duara RD, Guterman A, Hurwitz D, Berkowitz N, Weinberg G, Black B, Gittleman B, Eisdorfer C. (1989) A new scale for the assessment of functional status in Alzheimer's disease and related disorders. *Journals of Gerontology*, 44, 114-121.

B. Duara R, **Loewenstein DA**, Greig-Custo MT, Raj A, Barker W, Potter E, Schofield E, Small B, Schinka J, Wu Y, Potter H . (2010). Diagnosis and Staging of Mild Cognitive Impairment, using a modification of the Clinical Dementia Rating Scale: the mCDR. *International Journal of Geriatric Psychiatry*, 25(3), 282-289.

C. **Loewenstein DA**, Acevedo A, Czaja CJ, Duara R. (2004). Cognitive rehabilitation of mildly Impaired Alzheimer's disease patients on cholinesterase inhibitors. *American Journal of Geriatric Psychiatry*, 12, 395-402.

D. Acevedo A, **Loewenstein DA**. (2008). Non-Pharmacological Cognitive Interventions in Aging and Dementia. *Journal of Geriatric Psychiatry and Neurology*, 20(4), 239-249.

E. Czaja SJ, **Loewenstein DA**, Lee CC, Fu SH, Harvey PD. (2016). Assessing functional performance using computer-based simulations of everyday activities. *Schizophrenia Research*, 183, 130-136. PubMed PMID: 27913159.

4. Changes in MRI and PET scans for preclinical Alzheimer's. Fourth, our group has conducted a number of studies investigating preclinical Alzheimer's Disease and relating cognitive measures to changes in structural MRI and amyloid deposition on PET scans.

A. **Loewenstein DA**, Acevedo A, Small BJ, Agron J, Crocco E, Duara R. (2009). Stability of Different Subtypes of Mild Cognitive Impairment Among the Elderly Over a Two to Three Year Follow-Up Period. *Dementia and Geriatric Cognitive Disorders*, 17(5), 437- 440.

B. **Loewenstein DA**, Amarilis Acevedo A, Potter H, Schinka J, Raj A, Greig M, Agron J, Barker WW, Wu Y, Small B, Schoefield E, Duara R. (2009). Severity of Medial Temporal Atrophy and Amnesic MCI: Selecting type and number of memory tests. *American Journal of Geriatric Psychiatry*, 17(12), 1050-1058.

C. Apel J, Potter E, Shen Greig MT, **Loewenstein D**, Duara R. (2009). A comparative analysis of structural brain MRI in the diagnosis of Alzheimer's disease. *Behavioral Neurology*, 21(1), 9-13.

D. **Loewenstein DA**, Greig MT, Schinka JA, Barker W, Shen Q, Potter E, Raj A, Brooks L, Varon D, Schoenberg M, Banko J, Potter H, Duara R. (2012). An investigation of PreMCI: subtypes and longitudinal outcomes. *Alzheimer's & Dementia*, 8(3), 172-9.

E. Duara R, **Loewenstein DA**, Shen Q, Barker W, Potter E, Varon D, Heurlin K, Vandenberghe R, Buckley C. (2013). Amyloid positron emission tomography with (18) F-flutemetamol and structural magnetic resonance imaging in the classification of mild cognitive impairment and Alzheimer's disease. *Alzheimer's & Dementia*, 9(3), 295-30.

D. Additional Information: Research Support and/or Scholastic Performance

1R01AG047649-01A1
Loewenstein, David (PI)
(NIH)

02/01/2015 - 01/31/2020
2.4 CM

Novel Detection of Early Cognitive and Functional Impairment in the Elderly

This is an innovative longitudinal study that will examine the utility of two novel cognitive measures (LASSI-L; MPMT) and a series of newly developed computer-based functional task stimulations (FTS) in the detection of Amnesic mild cognitive impairment (aMCI) and PreMCI versus normal elderly subjects.

R01AG054009-01
Czaja, S and Loewenstein, D, PI's
(NIH-NIA)

09/01/2016- 04/30/2021
1.2 CM

A nonpharmacological intervention for patients with Alzheimer's Disease and their family caregivers.

This intervention provides a dual target intervention involving cognitive training and enhancing caregiver skills through an innovative technological platform

Grant Number: 8AZ23
PI: David Loewenstein PhD
State of Florida Ed and Ethel Moore Grant

02/01-18- 1/31/2020
.6 CM

The Relationships between Multimodal Neuroimaging Biomarkers and a Novel Cognitive Stress Test (CST) Among Ethnically Diverse Older Adults.

This is a two year cross-sectional study designed to examine tau and amyloid deposition as it relates to the CST in a modest number of Hispanic and non-Hispanic participants.

Grant Number: 7AZ18

02/2017- 02/2020

State of Florida Ed and Ethel Moore Grant

1.2 CM

PI: David Loewenstein PhD

Project Title: Brain Amyloid Load and Novel Cognitive Measures in Diverse Ethnic Groups

This project will examine amyloid load and its relation to structural MRI and novel cognitive stress tests in African American and Hispanic Elderly at Risk for AD.

1R01AG055638 - 01A1

04/01/2017-1/31/2023

Rosie Curiel (PI)

2.40 CM

(NIA/NIH)

Precision-Based Assessment for Detection of MCI in Older Adults

The major goals of this project are to examine the psychometric properties of novel sensitive cognitive assessment tools among participants 70+ years of age and determine which cognitive markers are most predictive of baseline and longitudinal atrophy in AD-related signature brain regions on MRI. The measures will be compared to widely used cognitive outcome measures in current Alzheimer's disease clinical trials.

Role: Co-Investigator

1P50AG047266-OA1

08/15/2015 – 05/31/2020

Todd E Golde (PI)

1.8 CM

(NIA/NIH)

Project II University of Florida – Mt. Sinai Medical Center AD Research Center

Core B will provide baseline clinical and imaging biomarker studies and longitudinal evaluations of 490 study participants, of which at least 50% will be Hispanic.

Role: (Loewenstein, PI) / Clinical Core (Co-Leader, Investigator)

1R01NR014434-01

04/01/2013 - 03/31/2018

Czaja, Sara (PI)

1.2 CM

(NINR/NIH)

A Tailored Technology Intervention for Diverse Family Caregivers of AD Patients

The focus of the study is to gather systematic data on the acceptability and efficacy of a unique technology based, culturally- tailored psycho-social intervention program that targets ethnically/culturally diverse family Caregivers of patients with Alzheimer's disease.

Role: Co-Investigator

2PO1AG017211-16

07/01/2015 - 03/31/2020

Czaja, Sara J (PI)

1.2 CM

(NIA/NIH)

Center on Research and Education for Aging and Technology Enhancement (CREATE IV)

CREATE is a highly successful, productive, and cohesive multidisciplinary Center for research and education on aging and technology.

Role: Co-Investigator, Data Management Core

6AZ04 (State of Florida)

01/01/2016 – 06/30/2018

Czaja, SJ (PI)

.6 CM

A Non-Pharmacological Intervention for Patients with Alzheimer's Disease

The proposed developmental study will develop and test the efficacy and feasibility of an integrated, dyadic based intervention program (DT), delivered through technology that will include cognitive/ functional training

for the AD patient and engage the caregiver (CG) as a therapy extender. The program will also include an evidenced-based caregiver component that emphasizes issues important in the earlier stages of caregiving and helps CGs prepare for caregiving transitions.

Role: Co-Investigator

Grant #7AZ14

03/1/2017 – 01/31/2020

Curiel, Rosie E. (PI)

.6 CM

State of Florida Department of Health, Ed and Ethel Moore AD Research Program

A Consortium to Study Precision-based Computerized Assessment for the Detection of Mild Cognitive Impairment in Older Adults

Novel computerized tests including the LASSI-L and Miami Prospective Memory Test (MPMT) obtained and the discriminative compared to traditional memory measures. This project is expected to provide critical data that facilitates an early career RO1 application to the National Institutes of Health, which will examine changes in cognitive performance using these instruments as they relate to longitudinal biological changes within the brain.

Role: Co-Investigator

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: McCabe, Philip M

eRA COMMONS USER NAME (credential, e.g., agency login): PMMCCABE

POSITION TITLE: Professor and Chairman of Psychology, Professor of Biomedical Engineering

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
University of Illinois, Urbana-Champaign	B.S	08/1975	Physiological Psychology
University of Illinois, Urbana-Champaign	Ph.D.	01/1982	Neuroscience
University of Miami	Postdoctoral	08/1982	Neuroscience/ Behavioral Medicine

A. Personal Statement

I am a Professor of Psychology and Biomedical Engineering and Chairman of the Psychology Department at the University of Miami, and a member of the University of Miami Neuroscience Ph.D. Program. For 11 years I was the Director of the Undergraduate Neuroscience Program. I have successfully trained graduate and undergraduate students in my laboratory for over 35 years, and have been involved with administration of student education and training for the past 25 years. My research deals with behavioral/cognitive neuroscience, and I have published in the neurobiology of emotional behavior, central autonomic regulation, and models of disease using electrophysiological, neuroanatomical, behavioral, quantitative, and molecular neurobiological methods.

1. Szeto, A., Sun-Suslow, N., Mendez, A.J., Hernandez, R.I., Wagner, K.V., McCabe, P.M. (2017) Regulation of the macrophage oxytocin receptor in response to inflammation. [Am J Physiol Endocrinol Metab.](#) 2017 Mar 1;312(3):E183-E189. PMID: PMC5374296
2. Noller, C.M., Mendez, A.M., Szeto, A., Boulina, M., Zaias, J., Schneiderman, N., McCabe, P.M. (2016) Structural remodeling of sympathetic innervation in atherosclerotic blood vessels: Role of atherosclerotic disease progression and chronic social stress. [Psychosom Med.](#) 2017 Jan;79(1):59-70.PMCID: [PMC5182089](#)
3. Noller, C.M., Boulina, M., McNamara, G., Szeto, A., McCabe, P.M., Mendez, A.M. (2016) A Systematic Approach for Quantitative Processing and Analysis of Small Biological Structures by Fluorescent Imaging. [J Biomol Tech.](#) 2016 Sep;27(3):90-7. PMID: [PMC4866578](#)
4. Szeto A, McCabe PM, Nation DA, Tabak BA, Rossetti MA, McCullough ME, Schneiderman N, Mendez AJ. [Evaluation of enzyme immunoassay and radioimmunoassay methods for the measurement of plasma oxytocin.](#) Psychosom Med. 2011 Jun;73(5):393-400. doi: 10.1097/PSY.0b013e31821df0c2. Epub 2011 Jun 2. PubMed PMID: 21636661; PubMed Central PMCID: PMC3118424.

B. Positions and Honors

Positions and Employment

1995-present	Professor of Psychology, University of Miami
2014-present	Chairman, Department of Psychology, University of Miami
1995-present	Professor of Biomedical Engineering, University of Miami
2003-2014	Director, University of Miami Undergraduate Neuroscience Program
1992-2014	Associate Chairman, Department of Psychology, University of Miami
1988-1995	Associate Professor of Psychology, University of Miami
1982-1988	Assistant Professor of Psychology, University of Miami

Other Experience, Professional Memberships, and Honors

2009-2010	President, Academy of Behavioral Medicine Research
2005-2008	Secretary, Academy of Behavioral Medicine Research
2003	Award for Excellence in Graduate Teaching, PGSA, Univ. Miami
1991-1995	NIMH, SBIR Study Section
1990	Fellow, Academy of Behavioral Medicine Research

C. Contribution to Science

1. My early publications dealt with the neurobiological substrates of learned emotional responses, using the classical fear-conditioning model. Our laboratory, along with others, identified the amygdala as a critical region in acquisition, retention and extinction of conditioned fear responses in animal models. We also studied how neutral and emotionally arousing stimuli are associated by via changes in synaptic strength in regions like the non-lemniscal medial geniculate. Other work examined the role of primary and higher sensory cortex in modulating learned fear responses.
 - a. Gentile CG, Jarrell TW, Teich A, McCabe PM, Schneiderman N. [The role of amygdaloid central nucleus in the retention of differential pavlovian conditioning of bradycardia in rabbits.](#) Behav Brain Res. 1986 Jun;20(3):263-73. PubMed PMID: 3741587.
 - b. Jarrell TW, Gentile CG, Romanski LM, McCabe PM, Schneiderman N. [Involvement of cortical and thalamic auditory regions in retention of differential bradycardiac conditioning to acoustic conditioned stimuli in rabbits.](#) Brain Res. 1987 Jun 2;412(2):285-94. PubMed PMID: 3607469.
 - c. Teich AH, McCabe PM, Gentile CG, Jarrell TW, Winters RW, Liskowsky DR, Schneiderman N. [Role of auditory cortex in the acquisition of differential heart rate conditioning.](#) Physiol Behav. 1988;44(3):405-12. PubMed PMID: 3222363.
 - d. McEchron MD, Green EJ, Winters RW, Nolen TG, Schneiderman N, McCabe PM. [Changes of synaptic efficacy in the medial geniculate nucleus as a result of auditory classical conditioning.](#) J Neurosci. 1996 Feb 1;16(3):1273-83. PubMed PMID: 8558255.
2. More recently, my laboratory has been focused on the role of social-emotional behavior on the progression of disease using animal models. Specifically, we have shown that social environment influences the progression of atherosclerosis in two well-established models of disease, the WHHL rabbit and the ApoE knockout mouse. This work has examined CNS, autonomic and hormonal factors that influence vascular inflammation, oxidative stress and other pathophysiological events occurring in the vessel wall. One important finding was that a stable social environment, characterized by increased affiliative social behavior, was associated with a 50% decrease in atherosclerotic disease in genetically prone animals. We have examined the role of the neuropeptide, oxytocin, in this effect, and have shown that oxytocin is both anti-inflammatory and antioxidant. Furthermore, exogenous chronic administration of oxytocin reduced the extent of disease in both animal models, and decreased the expression and release of inflammatory cytokines from adipose tissue. We have also demonstrated that sympathetic nervous system hyperinnervation of the vasculature occurs as atherosclerotic disease progresses, and are currently investigating the role this plays in the course of disease.

- a. McCabe PM, Gonzales JA, Zaias J, Szeto A, Kumar M, Herron AJ, Schneiderman N. [Social environment influences the progression of atherosclerosis in the watanabe heritable hyperlipidemic rabbit](#). *Circulation*. 2002 Jan 22;105(3):354-9. PubMed PMID: 11804992.
- b. Szeto A, Nation DA, Mendez AJ, Dominguez-Bendala J, Brooks LG, Schneiderman N, McCabe PM. [Oxytocin attenuates NADPH-dependent superoxide activity and IL-6 secretion in macrophages and vascular cells](#). *Am J Physiol Endocrinol Metab*. 2008 Dec;295(6):E1495-501. doi: 10.1152/ajpendo.90718.2008. Epub 2008 Oct 21. PubMed PMID: 18940936; PubMed Central PMCID: PMC2603556.
- c. Szeto A, Rossetti MA, Mendez AJ, Noller CM, Herderick EE, Gonzales JA, Schneiderman N, McCabe PM. [Oxytocin administration attenuates atherosclerosis and inflammation in Watanabe Heritable Hyperlipidemic rabbits](#). *Psychoneuroendocrinology*. 2013 May;38(5):685-93. doi: 10.1016/j.psyneuen.2012.08.009. Epub 2012 Sep 19. PubMed PMID: 22998949; PubMed Central PMCID: PMC3543511.
- d. Szeto, A., Sun-Suslow, N., Mendez, A.J., Hernandez, R.I., Wagner, K.V., McCabe, P.M. (2017) Regulation of the macrophage oxytocin receptor in response to inflammation. [Am J Physiol Endocrinol Metab](#). 2017 Mar 1;312(3):E183-E189. PMCID: PMC5374296
- e. Noller, C.M., Mendez, A.M., Szeto, A., Boulina, M., Zaias, J., Schneiderman, N., McCabe, P.M. (2016) Structural remodeling of sympathetic innervation in atherosclerotic blood vessels: Role of atherosclerotic disease progression and chronic social stress. [Psychosom Med](#). 2017 Jan;79(1):59-70. PMCID: [PMC5182089](#)

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

1 R01 HL116387-01A1 McCabe (PI) 07/13-06/18
 Social Environment, Sympathetic Nervous System & Atherosclerosis in WHHL Rabbits
 This project examines the influence of social environment on the progression of atherosclerosis in the WHHL rabbit, and assesses the role of vascular sympathetic nervous system remodeling as a function of disease and social environment.
 Role: P.I.

T32 HL-04726-38 Schneiderman (PI) 07/14-06/19
 Behavioral Medicine Training in Cardiovascular Disease
 This NHLBI training grant provides pre- and postdoctoral training in the biobehavioral mechanisms and treatment of cardiovascular disease.
 Role: Co-Director

Completed Research Support

PO1 HL-36588-24 Schneiderman (PI) 07/07-03/13
 Biobehavioral bases of CHD risk and management
 Project 3: Environment, CNS, and Atherosclerosis in WHHL Rabbits
 This project examined the influence of social environment on the progression of atherosclerosis in the WHHL rabbit, as well as autonomic and neuroendocrine factors involved in pathophysiology.
 Role: Project Leader

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.

Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Scott, William K.

eRA COMMONS USER NAME (credential, e.g., agency login): BSCOTT

POSITION TITLE: Professor of Human Genetics, Neurology, and Public Health Sciences

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Pennsylvania State University, University Park	B.S.	1991	Microbiology
University of South Carolina, Columbia	M.S.P.H.	1993	Epidemiology
University of South Carolina, Columbia	Ph.D.	1996	Epidemiology
Duke University Medical Center, Durham, NC	Postdoctoral	1996-1997	Genetic Epidemiology

A. Personal Statement

I am a genetic epidemiologist with 22 years' experience studying the genetic basis of complex traits, including gene-environmental interactions in Parkinson disease, age-related macular degeneration, and other complex traits associated with aging and infectious diseases. I led the clinical resources core for the University of Miami (UM) Udall Center from 1999-2018, directing the enrollment and longitudinal follow-up of participants in the genomic research studies and the tissue donation program. The UM Udall Center enrolled over 1,000 participants, including over 200 tissue donation program participants, and collected post-mortem tissue samples from 82 individuals. In these efforts, I worked extensively with the UM Brain Endowment Bank leadership and staff, and became Executive Director (and PI of the Miami NeuroBioBank contract) in December 2017. As Executive Director, I direct the operations committee including the Clinical Director, Medical Director, Associate Directors, and the Assistant Director of Operations. This management structure ensures day-to-day management by faculty investigators with expertise in the relevant areas of behavioral neurology, clinical neuropathology, anatomic pathology, and biorepository management. I will draw upon these varied experiences to provide advice to UM Evelyn F. McKnight Brain Institute leadership as part of the Scientific Advisory Board, in particular advising on the use of UM Brain Endowment Bank resources in McKnight Institute research projects.

B. Positions and Honors**Positions and Employment**

1996-1997 Research Associate, Department of Medicine, Section of Medical Genetics, Duke University Medical Center, Durham, North Carolina

1997-2006 Assistant Research Professor to Associate Professor, Section of Medical Genetics, Department of Medicine, Duke University Medical Center, Durham, North Carolina

2007-present Professor (tenured), Dr. John T. Macdonald Foundation Department of Human Genetics, Leonard M. Miller School of Medicine, University of Miami, Miami, Florida

Other Experience and Professional Memberships

2003-2008 Ad-hoc, then Standing Member, ECDA/NAME (NIH/CSR)

2007-2009 Adjunct Associate Professor, Section of Medical Genetics, Department of Medicine, Duke University Medical Center, Durham, North Carolina

2007-present Vice Chair for Education and Training, Dr. John T. Macdonald Foundation Department of Human Genetics, Leonard M. Miller School of Medicine, University of Miami, Miami, Florida

2008-2018 Graduate Program Director, Interdepartmental PhD Program in Human Genetics and Genomics, Leonard M. Miller School of Medicine, University of Miami, Miami, Florida

2010-2012 College of CSR Reviewers (NIH/CSR)

2012-present Graduate Program Director, Master of Science in Genomic Medicine, Leonard M. Miller School of Medicine, University of Miami, Miami, Florida

2012-present Program Director, Computational Ocular Genomics Training Program (NEI T32)

Honors

1995 Delta Omega (Public Health Honorary); 1991–1995, US Public Health Service Predoctoral Traineeship, University of South Carolina; 1989, Omicron Delta Kappa; 1987–1991, National Merit Scholar, Thomas J. Watson Scholar; 2018, Outstanding Graduate Program Director Award, Graduate School, University of Miami, Miami, Florida

C. Contribution to Science

My research has broadly focused on the integration of genetic and epidemiologic approaches to the study of complex chronic and infectious diseases. With a background in microbiology, epidemiology, and genetics, I actively participate in study design, data analysis, and interpretation of results for research projects on which I am an investigator. My research program has been collaborative and productive, resulting in 208 PubMed indexed publications (h-index = 63; Google Scholar, January 2019). My primary areas of research are outlined below.

1. **Epidemiologic and genetic studies of aging and physical function.** As a graduate student, I began studies to examine factors that influenced institutionalization and mortality in older adults. The observation that declining functional health status predicted institutionalization and mortality in older adults supported the idea that maintaining physical function and activities of daily living was a key component in ‘healthy longevity’ or ‘successful aging,’ and these measures formed part of the core phenotype used in the genetic studies of successful aging (SA) in the Amish. In those studies, we used mitochondrial haplogroup typing to identify a novel association of SA with mitochondrial haplogroup X and genome-wide screening to demonstrate linkage and association of SA to a region of chromosome 6.
 - a. **Scott WK**, Edwards KB, Davis DR, Cornman CB, Macera CA. Risk of institutionalization among community long-term care clients with dementia. *The Gerontologist* 1997;37:46-51.
 - b. **Scott WK**, Macera CA, Cornman CB, Sharpe PA. Functional health status as a predictor of mortality in men and women over 65. *Journal of Clinical Epidemiology* 1997;50:291-296.
 - c. Courtenay MD, Gilbert JR, Jiang L, Cummings AC, Gallins PJ, Caywood L, Reinhart-Mercer, L, Fuzzell D, Knebusch C, Laux R, McCauley JL, Jackson CE, Pericak-Vance MA, Haines JL, **Scott, WK**. Mitochondrial Haplogroup X is associated with successful aging in the Amish. *Hum Genet.* 2012 Feb;131(2):201-8. PMID: PMC4834861.
 - d. Edwards DR, Gilbert JR, Hicks JE, Myers JL, Jiang L, Cummings AC, Guo S, Gallins PJ, Konidari I, Caywood L, Reinhart-Mercer L, Fuzzell D, Knebusch C, Laux R, Jackson CE, Pericak-Vance MA, Haines JL, **Scott WK**. Linkage and association of successful aging to the 6q25 region in large Amish kindreds. *Age (Dordr).* 2013 Aug;35(4):1467-77. doi: 10.1007/s11357-012-9447-1. PMID: PMC3705095.
2. **Genetic epidemiology and gene-environment interaction in Parkinson disease.** I have spent over 15 years studying the complex etiology of Parkinson disease (PD). When these studies began, PD was considered the “quintessential environmentally-caused neurologic disease,” despite many reports of large families with apparent Mendelian inheritance. I was the primary data analyst for a large multi-center genome-wide linkage study of multiplex PD families, which identified several regions linked to PD (and led to the association of the MAPT locus with the disease). As a principal investigator of the UM Udall Center, I have led studies focused on the complex interactions among genes and environmental factors, demonstrating that the association of nitric oxide synthase variants depends on the history of cigarette smoking and pesticide exposure and that vitamin D deficiency is more common in PD than in age-matched controls. These studies have led to participation in several large genetic consortium efforts under item five. These results underscore the need to evaluate both genetic and environmental factors when examining the etiology of complex diseases.
 - a. **Scott WK**, Nance MA, Watts RL, Hubble JP, Koller WC, Lyons K, Pahwa R, Stern MB, Colcher A, Hiner BC, Jankovic J, Ondo WG, Allen FH Jr, Goetz CG, Small GW, Masterman D, Mastaglia F, Laing NG, Stajich JM, Slotterbeck B, Booze MW, Ribble RC, Rampersaud E, West SG, Gibson RA, Middleton LT, Roses AD, Haines JL, Scott BL, Vance JM, Pericak-Vance MA. Complete genomic screen in Parkinson disease: Evidence for multiple genes. *JAMA* 2001; 286(18): 2239-2244.
 - b. Wang L, Maldonado L, Beecham GW, Martin ER, Evatt ML, Ritchie JC, Haines JL, Zabetian CP, Payami H, Pericak-Vance MA, Vance JM, **Scott WK**. DNA variants in CACNA1C modify Parkinson disease risk only when vitamin D level is deficient. *Neurol Genet.* 2016 Apr 12;2(3):e72. doi: 10.1212/NXG.0000000000000072. eCollection 2016 Jun. PMID: PMC4830205.
 - c. Hancock DB, Martin ER, Vance JM, **Scott WK**. Nitric oxide synthase genes and their interactions with environmental factors in Parkinson’s disease. *Neurogenetics.* 2008 Oct;9(4):249-62. PMID: PMC2630458.
 - d. Wang L, Evatt ML, Maldonado LG, Perry WR, Ritchie JC, Beecham GW, Martin ER, Haines JL, Pericak-Vance MA, Vance JM, **Scott WK**. Vitamin D from different sources is inversely associated with Parkinson disease. *Mov Disord.* 2015 Apr;30(4):560-6. doi: 10.1002/mds.26117. PMID: PMC4390412.

3. **Genetic epidemiology of complex ocular diseases.** Similar to PD, age-related macular degeneration (AMD) is a complex disease with genetic and environmental risk factors. As a principal investigator of a multi-center study of AMD, I have directed studies of gene-environment interaction of the major genetic risk factors for AMD (CFH and ARMS2) and cigarette smoking (itself a significant risk factor) and evaluated interactions between exogenous estrogen use, estrogen receptor variants, and variation in the VEGF signalling pathway. These interactions suggest potential points of intervention in AMD focusing on modifiable (environmental) factors, rather than the immutable genetic risk factors. Additional studies are conducted in the context of large-scale consortia as described in item five.
 - a. Courtenay MD, Cade W, Schwartz SG, Kovach JL, Agarwal A, Wang G, Haines JL, Pericak-Vance MA, **Scott WK**. Set-based joint test of interaction between SNPs in the VEGF pathway and exogenous estrogen finds association with age-related macular degeneration. *Invest Ophthalmol Vis Sci*. 2014 Jul 11. pii: IOVS-14-14494. doi: 10.1167/iovs.14-14494. PMID: PMC4126792.
 - b. Edwards DR, Gallins P, Polk M, Ayala-Haedo J, Schwartz SG, Kovach JL, Spencer K, Wang G, Agarwal A, Postel EA, Haines JL, Pericak-Vance M, **Scott WK**. Inverse association of female hormone replacement therapy and oral contraceptive use with age-related macular degeneration and interactions with ARMS2 polymorphisms. *Invest Ophthalmol Vis Sci*. 2010 Apr;51(4):1873-9. PMID: PMC2868389.
 - c. Persad PJ, Heid IM, Weeks DE, Baird PN, deJong EK, Haines JL, Pericak-Vance MA, **Scott WK**; for the International Age-Related Macular Degeneration Genomics Consortium (IAMDGC). Joint Analysis of Nuclear and Mitochondrial Variants in Age-Related Macular Degeneration Identifies Novel Loci TRPM1 and ABHD2/RLBP1. *IOVS*. August 2017, Vol.58, 4027-4038. doi:10.1167/iovs.17-21734. PMID: PMC5559178.
 - d. Sardell RJ, Bailey JN, Courtenay MD, Whitehead P, Laux RA, Adams LD, Fortun JA, Brantley MA Jr, Kovach JL, Schwartz SG, Agarwal A, **Scott WK**, Haines JL, Pericak-Vance MA. Whole exome sequencing of extreme age-related macular degeneration phenotypes. *Mol Vis*. 2016 Aug 29;22:1062-76. PMID: PMC5007100.
4. **Studies of host-microbial interaction and susceptibility to infection.** Host genetic susceptibility to infection is a particularly interesting case of gene-environment interaction. I have directed genetic studies of susceptibility to tuberculosis (TB) that uncovered novel associations of TB with polymorphisms in pattern recognition receptors (toll-like receptors). I have collaborated on similar studies of susceptibility to candidiasis and Staphylococcal sepsis, supervising genetic analysis and interpretation. These studies have identified several novel candidate genes for these various infections, suggesting potential biological pathways that might be targeted for prevention or therapy.
 - a. Velez DR, Wejse C, Stryjewski ME, Abbate E, Hulme WF, Myers JL, Estevan R, Patillo SG, Olesen R, Tacconelli A, Sirugo G, Gilbert JR, Hamilton CD, **Scott WK**. Variants in Toll-like receptors 2 and 9 influence susceptibility to pulmonary tuberculosis in Caucasians, African-Americans, and West Africans. *Hum Genet*. 2010 Jan;127(1):65-73. PMID: PMC2902366.
 - b. Sobota RS, Stein CM, Kodaman N, Scheinfeldt LB, Maro I, Wieland-Alter W, Igo RP Jr, Magohe A, Malone LL, Chervenak K, Hall NB, Modongo C, Zetola N, Matee M, Joloba M, Froment A, Nyambo TB, Moore JH, **Scott WK**, Lahey T, Boom WH, von Reyn CF, Tishkoff SA, Sirugo G, Williams SM. A locus at 5q33.3 confers resistance to tuberculosis in highly susceptible individuals. *Am J Hum Genet*. 2016 Mar 3;98(3):514-24. doi: 10.1016/j.ajhg.2016.01.015. PMID: PMC4800052.
 - c. Yan Q, Sharma-Kuinkel BK, Deshmukh H, Tsalik EL, Cyr DD, Lucas J, Woods CW, **Scott WK**, Sempowski GD, Thaden J, Rude TH, Ahn SH, Fowler VG Jr. Dusp3 and Psme3 Are Associated with Murine Susceptibility to Staphylococcus aureus Infection and Human Sepsis. *PLoS Pathog*. 2014 Jun 5;10(6):e1004149. PMID: PMC4047107.
 - d. DeLorenze GN, Nelson CL, **Scott WK**, Allen AS, Ray GT, Tsai AL, Quesenberry CP Jr, Fowler VG Jr. Polymorphisms in HLA Class II Genes Are Associated With Susceptibility to Staphylococcus aureus Infection in a White Population. *J Infect Dis*. 2016 Mar 1;213(5):816-23. doi: 10.1093/infdis/jiv483. PMID: PMC4747615.
5. **Large-scale collaborative studies of common complex diseases of public health importance.** My work on common complex diseases has led to collaborations with similar groups around the world doing similar research. These consortium projects enable the discovery of genetic factors (and gene-environment interactions) that would go undetected in individual efforts. I have participated in the analysis group for each of these consortia, the results of which have been new discoveries published in widely read articles.
 - a. Velez DR, Wejse C, Stryjewski ME, Abbate E, Hulme WF, Myers JL, Estevan R, Patillo SG, Olesen R, Tacconelli A, Sirugo G, Gilbert JR, Hamilton CD, **Scott WK**. Variants in Toll-like receptors 2 and 9 influence susceptibility to pulmonary tuberculosis in Caucasians, African-Americans, and West Africans. *Hum Genet*. 2010 Jan;127(1):65-73. PMID: PMC2902366.

- b. Sobota RS, Stein CM, Kodaman N, Scheinfeldt LB, Maro I, Wieland-Alter W, Igo RP Jr, Magohe A, Malone LL, Chervenak K, Hall NB, Modongo C, Zetola N, Matee M, Joloba M, Froment A, Nyambo TB, Moore JH, **Scott WK**, Lahey T, Boom WH, von Reyn CF, Tishkoff SA, Sirugo G, Williams SM. A locus at 5q33.3 confers resistance to tuberculosis in highly susceptible individuals. *Am J Hum Genet.* 2016 Mar 3;98(3):514-24. doi: 10.1016/j.ajhg.2016.01.015. PMID: PMC4800052.
- c. Yan Q, Sharma-Kuinkel BK, Deshmukh H, Tsalik EL, Cyr DD, Lucas J, Woods CW, **Scott WK**, Sempowski GD, Thaden J, Rude TH, Ahn SH, Fowler VG Jr. Dusp3 and Psme3 Are Associated with Murine Susceptibility to Staphylococcus aureus Infection and Human Sepsis. *PLoS Pathog.* 2014 Jun 5;10(6):e1004149. PMID: PMC4047107.
- d. DeLorenze GN, Nelson CL, **Scott WK**, Allen AS, Ray GT, Tsai AL, Quesenberry CP Jr, Fowler VG Jr. Polymorphisms in HLA Class II Genes Are Associated With Susceptibility to Staphylococcus aureus Infection in a White Population. *J Infect Dis.* 2016 Mar 1;213(5):816-23. doi: 10.1093/infdis/jiv483. PMID: PMC4747615.

Complete List of Published Work in MyBibliography:

<http://www.ncbi.nlm.nih.gov/sites/myncbi/william.scott.1/bibliography/41141467/public/?sort=date&direction=ascending>

D. Additional Information: Research Support and/or Scholastic Performance

Most Relevant Research Support

HHSN271201300028C (Scott, WK)

09/01/2013 – 08/31/2021

NIH

“Brain and Tissue Repository Contract “

Development of a centralized brain and tissue biorepository to supply neurodegenerative, developmental and psychiatric diseased tissue to academic and industry scientists in order to advance biospecimen science and the economic opportunities emerging in the biomedical and biotechnology sectors. Role: Dr. Scott is PI.

HHSN271201300028C SUB 01 (Scott, WK)

09/01/2018 – 08/31/2019

NIH

“Contract Options Award”

Increased support for the processing, storage, archiving, and distribution of specimens in support of the GTEx project, an NIH Roadmap Initiative, which provides a research resource to the scientific community with which to study the relationship between genetic variation and regulation of gene expression. Role: Dr. Scott is PI.

Ongoing Research Support

1R01AI068804-10 (Fowler, (PI)) Duke University

05/01/2012 – 04/30/2019 (*no-cost extension*)

NIH/NIAID

“Host Susceptibility S. aureus”

The overall goal of this project is to further understand why some individuals develop Staphylococcus aureus infection, and of those with bacteremia, only some develop adverse outcomes. Dr. Scott is PI of a subcontract to conduct whole-exome sequencing of phenotypically discordant individuals, genotyping of candidate genes, and consult on data analysis. Role: Dr. Scott is Subcontract PI

1R56AI130947-01 (Williams S)

08/01/2017 – 07/31/2019 (*no-cost extension*)

NIH-NIAID/Case Western Reserve

“Genetics of TB resistance in HIV positive subjects”

We will coordinate GWAS genotyping in approximately 1,500 individuals from two TB cohorts. Dr. Scott will oversee all laboratory services performed by the Hussman Institute for Human Genetics Center for Genome Technology, and advise the principal investigators on the analysis and interpretation of the resulting data. Role: Dr. Scott is PI on the Subcontract

1R01EY023164-05 (Stambolian, D/Pericak Vance, M)

02/01/2013 – 01/31/2019 (*Years 2-5 only*) (*no-cost extension*)

NIH/UPenn Subcontract

“Genetic Epidemiology of Age-related Macular Degeneration in the Old Order Amish”

We propose to unravel the genetic architecture of AMD through the use of high resolution phenotyping and rare variant discovery will facilitate identification of disease-associated sequence variants that can be translated to and from model organisms for parallel pathway exploration. We will restrict our discovery of rare variants and “endophenotypes” to a very specific genetically and culturally isolated population, the AMISH living in Pennsylvania, Ohio and Indiana. UM will ascertain and sequence cases and controls from those Amish communities. Role: Dr. Scott is Co-Investigator.

M2018112 (Scott, WK)

07/01/2018 – 06/30/2020

BrightFocus Foundation

“Genetic Factors accelerating progression to advanced AMD”

We will use detailed clinical examinations of the eye and large-scale genetic analysis to identify new genetic factors that are associated with changes in the eye over time and with development of advanced AMD. The results of this study will improve our understanding of the AMD disease process and provide potential avenues for development of targeted therapies. Dr. Scott is PI.

1U54MD010722-03 (Wilkins C) 05/19/2016 – 03/31/2021

NIH-NIMHD/ Vanderbilt University (Weiss, RE subcontract PI)

“Center for Excellence in Precision Medicine and Population Health”

The Center will leverage unique assets and resources to develop novel methods and approaches to advance population health to examine determinants that drive disparity broadly and not for a specific disease phenotype. For this project, we will provide expertise, strategic advice and practical support to consortium members developing and implementing projects. Role: Dr. Scott is Co-Investigator on the Training and Mentoring Core.

1RF1AG058066-02 (Haines J/Pericak-Vance MA/Scott WK) 09/15/2017-06/30/2022 0.96 cal mo

NIH/Case Western Reserve

“Protective Genetic Variants for Alzheimer Disease in the Amish”

3RF1AG058066-01S1 (Haines J/Pericak-Vance MA/Scott WK) 09/15/2017-06/30/2022 *no effort requested*

NIH/Case Western Reserve

“Protective Genetic Variants for Alzheimer Disease in the Amish” - Supplement

Parent Grant: Alzheimer disease (AD) is the most common form of dementia in older individuals and carries a huge personal and societal emotional and financial burden. Although genetic variation significantly contributes to AD risk, studies to identify protective genetic variation are few. Studies of cognitively normal individuals in the genetically and culturally isolated Amish communities is a powerful approach toward identification of genetic variation that protects against AD. **Supplement:** The requested supplement is primarily to add ascertainment personnel at each site, with small amounts for miscellaneous supplies and coverage for local travel for the ascertainment personnel. These funds will both increase the speed of the ascertainment of CN individuals and allow collection of additional clinical and neuropsychological data (and samples, if necessary) on the cognitively impaired individuals. Dr. Scott is one of the Multiple Principal Investigators on both the Parent Grant and the Supplement.

Completed Research Support (Last Three Years)

1T32EY023194-05 (Scott, W) 01/01/2013 – 12/31/2018 (*no-cost extension*)

NIH/NEI

“University of Miami Computational Ocular Genomics Training Program”

To understand what causes eye disease requires scientists trained in both computational genomics and vision science; this program, located at one of the premier institutions for human genetics and ophthalmologic research, addresses that need for training scientists in this area. Role: Dr. Scott is PD/PI.

5R01GM034883-30 (Scott, WK) 01/01/2018 – 12/31/2018

NIH/Univ of Penn

“Role of Mitochondria-Targeted CYP2D6 in Chemical Toxicity”

The major objective and deliverable is to analyze cryopreserved brain regions for betacarbolines and isoquinolines and their respective metabolites by 2D LC/MS, and to correlate the levels of these compounds and metabolites with mt-CYP2D6 levels and neuronal pathology (Braak stage) in substantia nigra (pars compacta), amygdala and posterior putamen. Role: Dr. Scott is PI on the Subcontract.

5P50 NS071674-10 (Vance, JM) 09/01/2010 – 08/31/2018 (*no-cost extension*)

NIH/NINDS

“The Genetics of Parkinsonism Morris K. Udall Parkinson's Disease Research Center of Excellence”

“Core B: Clinical Resource Core”

The overall goal of this program project grant is to conduct a multidisciplinary investigation of the etiology of Parkinsonism, particularly Parkinson's disease (PD). Core B focuses on the ascertainment of discordant sibpairs for analysis of candidate genes and the collection of extensive environmental exposure information for use in studies of gene-environment interaction. Role: Dr. Scott is PI on Core B.

2R01EY012118-17 (Pericak-Vance, MA/Scott WK) 06/15/2000 – 07/31/2018 (*no-cost extension*)

NIH/NEI

“Genomic Architecture of Progression and Treatment Response in AMD”

The goal of this proposal is to increase our understanding of the genetic etiology of progression and treatment response in AMD, both of which have been understudied. Identifying the genes underlying clinical outcomes is directly relevant to better directing current treatments and developing new and better treatments and regimens for those suffering this disabling disorder. Role: Multiple PI

MEMBERS AND COLLABORATORS BIOSKETCHES



Ralph L. Sacco, M.D., M.S., FAHA, FAAN

**Evelyn F. McKnight Brain Institute Executive Director
and Scientific Advisory Board Member**

Professor and Olemberg Chair of Neurology
Director, Clinical and Translational Science Institute
Senior Associate Dean for Clinical and Translational Science
President, American Academy of Neurology 2017-2019
University of Miami, Miller School of Medicine



Tatjana Rundek, M.D., Ph.D. FANA

**Evelyn F. McKnight Brain Institute Scientific Director
and Scientific Advisory Board Member**

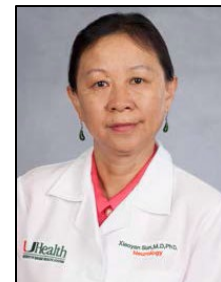
Executive Vice Chair of Research and Faculty Affairs
Director, Clinical and Translational Research Division
Director, Master of Science in Clinical Translational
Investigations
University of Miami, Miller School of Medicine



Xiaoyan Sun, M.D., Ph.D.

**Evelyn F. McKnight Brain Institute Education Director
and Scientific Advisory Board Member**

Assistant Professor
Department of Neurology
Clinical Director, Brain Endowment Bank
University of Miami, Miller School of Medicine



Bonnie E. Levin, Ph.D.

**Evelyn F. McKnight Brain Institute Cognitive Core Director,
and Scientific Advisory Board Member**

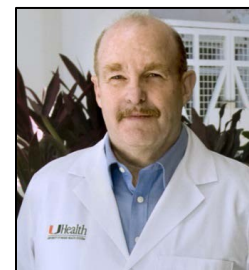
Bernard and Alexandria Schoninger Professor of Neurology
Director, Division of Neuropsychology
University of Miami, Miller School of Medicine



Noam Alperin, Ph.D.

Evelyn F. McKnight Brain Institute Member and Imaging Core Director

Professor of Radiology and Biomedical Engineering
Physiologic Imaging and Modeling Lab
Advance Image Processing Lab
University of Miami, Miller School of Medicine



Kunjan R. Dave, Ph.D.

Evelyn F. McKnight Brain Institute Member
Research Associate Professor
Department of Neurology
University of Miami, Miller School of Medicine



David Della-Morte, M.D., Ph.D.

Evelyn F. McKnight Brain Institute Member
Associate Professor
Department of Neurology
University of Miami, Miller School of Medicine



Joyce Gomes-Osman, PT, Ph.D.

Evelyn F. McKnight Brain Institute Member
Assistant Professor
Departments of Physical Therapy and Neurology
University of Miami, Miller School of Medicine



Hong Jiang, M.D., Ph.D.

Evelyn F. McKnight Brain Institute Member
Assistant Professor of Clinical
Neuro-ophthalmology & Neurology
Bascom Palmer Eye Institute
Department of Neurology
University of Miami, Miller School of Medicine



Miguel A. Perez-Pinzon, Ph.D.

**Evelyn F. McKnight Brain Institute Member and
Scientific Advisory Board Member**
Professor of Neurology & Neuroscience
Vice-Chair for Basic Science (Neurology)
Director, Cerebral Vascular Disease Research Laboratories
University of Miami, Miller School of Medicine



Stacy S. Merritt, M.A., CCRP

Evelyn F. McKnight Brain Institute Research and Administration Director
Department of Neurology
University of Miami, Miller School of Medicine



Susan Fox-Rosellini, M.B.A.

Evelyn F. McKnight Brain Institute Development & Marketing Director
Department of Neurology
University of Miami, Miller School of Medicine



Olveen Carrasquillo, M.D., M.P.H.

Evelyn F. McKnight Brain Institute Scientific Advisory Board Member
Professor of Medicine and Public Health Sciences
Chief, Division of General Internal Medicine
University of Miami, Miller School of Medicine



David Loewenstein, Ph.D., ABPP/CN

Evelyn F. McKnight Brain Institute Scientific Advisory Board Member
Director, Center for Cognitive Neuroscience and Aging
Professor, Psychiatry and Behavioral Sciences
Department of Psychiatry and Behavioral Sciences
University of Miami, Miller School of Medicine



Phillip McCabe, Ph.D.

Evelyn F. McKnight Brain Institute Scientific Advisory Board Member
Professor and Chairman
Department of Psychology
University of Miami, Miller School of Medicine



William K. Scott, Ph.D.

Evelyn F. McKnight Brain Institute Scientific Advisory Board Member
Professor of Human Genetics
Neurology and Public Health Sciences
Vice Chair for Education and Training
John P. Hussman Institute for Human Genomics
Dr. John T. Macdonald Department of Human Genetics
University of Miami, Miller School of Medicine



Anita Seixas Dias Saporta, M.D.

Evelyn F. McKnight Brain Institute Research Fellow
Department of Neurology
University of Miami, Miller School of Medicine



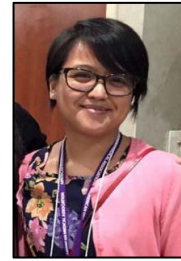
Michelle Rae Caunca, B.S.

Evelyn F. McKnight Brain Institute Formal Trainee

M.D./Ph.D. Candidate

Department of Neurology

University of Miami, Miller School of Medicine



Antoni Barrientos, Ph.D.

Evelyn F. McKnight Brain Institute Collaborator

Associate Professor of Neurology

Associate Professor of Biochemistry & Molecular Biology

University of Miami, Miller School of Medicine



Susan Halloran Blanton, Ph.D.

Evelyn F. McKnight Brain Institute Collaborator

Executive Director, Hussman Institute for Human Genomics

Associate Professor of Human Genetics and Neurology

Dr. John T. Macdonald Department of Human

Genetics Associate Director of Communications and

Compliance Hussman Institute for Human Genomics



Scott Brown, Ph.D.

Evelyn F. McKnight Brain Institute Collaborator

Research Associate Professor

Department of Public Health Sciences

University of Miami, Miller School of Medicine



Christian Camargo, M.D.

Evelyn F. McKnight Brain Institute Collaborator

Instructor, Department of Neurology

Cognitive Division

University of Miami, Miller School of Medicine



Elizabeth Crocco, M.D.

Evelyn F. McKnight Brain Institute Collaborator

Chief, Division of Geriatric Psychiatry

Department of Psychiatry and Behavioral Sciences

University of Miami, Miller School of Medicine

Geriatric Psychiatry Training Director

Jackson Memorial Hospital



Chuanhui Dong, Ph.D.

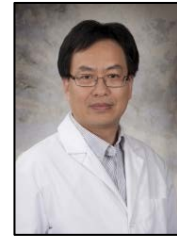
Evelyn F. McKnight Brain Institute Collaborator

Biostatistician

Research Associate Professor

Department of Neurology

University of Miami, Miller School of Medicine



Hannah Gardener, Sc.D.

Evelyn F. McKnight Brain Institute Collaborator

Assistant Scientist

Department of Neurology

University of Miami, Miller School of Medicine



Sarah Getz, Ph.D.

Evelyn F. McKnight Brain Institute Collaborator

Instructor of Neuropsychology

Department of Neurology, Division of Neuropsychology

University of Miami, Miller School of Medicine



Katalina Fernández McInerney, Ph.D.

Evelyn F. McKnight Brain Institute Collaborator

Assistant Professor

Department of Neurology, Division of Neuropsychology

University of Miami, Miller School of Medicine



Carlos T. Moraes, Ph.D.

Evelyn F. McKnight Brain Institute Collaborator

Esther Lichtenstein Professor in Neurology

Department of Neurology and Cell Biology

University of Miami, Miller School of Medicine



Milena Pinto, Ph.D.

Evelyn F. McKnight Brain Institute Collaborator

Research Assistant Professor

Department of Neurology

University of Miami, Miller School of Medicine



Alberto Ramos, M.D., MSPH, FAASM

Evelyn F. McKnight Brain Institute Collaborator

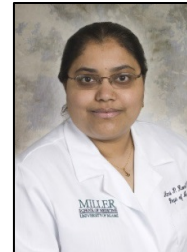
Associate Professor of Clinical Neurology
Co-Director of the Sleep Disorders Program
University of Miami, Miller School of Medicine



Ami Pravinkant Raval, Ph.D.

Evelyn F. McKnight Brain Institute Collaborator

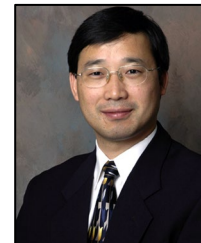
Research Associate Professor
Basic Science Division
Department of Neurology
University of Miami, Miller School of Medicine



Jianhua Wang, M.D., Ph.D.

Evelyn F. McKnight Brain Institute Collaborator

Associate Professor
Department of Ophthalmology Bascom Palmer Eye Institute
University of Miami, Miller School of Medicine



BIOGRAPHICAL SKETCHFollow this format for each person. **DO NOT EXCEED FIVE PAGES.**NAME: **BARRIENTOS, Antoni**POSITION TITLE: **Professor**ERA Commons ID: **abarrientos****EDUCATION/TRAINING**

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
Univ. of Barcelona. Teachers' School. SPAIN	B.S.	1981-1984	Science Education
Univ. of Barcelona. School of Biology. SPAIN	B.S.	1986-1992	Fundamental Biology
Univ. of Barcelona. School of Medicine. SPAIN	Ph.D.	1993-1997	Mitochondrial Genetics and Biochemistry
Univ. of Miami. School of Medicine. FL. USA	Post-doctoral fellow	1997-1999	Mitochondrial Biology
Columbia University. New York. NY. USA	Post-doctoral fellow	1999-2000	Yeast mitochondrial Genetics and Biochemistry

A. Personal Statement

My main research interest focuses on the biogenesis of mitochondrial membrane complexes in health, disease and aging. Such complexes are involved in biological energy transduction, and I am specifically interested in the components of the mitochondrial oxidative phosphorylation system, such as cytochrome *c* oxidase.

I have devoted my entire career to mitochondrial research, initially studying samples from patients and later developing novel mammalian and yeast culture models. We routinely use the facultative aerobe/anaerobe yeast *Saccharomyces cerevisiae* for mechanistic discovery and human cells in culture to generate findings that are relevant to human biology and diseases. The two main research interests in my lab are on the biogenesis of mitochondrial membrane complexes and on mitochondria-related mechanisms of neuromuscular and metabolic disease, neurodegenerative disease and aging. Over the last 16 years we have been extensively working on the basic mechanisms underlying the biogenesis of mitochondrial cytochrome *c* oxidase, the mitochondrial ribosomes and in mitochondrial dynamics and physiology with the support of NIH, American Heart Association and several Muscular Dystrophy Association (MDA) Research Grants. I recently obtained a MIRA (R35) award that consolidates my RO1 NIGMS grants. We have been also working on the role of mitochondrial mechanisms of neurodegeneration and aging with the support of an RC1 grant from the Florida Department of Health and more recently with the support of the Army Research Office (ARO). I also obtained a Merit Award and became a VA investigator in 2016. During my 16 years as an academic faculty I have trained 11 postdoctoral trainees; I have mentored 11 PhD students (5 currently), have been in the dissertation committee of 22 graduate students and was a mentor of 10 undergraduate students.

B. Positions and Honors**Positions:**

1985-1992. Permanent position as Teacher of Sciences in Secondary Public Schools. Barcelona. SPAIN.

2000-2003. Associate Research Scientist. Dept Biological Sciences. Columbia University (New York, NY).

2003-2007. Tenure-earning track Assistant Professor. Department of Neurology. Dept of Biochemistry & Molecular Biology. University of Miami (Miami. FL)

June 2007 – June 2009. Tenure-earning track Associate Professor. Department of Neurology and Department of Biochemistry & Molecular Biology. University of Miami (Miami. FL)

June 2009 - June 2013. Tenured Associate Professor. Department of Neurology and Department of Biochemistry & Molecular Biology. University of Miami (Miami. FL)

June 2013 until present. Tenured Professor. Department of Neurology and Department of Biochemistry & Molecular Biology. University of Miami (Miami. FL)

Honors:

1993-1996. Pre-Doctoral Scholarship from the Spanish Government: Education of University' Professors.

1997-1999. Post-Doctoral Scholarship from the Spanish Government: Program for Research Profs. Abroad.

2003-2004. Selected candidate to represent the University of Miami for the Pew Award in Biomedical Sciences.

2004-2005. Selected to represent the University of Miami for the Ellison Foundation award in Aging Research.

Editorial Responsibilities:

Ad hoc reviewer for: Cell Metabolism, Nature Genetics, Journal of Biological Chemistry, Human Molecular Genetics, Molecular Biology of the Cell, Journal of Molecular Biology, Trends Mol Med, Mitochondrion, Antioxidants and Redox Signaling, Biochemical Journal, FEBS Letters, Aging: clinical and experimental Research, Genetics in Medicine, Annals of Neurology and Neurology.

Advisory panels:

Federal Agencies

- Ad hoc reviewer for the Cellular Mechanisms of Aging and Development (CMAD) study section (NIH) and the Membrane Biology and Protein Processing (MBPP) Study Section (2011-2013).
- Ad hoc reviewer for R13 Scientific Conference Grant (NIH) since 2011.
- Stage 1 reviewer for The Fellowships ZRG1 F05-Cell Biology and Development study section (NIH) (2010)
- Stage 1 reviewer for Recovery Act RC1 (2009) and RC4 (2010) applications (NIH)
- Regular member of the Membrane Biology and Protein Processing (MBPP) Study Section since 2014.

Reviewer of research grants from:

Muscular Dystrophy Association (MDA) (*ad hoc* reviewer since 2008); Italian Telethon (*ad hoc* reviewer since 2006); The British Medical Research Council (MRC) (*ad hoc* reviewer since 2008); The Spanish National Evaluation and Foresight Agency (ANEP) from the Spanish Government Ministry of Education and Science - Secretary for Universities and Research (permanent reviewer since 2004).

C. Contribution to Science

I believe I have significantly contributed to the field of mitochondrial biogenesis in health, disease and aging. Among my most notable contributions are:

(i) Discovered a translational negative feedback regulatory system that coordinates the synthesis of mitochondrial cytochrome c oxidase (COX) subunit 1 with the assembly of the multimeric COX enzyme. COX, the terminal oxidase of the respiratory chain, is a hetero-oligomeric enzyme formed by subunits encoded in the nuclear and the mitochondrial DNA. Because COX contain highly reactive heme A and copper prosthetic groups, the biogenesis of this enzyme must be tightly regulated to prevent the accumulation of pro-oxidant assembly intermediates. We discovered and characterized in yeast mitochondria the existence of a negative feedback translational regulatory system. This system coordinates the synthesis of Cox1, a mtDNA-encoded catalytic subunit containing heme A and copper centers, with its assembly into the holoenzyme. We identified a COX1 mRNA-specific translation activator, Mss51, as the key element of the system [1]. Mss51 is a bi-functional protein that interacts with the 5'UTR of COX1 mRNA to promote translation and subsequently interacts with the newly synthesized Cox1 protein to facilitate its stability in pre-assembly complexes. Mss51 does not act alone. The mitochondrial Hsp70 chaperone Ssc1 [2] and the COX specific chaperones Cox14 [1] and Coa3 [3] dynamically interact with Mss51-containing complexes to coordinate Cox1 synthesis and assembly, and to facilitate Mss51 recycling between its two functions. Our discoveries sparked lines of investigations in several groups who have contributed to the understanding of the translational regulatory mechanism in yeast and in mammalian cells. More recently, we discovered that Mss51 binds heme [4]. This specific finding has provided a key element for a regulatory mechanism that coordinates assembly of COX, the major oxygen-consuming mitochondrial enzyme, with heme and oxygen availability for respiration and aerobic energy production. Over the last few years, researchers have found similar translational regulation mechanisms operating on the assembly of other mitochondrial OXPHOS complexes, namely the *bc*₁ complex or complex III and the F₀F₁ ATPase.

1 Barrientos, A., *et al.* (2004) Mss51p and Cox14p jointly regulate mitochondrial Cox1p expression in *Saccharomyces cerevisiae*. **EMBO J.** 23, 3472-3482

2 Fontanesi, F., *et al.* (2010) Mss51 and Ssc1 facilitate translational regulation of cytochrome c oxidase biogenesis. **Mol. Cell. Biol.** 30, 245-259

3 Fontanesi, F., *et al.* (2011) Cox25 teams up with Mss51, Ssc1, and Cox14 to regulate mitochondrial COX subunit 1 expression and assembly in *Saccharomyces cerevisiae*. **J. Biol. Chem.** 286, 555-566

4 Soto, I.C., *et al.* (2012) A heme-sensing mechanism in the translational regulation of mitochondrial cytochrome c oxidase biogenesis. **Cell Metab.** 16, 801-813

(ii) Discovered and characterized an array of cytochrome c oxidase assembly factors in human cells. Over the last 15 years we have contributed to the characterization of the human cytochrome c oxidase assembly process in health and disease. Have discovered multiple assembly factors required for the assembly and maturation of either COX2 [5, 6] or COX1 [7, 8] and have been frequently invited to write review articles on the topic [9].

5 Bourens, M. *et al.* (2014) Human COX20 cooperates with SCO1 and SCO2 to mature COX2 and promote the assembly of cytochrome c oxidase. **Hum. Mol. Genet.** 23, 2901-13.

6 Bourens, M. and Barrientos, A. (2017) Human mitochondrial cytochrome c oxidase assembly factor COX18 acts transiently as a membrane insertase within the subunit 2 maturation module. *J. Biol. Chem.* 292, 7774-7783

7 Bourens, M. and Barrientos, A. (2017) A CMC1-Knockout reveals translation-independent control of human mitochondrial Complex IV biogenesis. *EMBO Rep.* 18, 477-494

8 Clemente, P. et al. (2013) hCOA3 stabilizes cytochrome c oxidase 1 (COX1) and promotes cytochrome c oxidase assembly in human mitochondria. *J. Biol. Chem.* 288, 8321-31.

9 Timon-Gomez, A. et al. (2018) Mitochondrial cytochrome c oxidase biogenesis: Recent developments. *Semin. Cell Dev. Biol.* 76, 163-178.

(iii) Discovered that mitochondrial supercomplexes or respirasomes are assembled by incorporation of individual complex subunits rather than by assembly of preexisting fully assembled complexes [10]. The structural and functional organization of the mitochondrial respiratory chain (MRC) has been a matter of debate for more than 50 years. Two models have been historically hypothesized. Following the “fluid state” model, individual MRC complexes diffuse freely in the mitochondrial inner membrane and electron transport occurs when the complexes randomly collide. Conversely, the “solid state” model proposes that OXPHOS complexes are organized in rigid higher-order assemblies known as supercomplexes or respirasomes. It is currently accepted that both organizations probably coexist, giving rise to the “dynamic aggregate” or “plasticity” model. This model suggests that OXPHOS complexes switch from freely moving to fixed structures and vice versa to adapt to changes in cellular metabolism. The mechanisms that regulate the biosynthesis of mitochondrial supercomplexes remain largely unsolved. It has been thought that supercomplexes originate by the direct association of single preassembled complexes. However, some observations had suggested that the formation of these macromolecular assemblies does not necessarily require the preassembly of individual holoenzymes, but could also be achieved through a coordinated association of partially assembled complexes and free subunits. In collaboration with Dr. Cristina Ugalde (Spain), we reported the first human mitochondrial respirasome assembly pathway, which involves a paradigm-shifting model. Our data indicate that respirasome biogenesis involves a complex I assembly intermediate acting as a scaffold for the combined incorporation of complexes III and IV subunits, rather than originating from the association of preassembled individual holoenzymes [10]. This model allows us to explain the requirements for CI assembly, the structural interdependences among OXPHOS complexes, and why certain genetic defects affecting a single complex may lead to combined RC enzyme defects in patients. Multiple research groups are now contributing to define the proposed pathway and to identify respirasome assembly factors as facilitators the assembly process [11] and we have now described the function of human COX7A2L [12].

10 Moreno-Lastres, D., et al. (2012) Mitochondrial Complex I Plays an Essential Role in Human Respirasome Assembly. *Cell Metab.* 15, 324-335

11 Barrientos, A. and Ugalde, C. (2013) I Function, Therefore I Am: Overcoming Skepticism about Mitochondrial Supercomplexes. *Cell Metab.* 18, 147-149

12 Lobo-Jarne, T. et al. (2018) Human COX7A2L regulates Complex III biogenesis and promotes supercomplex organization remodeling without affecting mitochondrial bioenergetics. *Cell Rep.* 25, 1786-1799

(iv) Discovered the first DEAD box RNA helicases that play roles in the assembly of the mitochondrial ribosomes in yeast and in mammals. Over the last few years we have been working on the biogenesis of the mitochondrial ribosomes. Our interest is timely because in the years of 2014-15 the structure of yeast, porcine and human mitochondrial ribosomes have been resolved by cryo-EM at a 3.4-3.9 Å resolution. The process of mitoribosome assembly is complicated by the fact that the two mitoribosomal RNAs (rRNAs) are universally mitochondrion-encoded whereas all ribosomal proteins (with a single exception in yeast) are encoded in the nuclear DNA. Even though during the last decade there have been advances on the identification mitoribosome assembly factors and the complement of mitoribosome proteins, a detailed map of the assembly pathway is yet to be determined. Several factors may have contributed to the paucity of information on this process both, in yeast and human cells. First, many assembly factors are yet to be identified. In this regard, we described MTG1 as the first conserved GTPase involved in the assembly of the large subunit (LSU) in yeast [13] and humans [14] and more recently we have characterized the first DEAD box helicase that plays a role in LSU assembly, called Mrh4 in yeast [15] and DDX28 in mammals [16]. For example, we have reported that Mrh4 binds to the 21S rRNA to facilitate the incorporation of three late-assembly LSU subunits [15]. Second, yeast ribosome assembly mutants tend to lose their mitochondrial DNA, therefore complicating their analyses. To bypass this challenge in yeast we have recently identified genetic suppressors that maintain mtDNA stability in the absence of mitoribosome assembly, thus allowing the study of assembly intermediates [15]. We have identified several additional mitoribosome assembly factors in yeast and human cells [17]

A recent breakthrough on mitoribosome assembly relates to the mitochondrial compartmentalization of this process. At least three distinct types of foci relevant to mtDNA expression have been identified and visualized within the mitochondrial matrix of human cells. Those are the mitochondrial nucleoids, RNA granules and the RNA degradosome. While it has been proposed that mitoribosome assembly could start near the nucleoids, our results show that the distinct compartment in the vicinity of the nucleoids are the RNA granules, where DDX28 and several other assembly factors localize [16]. Newly transcribed rRNAs and/or early mitoribosome assembly intermediates are probably transferred from nucleoids to the RNA granules, where mitoribosome assembly is completed. These RNA granules are therefore reminiscent of the nucleolus. Within the nucleus, the membrane-less nucleolus is organized around the chromosomal regions that contain the genes for the rRNAs, and is the site of rRNA transcription and processing, and of ribosome assembly. Equivalent features pertain to the mitochondrial RNA granule, which we have proposed to term “the mitochondriolus” [16].

13 Barrientos, A., *et al.* (2003) *MTG1* codes for a conserved protein required for mitochondrial translation. *Mol. Biol. Cell* 14, 2292-2302.

14 Kim, H.-J. and Barrientos, A. (2018) *MTG1* couples mitoribosome large subunit assembly and intersubunit bridge formation. *Nucleic Acid Res.* 2018 Oct 13. doi: 10.1093/nar/gky938

15 De Silva, D., *et al.* (2013) The DEAD-Box protein Mrh4 functions in the assembly of the mitochondrial large ribosomal subunit. *Cell Metab.* 18, 712-725

16 Tu, Y.T. and Barrientos, A. (2015) The Human Mitochondrial DEAD-Box Protein DDX28 Resides in RNA Granules and Functions in Mitoribosome Assembly. *Cell Rep.* 12, 00058-00053

17 De Silva D, Poliquin S, Zeng R, Zamudio-Ochoa A, Marrero N, Perez-Martinez X, Fontanesi F, Barrientos A. (2017) The DEAD-box helicase Mss116 plays distinct roles in mitochondrial ribogenesis and mRNA-specific translation. *Nucleic Acids Res.* 2017 45(11):6628-6643

(v) Discovered that mitochondrial respiratory thresholds and ROS signaling regulate yeast chronological life span and its extension by TORC1 inhibition or caloric restriction (CR). Metabolic and mitochondrial abnormalities are a prominent feature of aging and neurodegeneration. However, the literature reports conflicting results concerning the extent and causality of the aging associated aerobic energy production decline and mitochondrial ROS-induced damage, as well as their interplay with nutritional cues. Single cell models have provided key information concerning mechanisms of aging and neurodegeneration. In collaboration with Dr. G. Shadel (Yale University, USA), we have gained insight into the mechanism by which *tor1* mutations extend yeast chronological lifespan. We discovered that TORC1 inhibition results in increased mitochondrial respiration and enhanced ROS production, which induced an adaptive signaling that enhances stress resistance and extends chronological life span [18]. This is a clear example of mitohormesis, in which low-level of a stressor (i.e. ROS) promote adaptive changes resulting in stress resistance. Furthermore, we have characterized the role of mitochondrial respiration in regulating yeast lifespan and its extension by CR. We have shown that a 40% of wild-type respiration is enough to support regular life span and to allow the cells to benefit from CR-induced life span extension. However, while CR increases respiratory capacity and ROS production during growth, it induces shutdown of OXPHOS and ROS generation during chronological aging, thus contributing to extend life span [19]. Together, our data support a model in which ROS signaling and respiratory thresholds are complementary aging modulators that utilize two distinct mechanisms to achieve the same adaptive endpoint: increased stress resistance, efficient use of energy stores, and probably other beneficial effects in the stationary phase, all of which extend chronological life span [20].

18 Pan, Y., *et al.* (2011) Regulation of yeast chronological life span by TORC1 via adaptive mitochondrial ROS signaling. *Cell Metab.* 13, 668-678.

19 Ocampo, A., *et al.* (2012) Mitochondrial respiratory thresholds regulate yeast chronological life span and its extension by caloric restriction. *Cell Metab.* 16, 55-67

20 Ruetenik AL and Barrientos A. Dietary restriction, mitochondrial function and aging: from yeast to humans. *BBA: Bioenergetics.* (2015) 1847:1434–1447

21 Ruetenik AL, Ocampo A, Ruan K, Zhu Y, Li C, R. Zhai GR and Barrientos A. Attenuation of polyglutamine-induced toxicity by enhancement of mitochondrial OXPHOS in yeast and fly models of aging. *Microbial Cell*, 3 (8):338-51 (2016)

(vi) Discovered that proteotoxicities can be suppressed in yeast models by either enhancement of mitochondrial biogenesis or by increasing the levels of NAD⁺ salvage biosynthetic enzymes.

Transgenic yeast expressing human neurodegenerative disease-relevant proteins recapitulate key features of neuronal proteotoxicity. They have facilitated the elucidation of basic cellular mechanisms of toxicity triggered by human neurotoxic proteins. For example, we reported that they reproduce the mitochondrial defects seen in patients [21]. More recently, we have developed novel models that screen for suppressors of proteotoxicity. We have shown that proteotoxicity can be suppressed by enhancement of mitochondrial biogenesis [22], which brought to a similar discovery in mouse models. We have also discovered that proteotoxicity can be suppressed by overexpressing several enzymes in the NAD⁺ salvage biosynthetic pathway, specifically NMA1/2, QNS1,

NPT1 and PNC1 [23]. Our results are consistent with those obtained in fly models for NMNAT (NMA1 homologue). We are now establishing collaborations with Dr. Grace Zhai (Molecular & Cellular Pharmacology, University of Miami) and with Dr. Lisa Ellerby (Bucks Institute, California) to test whether the four enzymes act as suppressors respectively in *Drosophila* and patient derived-iPSC-neuronal models of polyglutamine disorders. Results from ongoing experiments indicate that suppression is independent of sirtuins and of the catalytic activity of the enzymes. Rather, under stress, these proteins act as molecular chaperones to combat proteotoxicity [23].

22 Solans, A., *et al* (2006) Cytotoxicity of a mutant huntingtin fragment in yeast involves early alterations in mitochondrial OXPHOS complexes II and III. *Hum. Mol. Genet.* 15, 3063-3081

23 Ocampo, A., *et al.* (2010) Suppression of polyglutamine-induced cytotoxicity in *Saccharomyces cerevisiae* by enhancement of mitochondrial biogenesis. *FASEB J.* 24, 1431-1441

24 Ocampo, A., *et al* (2013) NAD⁺ salvage pathway proteins suppress proteotoxicity in yeast models of neurodegeneration by promoting the clearance of misfolded/oligomerized proteins. *Hum. Mol. Genet.* 22, 1699-1708

Public URL for my bibliography collection in My NCBI is:

<http://www.ncbi.nlm.nih.gov/sites/myncbi/antoni.barrientos.1/bibliography/41138774/public/?sort=date&direction=ascending>.

D. Research Support

Ongoing Research Support

6-1-2016–5-31-2021. MIRA (R35) Grant from NIH/NIGMS (R35GM118141-01). “*Mitochondrial Biogenesis in Health and Disease*”. This award consolidates 3 RO1 grants to study the biogenesis of mitochondrial respiratory chain complexes and supercomplexes and the biogenesis and function of mitochondrial ribosomes.

2-1-2016 / 1-31-2019. Research Grant from the Muscular Dystrophy Association. Research project: “*Role of cysteine rich proteins in mitochondrial cytochrome c oxidase biogenesis*”. **PI: Antoni Barrientos**.

6-1-2016 / 5-31-2019. Research grant from The Army Research Office (ARO) # W911NF-16-1-0311. “*Mitochondrial Regulation of Neurodegenerative Proteotoxic Stress*”. **PI: Antoni Barrientos**.

3/1/2017–2/29/2021. Merit Award from the VA-Biomed Lab Research & Development 1101BX003303-01. “*Slowing Proteotoxic Neurodegeneration by Boosting Mitochondrial Bioenergetics*”. **PI: Antoni Barrientos**

Completed Research Support over the last three years

1-1-2012 / 12-31-2015. RO1 grant from NIH (NIH # 2 R01 GM071775-06A1). “*Cytochrome c oxidase assembly in health and disease*”. We use the yeast *Saccharomyces cerevisiae* and human cultured cells as models to study cytochrome c oxidase (COX) assembly in wild-type strains and other carrying mutations in evolutionary conserved COX assembly factors, relevant for human mitochondrial diseases. **PI: Antoni Barrientos**.

1-1-2013 / 12-31-2015. Supplement to RO1 grant from NIH (NIH # 2 R01 GM071775-06A1S3). “*Macromolecular assemblies in cells*”. We use the human cell culture models to study COX assembly and how it is regulated at the translational level through dynamic protein-protein interactions. **PI: Antoni Barrientos**.

1-1-2014 / 12-31-2018. RO1 grant from NIH (NIH # R01 GM105781A). “*The biogenetic pathway of mitochondrial respirasomes*”. We use the yeast *Saccharomyces cerevisiae* and human cultured cells as models to study the assembly of mitochondrial supercomplexes and respirasomes. **PI: Antoni Barrientos**. *Substituted by MIRA grant*

3-1-2015 / 2-28-2019. RO1 grant from NIH (NIH # R01 GM105781A). “*Biogenesis of the Mitochondrial Translation Machinery*”. We use the yeast and human cultured cells as models to study the assembly of mitochondrial ribosomes, with a focus on the function of DEAD box proteins. **PI: Antoni Barrientos**. *Substituted by MIRA grant*

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Christian Johann Camargo

eRA COMMONS USER NAME (credential, e.g., agency login): CHRISTIANCAMARGO

POSITION TITLE: Instructor of Clinical Neurology

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Massachusetts Institute of Technology, Cambridge, MA	SB, SB	06/2007	Brain and Cognitive Sciences; Music
Cleveland Clinic Lerner College of Medicine of Medicine of Case Western Reserve University, Cleveland, OH	MD	06/2012	Medicine
Washington Hospital Center, Washington, DC	Internship	06/2013	Preliminary Surgery
Jackson Memorial Hospital / University of Miami Miller School of Medicine, Miami, FL	Residency	06/2017	Neurology
University of Miami Miller School of Medicine, Miami, FL	Fellowship	06/2018	Cognitive Neurology

A. Personal Statement

I am presently a neurologist in the Division of Cognitive Neurology at the University of Miami Department of Neurology, and Instructor in Clinical Neurology at the University of Miami Miller School of Medicine. My research interests include identification of biomarkers for prediction of cognitive decline, utilizing mesenchymal stem cells to treat primary neurodegenerative diseases, and therapeutic interventions focused on synaptic repair for the treatment of cognitive dysfunction. My research background has been focused on the study of the molecular and electrophysiological mechanisms of synaptic plasticity, and functional brain stimulation to treat mood and behavioral disorders through neuromodulation. As a faculty in the Department of Neurology, I have also had a direct educational role: first, in direct Neurology resident clinical training, second, by promoting and educating the local Miami community on brain health via radio and in-person engagement in retirement communities, and finally as a founding member of the McKnight Brain Research Foundation / McKnight Brain Institutes (MBRF/MBI) Communications Working Group. My goals include attaining a better understanding of the underlying process behind cognitive dysfunction in neurodegenerative disorders for the purposes of therapeutic development and intervention, and implementing these novel strategies. In the present study, I hope to investigate the feasibility of a study to determine whether or not an oral nutrient which provides the components essential for synaptic membrane synthesis (e.g., phospholipids, choline, uridine) can improve memory and cognition in patients with age-related cognitive decline.

B. Positions and Honors**Positions and Employment**

2018 – Present MBRF / MBI Communications Working Group Member
2017 – Present Instructor of Clinical Neurology, University of Miami Miller School of Medicine

Honors

MIT Honorable Mention for Outstanding Research (2005)

MIT Walle J.H. Nauta Award for Outstanding Research (2007)

Silvero Cabellon Award, Best Performance by a Jr. Resident, Washington Hospital Center Dept. of Vascular Surgery (2013)

C. Contributions to Science

1. **Predicting progression to Alzheimer's Disease in patients with Mild Cognitive Impairment.** Based on the observation that about half of patients with Mild Cognitive Impairment will go on to develop further cognitive dysfunction and dementia while half remain with stable cognition, we sought to identify potential biomarkers that could predict this transformation. Our research led us to investigate Neurogranin as such a potential biomarker.

a. Supporting Publications

- i. Headley, A., De Leon, A., Dong, C., Levin, B., Loewenstein, D., **Camargo, C.**, Rundek, T., Zetterberg, H., Blennow, K., Wright, C., Sun, X. "Neurogranin as a predictor of memory and executive function decline in MCI patients." *Neurology*. (Accepted for publication; not yet published.)

2. **Utilizing Deep Brain Stimulation to Investigate Reward Function in Ventral Striatal Cells, and as a novel therapy.** Towards this end, we analyzed single-unit electrophysiological recordings of the ventral striatum in patients receiving Deep Brain Stimulation for Depression and OCD. Utilized single unit-acquisition and analysis techniques utilizing customized MATLAB scripts, Offline Spike Sorter, and Spike2. Further conducted and analyzed recordings in a patient with Pelizaeus-Merzbacher Disease as a potential therapy via compassionate-use. Separately, I designed and executed a retrospective consecutive case review/repeated-measures study for analysis of dystonia outcomes following Deep Brain Stimulation (DBS.)

a. Supporting Oral Presentations / Conference Posters

- i. **Camargo, C.**, Sheth, S., Gale J., Mian, M., Patel, S., Gerard, J., Dougherty, D., Eskandar, E. "Single-Unit Reward Encoding in the Human Nucleus Accumbens" Massachusetts General Hospital Department of Neurosurgery, Cleveland Clinic Neurological Institute Research Day, 05/2010, Cleveland, OH (Oral Presentation)
- ii. **Camargo, C.**, Sheth, S., Patel, S., Mian, M., Flaherty, A., Eskandar, E., Gale J "Thalamic Deep Brain Stimulation as a Treatment Option for Tremor in Pelizaeus-Merzbacher Disease " Massachusetts General Hospital Department of Neurosurgery, American Association of Neurological Surgeons Annual Meeting, 05/2010, Philadelphia, PA (Abstract/e-Poster)
- iii. Sheth S, Mian M, Gale J, Patel S, **Camargo C**, Gerrard J, Eskandar E. "Human Ventral Striatum Neurons Encode Reward Expectation" Massachusetts General Hospital Department of Neurosurgery, American Association of Neurological Surgeons Annual Meeting, 05/2010, Philadelphia, PA (Oral Presentation)
- iv. **Camargo, C.**, Monsalve G., Kubu C., Deogaonkar M. "A Proposed Retrospective Consecutive Case- Review for the Study of Dystonia Outcomes post-DBS" Cleveland Clinic Center for Neurological Restoration, Cleveland Clinic Neurological Institute Research Day Poster Session, 05/2009, Cleveland, OH. (Poster)

3. **Identifying the molecular mechanisms of hippocampal synaptic plasticity in rodent hippocampal neurons.** I assisted postdoctoral fellow Kensuke Futai in investigating PSD-95 modulation of presynaptic glutamate release probability by designing and creating a viral vector for overexpression of PSD-95 in rat hippocampal slices. Established developmental profiles for various synaptic plasticity-related hippocampal synaptic proteins in the rat by utilizing the Odyssey LI-COR IR Scanner to perform a novel quantifiable expression analysis of immunoblots. Initiated process for purifying GluR1 from hippocampal membrane

fractions in order to apply quantitative tandem mass spectrometry techniques to characterize GluR1 phosphorylation in naïve synapses at various developmental points.

a. Supporting Oral Presentations / Conference Posters

- i. **Camargo, C.**, Futai, K., Hayashi, Y., "Investigation of the Developmental Changes of Rat Hippocampal Synaptic Proteins," MIT Picower Institute for Learning and Memory, RIKEN Neuroscience Research Institute, RIKEN Retreat Poster Session, 11/2006, Shinrin-Koen, Saitama, Japan (Poster)
- ii. **Camargo, C.**, Futai, K., Hayashi, Y., "Comparison of the Expression of PSD95 in Rat Hippocampal Slice Culture and Tissue from Various Postnatal Ages," MIT Picower Institute for Learning and Memory, RIKEN Neuroscience Research Institute, MIT Department of Brain and Cognitive Sciences CPW Poster Session, 04/2004, Cambridge, MA. (Poster)

D. Additional Information: Research Support and/or Scholastic Performance

2007-2012 Physician Investigator Training Scholarship, Cleveland Clinic Lerner College of Medicine

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Kunjan R. Dave

eRA COMMONS USER NAME (credential, e.g., agency login): krdave

POSITION TITLE: Research Associate Professor

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Gujarat University, Ahmedabad, India	B.Sc.	12 / 1993	Biochemistry
The M. S. University of Baroda, Vadodara, India	M.Sc.	12 / 1995	Biochemistry
The M. S. University of Baroda, Vadodara, India	Ph.D.	06 / 2000	Biochemistry
University of Miami School of Medicine, Miami	Post-doc	05 / 2003	Neurology

A. Personal Statement

I completed my training in the field of cerebral ischemia at the Cerebral Vascular Disease Research Center (CVDRC), University of Miami Miller School of Medicine. Since joining CVDRC I have participated in several projects studying different aspects of cerebral ischemia. Presently, my laboratory works on research projects with ultimate goal of lowering the incidence and severity of cerebral ischemia. One of the projects is focused on improving neurological health of diabetics by decreasing the severity and incidence of cerebral ischemia in diabetics as cerebral ischemia and heart disease are the most serious complications of diabetes, accounting for more than 84% of the mortality among diabetics. We are in the process of renewing this R01 grant. Another project in my lab evaluates a strategy to lower hematoma growth following intracerebral hemorrhage. In this collaborative project, we propose to evaluate deleterious effects of nicotine treatment on outcomes following intracerebral hemorrhage.

B. Positions and Honors**Professional experience:**

- Associate Director (2014 – present), Cerebral Vascular Disease Research Laboratories, Department of Neurology, University of Miami Miller School of Medicine, Miami, FL.
- Affiliate faculty Neuroscience Graduate Program (2014 – present), University of Miami Miller School of Medicine, Miami, FL.
- Research Associate Professor (2013 – present) Department of Neurology, University of Miami Miller School of Medicine, Miami, FL.
- Research Assistant Professor (2006 - 2013) Department of Neurology, University of Miami Miller School of Medicine, Miami, FL.
- Assistant Scientist (2003 - 2006) Department of Neurology, University of Miami Miller School of Medicine, Miami, FL.
- Biochemist (September, 1999 – February, 2000) Pharmacology Division, Research and Development, The Zandu Pharmaceutical works, Mumbai (Bombay), India.

Scholarship / Award:

- Stanley J. Glaser Foundation biomedical research award, University of Miami Miller School of Medicine 2007 - 2008.

- Recipient of award of Bursaries for young scientists to attend Brain'05 conference (Amsterdam, The Netherlands, June 2005) organized by the International Society for Cerebral Blood Flow and Metabolism.
- Received "Hari Ohm Ashram Prerit Shri Bhaikaka Inter-University Smarak Trust" Award, Sardar Patel University, Vallabh Vidyanagar, Gujarat, India for two research papers in year 1999-2000.
- Recipient of award of The Lady Tata Memorial Trust Research Scholarship, Mumbai (Bombay), India for years 1996-98.
- Recipient of Scholarship from Higher Education Commissioner, Government of Gujarat, India for year 1996.

Membership in Professional Societies:

- Society for Neurosciences
- International Society for Cerebral Blood Flow and Metabolism
- American Heart Association

Role as a reviewer:

- AHA Brain 5 Study section Spring 2013, Spring 2014, Spring 2015
- AHA Brain 1 study section Fall 2013
- Bando Giovani Ricercatori "Alessandro Liberati" 2013 (Italian funding agency)
- Abstract reviewer, International Stroke Conference 2014, 2015, 2016
- AHA Innovative Research Grant Study section Fall 2014, Fall 2015, Fall 2016
- Croatian Science Foundation 2014
- Abstract reviewer Brain 2015, Brain 2017 (International symposium on Cerebral blood flow, metabolism and function)
- AHA Cardiac Arrest Resuscitation Basic Study section; Spring 2015, Spring 2016
- AHA Cardiac Arrest Resus CL/Pop Merge with Basic Science Study section; Fall 2015
- AHA scientific sessions abstracts June 2016
- NIH- Acute Neural Injury and Epilepsy Study Section (ANIE) 6/2015, 10/2015, 2/2016, 6/2016, 10/2016, 2/2017, 10/2017, 6/2018, 10/2018
- AHA Brain 3 Study section Spring 2016, Fall 2016, Spring 2017
- Co-Chair AHA Brain 3 Study section Spring 2017
- Co-Chair AHA Brain 2 fellowship Study section, Spring 2018
- Chair AHA Brain 2 fellowship Study section Fall 2018
- AHA/Allen Initiative in Brain Health and Cognitive Impairment study section Phase 1 and 2

C. Contribution to Science

1. Cerebral ischemia and heart disease are the most serious complications of diabetes, accounting for more than 84% of the mortality among diabetics. Epidemiological studies of cerebral ischemia suggest that diabetes increases both the risk of incidence and exacerbates the consequences of cerebral ischemia. Hyperglycemia is one of the contributing factors. In clinical studies, intensive anti-diabetic therapy was able to delay the onset and slow the progression of secondary complications of diabetes. The major side-effect of intensive diabetic therapy is hypoglycemia. Using the streptozotocin-diabetic rat, we observed that recurrent hypoglycemia (RH) renders the insulin-treated diabetic (ITD) rat brain more sensitive to global cerebral ischemia and results in greater brain damage. Presently, we are investigating the mechanism by which RH increases ischemic damage in ITD.
 - a. Dave K. R., Pileggi A., Raval A. P. Recurrent hypoglycemia increases oxygen glucose deprivation-induced damage in hippocampal organotypic slices. *Neurosci Lett.* 496:25-9, 2011.
 - b. Dave K. R., Tamariz J, Desai KM, Brand FJ, Liu A, Saul I, Bhattacharya SK, Pileggi A. Recurrent hypoglycemia exacerbates cerebral ischemic damage in streptozotocin-induced diabetic rats. *Stroke.* 42:1404-11, 2011.
 - c. Rehni A. K., Nautiyal N., Perez-Pinzon M. A., Dave K.R. Hyperglycemia / hypoglycemia-induced mitochondrial dysfunction and cerebral ischemic damage in diabetics. *Metab Brain Dis.* 2014 (In press)

2. Ischemic tolerance in brain develops when a sublethal ischemic insult occurs before a period of "lethal" cerebral ischemia. While working at Dr. Perez-Pinzon's laboratory, I participated in studies aimed to determine mechanisms of ischemia tolerance induced by cerebral ischemia and pharmacological preconditioning.

- a. Della-Morte D., Dave K. R., Defazio R. A., Bao Y. C., Raval A. P., Perez-Pinzon M. A. Resveratrol pretreatment protects rat brain from cerebral ischemic damage via a sirtuin 1 - uncoupling protein 2 pathway. *Neuroscience*. 159:993-1002, 2009.
- b. Dave K. R., DeFazio R. A., Raval A. P., Torraco A., Saul I., Barrientos A., Perez-Pinzon M. A. Ischemic preconditioning targets the respiration of synaptic mitochondria via protein kinase C epsilon. *J Neurosci*. 28:4172-82, 2008.
- c. *Raval A. P., Dave K. R., Perez-Pinzon M. A. Resveratrol mimics ischemic preconditioning in the brain, *J Cereb Blood Flow Metab*, 26:1141-7, 2006.
- d. *Dave K. R., Lange-Asschenfeldt C., Raval A. P., Prado R., Busto R., Saul I., Perez-Pinzon M. A. Ischemic preconditioning ameliorates excitotoxicity by shifting glutamate/gamma-aminobutyric acid release and biosynthesis, *J Neurosci Res.*, 82:665-673, 2005.

3. Cardiopulmonary arrest remains one of the leading causes of death and disability in the U.S.A. Cardiac arrest with its consequent disruption of blood flow sets in motion a cascade of cellular and systemic derangements that result in selective brain damage. I participated in project aimed to determine the mechanism of neuronal death following cardiac arrest-induced cerebral ischemia.

- a. Lin H. W., Gresia V. L., Stradecki H. M., Alekseyenko A., Dezfulian C., Neumann J. T., Dave K. R., Perez-Pinzon M. A. Protein kinase C delta modulates endothelial nitric oxide synthase after cardiac arrest. *J Cereb Blood Flow Metab*. 2014, 34:613-20.
- b. Dave K. R., Della-Morte D., Saul I., Prado R., Perez-Pinzon M. A. Ventricular fibrillation-induced cardiac arrest in the rat as a model of global cerebral ischemia. *Transl Stroke Res*. 2013, 4:571-8.
- c. Dave K. R., Bhattacharya S. K., Saul I., DeFazio R. A., Dezfulian C., Lin H. W., Raval A. P., Perez-Pinzon M. A. Activation of protein kinase C delta following cerebral ischemia leads to release of cytochrome C from the mitochondria via bad pathway. *PLoS One*. 6:e22057, 2011.
- d. Raval A. P., Dave K. R., Prado R., Katz L. M., Busto R., Sick T. J., Ginsberg M. D., Mochly-Rosen D., Perez-Pinzon M. A. Protein kinase C delta cleavage initiates an aberrant signal transduction pathway after cardiac arrest and oxygen glucose deprivation, *J Cereb Blood Flow Metab*, 25:730-741, 2005.

4. Amyotrophic lateral sclerosis (ALS) is a devastating disease, which results in degeneration of both upper and lower motor neurons of the brain, brain stem and spinal cord. The cause of most types of ALS remains uncertain, and the disease is incurable. I participated in projects aimed to determine mechanisms of cell death in mouse models of motor neuron disease.

- a. Dave K. R., Raval A. P., Purroy J., Kirkinetzos I. G., Moraes C. T., Bradley W. G., Perez-Pinzon M. A. Aberrant delta PKC activation in the spinal cord of Wobbler mouse: a model of motor neuron disease. *Neurobiol Dis*, 18:126-133, 2005.
- b. Dave K. R., Bradley W. G., Perez-Pinzon M. A. Early mitochondrial dysfunction occurs in motor cortex and spinal cord at the onset of disease in the Wobbler mouse. *Experimental Neurology*, 182:412-420, 2003.
- c. Dave K. R., Prado R., Busto R., Raval A. P., Bradley W. G., Torbati D., Perez-Pinzon M. A. Hyperbaric oxygen therapy protects against mitochondrial dysfunction and delays onset of motor neuron disease in the wobbler mice. *Neuroscience*, 120:113-20, 2003.
- d. Xu, G-P, Dave K. R., Moraes C. T., Busto R., Sick T. J., Bradley W. G., Perez-Pinzon M. A. Dysfunctional mitochondrial respiration in the Wobbler mouse brain. *Neuroscience Letters*, 300:141-144, 2001.

5. Arctic ground squirrels (AGS; *Spermophilus parryii*) is a species of heterothermic mammals; i.e., a species that hibernates. Hibernating creatures experience fluctuating metabolic rates and body temperatures as they cycle into and out of periods of prolonged torpor. One of the main reasons for their ischemia tolerance during hibernation is hypothermia. However, during euthermia several ischemia tolerance pathways are active in AGS. In an experiment aimed to determine if AGS tolerate cerebral ischemia during euthermia, we demonstrated that AGS can be readily resuscitated from prolonged cardiac arrest (CA) without evidence of neuropathology. Tolerance to global cerebral ischemia was observed even when animals were not hibernating

and when brain temperature was maintained at 37 °C. In another study we observed that epsilon PKC activation delays the collapse of ion homeostasis during ischemia in AGS but not rat.

- a. Dave K. R., Christian S. L., Perez-Pinzon M. A., Drew K. L. Neuroprotection: lessons from hibernators. *Comp Biochem Physiol B Biochem Mol Biol.* 162:1-9, 2012.
- b. Dave K. R., Defazio R. A, Raval A. P., Dashkin O., Saul I., Iceman K. E., Perez-Pinzon M.A., Drew K.L. Protein kinase C epsilon activation delays neuronal depolarization during cardiac arrest in the euthermic arctic ground squirrel. *J Neurochem.* 110:1170-9, 2009.
- c. Dave K. R., Prado R., Raval A. P., Drew K. L., Perez-Pinzon M. A. The arctic ground squirrel brain is resistant to injury from cardiac arrest during euthermia, *Stroke*, 37:1261-1265, 2006.

Complete List of Published Work in PubMed:

<https://www.ncbi.nlm.nih.gov/sites/myncbi/kunjan.dave.1/bibliography/44169146/public/?sort=date&direction=descending>

D. Research Support

American Stroke Association-Bugher Foundation Centers for Excellence in Stroke Collaborative Research for Regeneration, Resilience and Secondary Prevention, Ralph S. Sacco (PI): Project 2: Enriched Environment, Exercise and Neurotherapeutics to Enhance Functional Recovery Following Stroke. Project PI: Dr. Perez-Pinzon 4/1/2014 – 3/31/2018 (no cost extension) Role: co-investigator project 2

2R01NS034773 Dr. Perez-Pinzon, P.I. 6/1/2015 – 5/31/2020

NIH/NINDS

Ischemic preconditioning: mechanisms of neuroprotection.

The major goals of this project are to define the specific molecular targets of resveratrol preconditioning that promote ischemic tolerance and to further define the molecular mechanisms of a chronic ischemic tolerant state.

Role: co-investigator

R21NS094896 (IGNITE mechanism) Dr. Dave, P.I. R21 phase: 2/1/2016 – 1/31/2017

NIH/NINDS

R33 phase: 2/1/2017 – 1/31/2019

Red blood cell microparticles (RMPs) to reduce bleeding following hemorrhagic stroke.

The major goal of this project is to lower hematoma growth following intracerebral hemorrhage using RMPs.

Role: Principal Investigator

R01 NS097658 Dr. Perez-Pinzon, P.I. 08/2017 – 04/2022

NIH/NINDS

Metabolic master regulators for ischemic neuroprotection

Role: co-investigator

R21NS098896-01 Dr. Perez-Pinzon, P.I. 06/2016 – 05/2018 (no cost extension)

NIH/NINDS

Decellularized extracellular matrix biomaterials as therapy to ameliorate cerebral ischemia damage.

Role: co-investigator

Univ. of Miami SAC 2017-27 Dr. Koch, P.I. 3/17 – 3/18 (no cost extension)

Preconditioning with resveratrol and limb ischemia for subarachnoid hemorrhage.

Role: co-investigator

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
 Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: David Della-Morte

eRA COMMONS USER NAME (credential, e.g., agency login): ddellamorte

POSITION TITLE: Assistant Professor of Neurology, (Associate Professor Pending Position) University of Miami Miller School of Medicine

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Medical School University of Naples, Italy	MD	1996-2002	Medicine
Medical School University of Naples, Italy	Residency	2003-2006	Internal Medicine/ Geriatrics
Medical School University of Naples, Italy	Ph.D.	2006-2010	Neuroscience
Miller School of Medicine, University of Miami, Miami, FL, U.S.A.	Fellowship	2006-2009	Neuroscience

A. Positions and Honors

Positions and Employment

2003-05	Emergency Service	Clinical Thermal Center, Fiuggi, Italy.
2003-06	Chief of Residents	Dept. of Internal Medicine, University of Naples, Italy.
2006-09	Postdoctoral Associate	Miller School of Medicine, Univ. of Miami, Miami, FL
2009-	Assistant Professor of Neurology	Miller School of Medicine, Univ. of Miami, Miami, FL
2010-	Director of Center of Research of Physiopathology of Aging	IRCCS, San Raffaele Pisana, Rome, Italy
2013-	Assistant Professor of Internal Medicine (Associate Professor Position Pending)	Dept. of Systems Medicine, University of Rome, Italy
2014-	Qualification as Associate Professor	Italian National Scientific Council

Honors

2003-	Awarded for the best research and scientific contribute to the 48° National Congress of Italian Geriatric Society; Florence, Italy.
2007-	Awarded American Heart Association (AHA identification number - 0625318B) Percentile rank: 7.53 (considered excellent).
2008-	Awarded with Travel Grant for the best abstract presented at International Symposium, University of Miami, FL, USA.
2008-	Ad hoc reviewer of several peer reviewed international journals such as: <i>Stroke, Circulation and Neurology.</i>
2010-	Editorial Board Member of <i>International Journal of Diabetology & Vascular Disease Research, Cell R4, Clinical & Experimental Cardiology, JSM Alzheimer's Disease and Related Dementia, Journal of Novel Physiotherapies.</i>
2012-	Member of Health Research Board (HRB), National Health Institute of Ireland: ad hoc reviewer for Health Research Awards.
2012-	Member of American Association for the Advancement of Science (AAAS), European Association for the Study of Diabetes (EASD).
2014-	US O1 VISA for Extraordinary Ability in Science.

- 2014- Committee Member - Thesis in Master in Diabetes and its Management, School of Medicine, University of Rome Tor Vergata, Rome, Italy.
- 2015-17 Co-Editor in Chief of Clinical Immunology, Endocrine & Metabolic Drugs.
- 2015- Committee Member - Test for Admission at School of Medicine, School of Medicine University of Rome Tor Vergata, Rome, Italy.
- 2016- Coordinator of the Internal Medicine Course, Faculty of Dentistry, School of Medicine, University of Rome Tor Vergata, Rome, Italy.

B. Contribution to Science

1. Genetic contribution to atherosclerosis and stroke. My focus was to investigate the association between Genetics and subclinical phenotypes of atherosclerosis, such as carotid plaque and carotid intima media thickness, in the risk for vascular diseases. In the past 9 years by using Northern Manhattan Study (NOMAS) and Family Study as Collaborator of Drs. Sacco and Rundek (PIs of NOMAS), I studied the interaction of genetics with vascular risk factors in determining the risk for stroke. These researches yielded novel findings regarding variation in stroke predisposition among different race-ethnicities.
 - a. **Della-Morte D**, Beecham A, Rundek T, Slifer S, Boden-Albala B, McClendon MS, Blanton SH, Sacco RL. Genetic linkage of serum homocysteine in Dominican families: the Family Study of Stroke Risk and Carotid Atherosclerosis. *Stroke*. 2010 Jul;41(7):1356-62. PMID: PMC2914470
 - b. **Della-Morte D**, Beecham A, Rundek T, Wang L, McClendon MS, Slifer S, Blanton SH, Di Tullio MR, Sacco RL. A follow-up study for left ventricular mass on chromosome 12p11 identifies potential candidate genes. *BMC Med Genet*. 2011 Jul 26;12:100. PMID: PMC3199748
 - c. **Della-Morte D**, Beecham A, Dong C, Wang L, McClendon MS, Gardener H, Blanton SH, Sacco RL, Rundek T. Association between variations in coagulation system genes and carotid plaque. *J Neurol Sci*. 2012 Dec 15;323(1-2):93-8. PMID: PMC3483411
 - d. **Della-Morte D**, Wang L, Beecham A, Blanton SH, Zhao H, Sacco RL, Rundek T, Dong C. Novel genetic variants modify the effect of smoking on carotid plaque burden in Hispanics. *J Neurol Sci*. 2014 Sep 15;344(1-2):27-31. PMID: PMC4143440

2. Epidemiology of vascular risk factors, subclinical phenotypes of atherosclerosis, and cardiovascular disease. Since the beginning of my medical and scientific career, I have started to investigate the role of vascular risk factors, including diabetes, hypertension, dyslipidemia, homocysteine in the mechanisms leading to atherosclerosis and then cardiovascular diseases, especially in aged population. We conducted several epidemiological studies where we strongly reported different prevalence of these vascular risk factors among Hispanics, blacks and white. We were also the first to suggest a revision of the AHA guideline concerning treatment for hypertension in elderly Hispanics. In this field, I maintained international collaborations, particularly with Italian research teams involved in studying cardiovascular disease and aging.
 - a. Dong C, **Della-Morte D**, Rundek T, Wright CB, Elkind MS, Sacco RL. Evidence to Maintain the Systolic Blood Pressure Treatment Threshold at 140 mm Hg for Stroke Prevention: The Northern Manhattan Study. *Hypertension*. 2016 Mar;67(3):520-6. PMID: PMC4752407
 - b. Rundek T, **Della-Morte D**, Gardener H, Dong C, Markert MS, Gutierrez J, Roberts E, Elkind MSV, DeCarli C, Sacco RL, Wright CB. Relationship between carotid arterial properties and cerebral white matter hyperintensities. *Neurology*. 2017 May 23;88(21):2036-2042. PMID: PMC5440241
 - c. **Della-Morte D**, Gardener H, Dong C, Markert M, Cabral D, Elkind MSV, Sacco RL, Rundek T. Association Between Carotid Artery Function and Structure in the Northern Manhattan Study. *Front Neurol*. 2018 Apr 16;9:246. PMID: 29713306. PMID: PMC5911635
 - d. **Della-Morte D**, Dong C, Markert MS, Elkind MSV, Sacco RL, Wright CB, Rundek T. Carotid Intima-Media Thickness Is Associated With White Matter Hyperintensities: The Northern Manhattan Study. *Stroke*. 2018 Feb;49(2):304-311. PMID: 29284725. PMID: PMC5780238

3. Role of cerebral ischemic precondition (IPC) as endogenous mechanism of protection against cerebral and cardiac ischemia. Our studies, since 2005, were among the first demonstrating the reduction of the protective effect of IPC in aged animals and in elderly subjects compared with young control at both cardiac and cerebral levels. With research in this field, by using experimental *in vivo* and *in vitro* models, we showed novel pathways of neuroprotection IPC-mediated. We also demonstrated that IPC protection was induced by resveratrol administration and was mediated by Sirtuin-1 and Uncoupling-2 activation pathway. Through these researches I received the AHA fellowship award.

- a. **Della Morte D**, Abete P, Gallucci F, Scaglione A, D'Ambrosio D, Gargiulo G, De Rosa G, Dave KR, Lin HW, Cacciatore F, Mazzella F, Uomo G, Rundek T, Perez-Pinzon MA, Rengo F. Transient ischemic attack before nonlacunar ischemic stroke in the elderly. *J Stroke Cerebrovasc Dis*. 2008 Sep;17(5):257-62. PMID: PMC2676578
 - b. **Della-Morte D**, Dave KR, DeFazio RA, Bao YC, Raval AP, Perez-Pinzon MA. Resveratrol pretreatment protects rat brain from cerebral ischemic damage via a sirtuin 1-uncoupling protein 2 pathway. *Neuroscience*. 2009 Mar 31;159(3):993-1002. PMID: PMC2668125
 - c. **Della-Morte D**, Raval AP, Dave KR, Lin HW, Perez-Pinzon MA. Post-ischemic activation of protein kinase C ϵ protects the hippocampus from cerebral ischemic injury via alterations in cerebral blood flow. *Neurosci Lett*. 2011 Jan 7;487(2):158-62. PMID: PMC3004991
 - d. Koch S, **Della-Morte D**, Dave KR, Sacco RL, Perez-Pinzon MA. Biomarkers for ischemic preconditioning: finding the responders. *J Cereb Blood Flow Metab*. 2014 Jun;34(6):933-41. PMID: PMC4050240
4. Experimental studies on the effect of antioxidant proteins against vascular risk factors and atherosclerosis. In the recent years, we focused our research in specific proteins such as Serum and Glucocorticoid-Inducible Kinase (SGK)-1, which have been demonstrated to have powerful antioxidant effects. By using *in vitro* models of endothelial and coronary cells we demonstrated as SGK-1, when activated is able to protect the vessel against hyperglycemia and pro-oxidant stimuli. However, more important, we were the first showing a direct effect of SGK-1 on the length of the telomeres, and therefore its capacity in delay endothelial senescence. These researches yielded a grant of \$400k from Fondazione Roma (Italy). We are continuing these studies in animal models and we are investigating the association between genetic variants of SGK-1 and atherosclerosis in NOMAS with promising results.
- a. Ferrelli F, Pastore D, Capuani B, Lombardo MF, Blot-Chabaud M, Coppola A, Basello K, Galli A, Donadel G, Romano M, Caratelli S, Pacifici F, Arriga R, Di Daniele N, Sbraccia P, Sconocchia G, Bellia A, Tesauro M, Federici M, **Della-Morte D**, Lauro D. Serum glucocorticoid inducible kinase (SGK)-1 protects endothelial cells against oxidative stress and apoptosis induced by hyperglycaemia. *Acta Diabetol*. 2015 Feb;52(1):55-64. PMID: 24961472
 - b. Basello K, Pacifici F, Capuani B, Pastore D, Lombardo M, Ferrelli F, Coppola A, Donadel G, Arriga R, Sconocchia G, Bellia A, Rogliani P, Federici M, Sbraccia P, Lauro D, **Della-Morte D**. Serum- and Glucocorticoid-Inducible Kinase (SGK)1 delay the onset of Endothelial Senescence by Directly Interacting with hTERT. *Rejuvenation Res*. 2016 Feb;19(1):79-89. PMID: 26230157
 - c. Lauro D, Pastore D, Capuani B, Pacifici F, Palmirotta R, Abete P, Roselli M, Bellia A, Federici M, Di Daniele N, Sbraccia P, Guadagni F, Lauro R, **Della-Morte D**. Role of Serum and Glucocorticoid-Inducible Kinase (SGK)-1 in Senescence: a Novel Molecular Target against Age-Related Diseases. *Curr Med Chem*. 2015;22(33):3765-88. PMID: 26264924
 - d. Pastore D, **Della-Morte D**, Coppola A, Capuani B, Lombardo MF, Pacifici F, Ferrelli F, Arriga R, Mammi C, Federici M, Bellia A, Di Daniele N, Tesauro M, Donadel G, Noto D, Sbraccia P, Sconocchia G, Lauro D. SGK-1 protects kidney cells against apoptosis induced by ceramide and TNF- α . *Cell Death Dis*. 2015 Sep 17;6:e1890. PMID: PMC4650437

Complete List of Published Work in MyBibliography: <https://www.ncbi.nlm.nih.gov/pubmed/?term=della+morte+d>

C. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

Award: M1800195

Rundek (PI)

09/01/2018-8/31/2023

NIH

Title: Family Study of Carotid Atherosclerosis and Stroke Risk.

The major goal of this study is to evaluate heritability and genetic linkage of novel vascular risk factors such as carotid intima-media thickness among the families of high-risk Caribbean Hispanics.

Role: Co-I: David Della-Morte

ARISTA---USA Protocol ID# CV185-564

Rundek (PI)

01/01/2017-12/31/2019

Pfizer

Title: "Disparities in Stroke Outcomes and Care Delivery in Patients with Atrial Fibrillation: FLiPER

--- AF Florida Puerto Rico Atrial Fibrillation Stroke Study"

The major goal of this study is to evaluate the effect of Atrial Fibrillation on ischemic stroke/TIA outcomes overall,

and by sex and race/ethnicity by using a large Florida-Puerto Rico (FL---PR) Stroke Registry.

Role: Co-PI: David Della-Morte

No Award No. B88F12000730005

Italian Minister of Health

Guadagni (PI)

01/01/2014-12/30/2020

POR FESR CAMPANIA 2014-2020 – B-TECHNOLOGY PLATFORM AGAINST RARE CANCERS

Title: RARE.PLAT.NET. Innovazioni diagnostiche e terapeutiche per tumori neuroendocrini, endocrini e per il glioblastoma attraverso una piattaforma tecnologica integrata di competenze cliniche, genomiche, ICT, farmacologiche e farmaceutiche.

This award is specifically designed to develop through a cluster of National Biological Banks and Big Data a technological platform that will be able to improve prevention, prediction and treatment for brain cancers, neuroendocrin cancers, and cerebrovascular diseases. To find novel algorithms of prediction developed by using genetic, IT, and biological data is the main scope of this project.

Role: Co-I: David Della-Morte

No Award No. F/050383/01-03/X32

Guadagni (PI)

01/01/2014-12/31/2020

Italian Minister of Economic Development - Divisione VII – Interventi per ricerca e sviluppo.

NET4HEALTH - NETWORK for HEALTH management. Title: "HORIZON 2020" PON I&C 2014-2020 MISE – Direzione Generale per gli Incentivi alle Imprese.

This project is mainly aimed to develop a National central Biobank by clustering the most important Italian Biobanks. These Biobanks are especially dedicated in collecting biospecimens from patients with chronic diseases (e.g. cancer, diabetes, cardiovascular diseases). A central Biobank would further help researchers in better analyzing data and to reach in a better prediction and prevention for these pandemic diseases.

Role: CoI: David Della-Morte

Lauro (PI)

09/23/2018-09/22/2021

Rome Foundation- Title: "Diabetes Mellitus, Regenerative and Reparative Processes, and Improvement of Pancreatic Beta Cell Function: Role of Bone Marrow-Mesenchymal Stem Cells, Micrnas, M2 Macrophages And Myeloid Derived Suppressor Cells". This project is mainly aimed to develop novel therapeutic strategies to regenerate and preserve pancreatic beta cell mass, which is dramatically affected in diabetes mellitus.

Role: CoPI: David Della-Morte

No Award No. PNR 2015-2020 ARS01_01163 PerMedNet Guadagni (PI)

10/01/2018-09/31/2021

European Social Fund, under the Italian Ministries of Education, University and Research. Title: "Personalized medicine for innovative strategies in neuropsychiatric and vascular diseases".

This project is mainly aimed to develop novel and more personalized drugs for neurodegenerative disorders particularly focused on stroke.

Role: CoPI: David Della-Morte

Completed Research Support

American Heart Association AHA 0625318B Della-Morte (PI)

05/07/07-05/30/09

Potential mechanism by which resveratrol mimics cerebral ischemic preconditioning

This is a study to investigate the potential role of polyphenols in neuroprotection against cerebral ischemia by the capacity to mimic the endogenous mechanism of protection called ischemic preconditioning.

Role: PI

UM/SAC 2014-3R2 Pilot Award

Bianchi (PI)

01/01/15-12/31/15

Role of Sirtuins in Neurodegeneration

This is an award aimed to generate preliminary data for NIH Grant on the role of Sirtuins in Neurodegeneration by using a unique model of cerebral damage in *C. elegans*.

Role: Co-PI

NIH/NINDS R01 NS 065114

Rundek (PI)

07/01/10-06/30/16

Novel Factors for Unexplained Phenotypes of Subclinical Carotid Atherosclerosis

This is a selective genotype study of the extreme phenotypes of subclinical atherosclerosis among individuals with high burden of atherosclerosis and no risk factors (RF) and high burden of RF but no atherosclerosis.

Role: Co-I

NIH/NINDS K24 NS 062737

Rundek (PI)

09/30/09-08/31/16

Genetic Determinants of Extreme Phenotypes of Subclinical Atherosclerosis

This is an award to train young investigators in patient-oriented research, perform research on genetic factors of extreme phenotypes of subclinical atherosclerosis, and enhance career development in genetic epidemiology.

Role: Co-I

Rome Foundation

Pontecorvi (PI)

01/01/15-12/31/17

Diabetes and sarcopenia in the elderly; age-associated inflammation as a shared pathogenic mechanism and Potential therapeutical target

The major goal of this study is to evaluate the antioxidant protein such as Peroxiredoxin6 in the mechanism linked with diabetes and muscle mass deterioration in aging population.

Role: Co-PI

NIH/NINDS R01 NS 40807

Rundek, Sacco (Multi-PI)

05/01/02-09/30/17

Family Study of Stroke Risk and Carotid Atherosclerosis

The major goal of this study is to evaluate heritability and genetic linkage of novel vascular risk factors such as carotid intima-media thickness among the families of high-risk Caribbean Hispanics.

Role: Co-I

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: **Hannah Gardener, ScD**

eRA COMMONS USER NAME (credential, e.g., agency login): **HGARDENER**

POSITION TITLE: **Associate Scientist**

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Dartmouth College	AB	06/2000	Psychological and Brain Sciences
Harvard School of Public Health	ScD	08/2007	Epidemiology

A. Personal Statement

Hannah Gardener, ScD, Associate Scientist in the Department of Neurology at the University of Miami, is an epidemiologist with a particular interest in neuroepidemiology and the epidemiology of aging. She received her doctorate in Epidemiology in 2007 from the Harvard School of Public Health. With 79 publications, she has been conducting research on risk factors for clinical and subclinical vascular outcomes in the Northern Manhattan Study for over ten years. She is particularly interested in diet and other modifiable vascular risk factors in relation to cognitive impairment and decline, vascular events, carotid disease, and age-related changes in brain structure. She is responsible for study design, data management, design and completion of statistical analyses, interpretation of results, presentations and manuscript writing.

B. Positions and Honors**POSITIONS AND EMPLOYMENT****Traineeship**

2002-04 Senior Research Assistant, Department of Society, Human Development and Health, Harvard School of Public Health

2007-09 Epidemiology Post-Doctoral Fellow, Department of Neurology, University of Miami Miller School of Medicine

Academic Appointments:

2016-present Associate Scientist Department of Neurology, University of Miami Miller School of Medicine

2009-2016 Assistant Scientist Department of Neurology, University of Miami Miller School of Medicine

2009 Research Assistant Professor Departments of Neurology and Pediatrics, University of Miami Miller School of Medicine

Memberships:

2008- American Academy of Neurology

2007-2008 Society for Epidemiologic Research

Honors:

- 2006-2007 Certificate of Distinction in recognition of outstanding accomplishments and contributions in teaching: Harvard School of Public Health, Department of Epidemiology
- 2004-2006 National Research Service Award grant from the Training Program in Psychiatric Epidemiology and Biostatistics (T32 MH17119):
- 2000 Phi Beta Kappa, Dartmouth College
- 2000 Benner Award for Excellence in Research, Dartmouth College

C. Contribution to science

C.1. Predictors of cognitive function and decline in the population. An area of research focus is the role of novel and traditional vascular risk factors in cognitive performance and decline over time. Most notable is our finding of a role for infectious burden in executive function as well as memory decline over time, and our studies showing relationships between sleep disturbance, physical activity, and cardiovascular health factors with decline in cognitive domains.

1. **Gardener H**, Caunca MR, Dong C, Cheung YK, Elkind MSV, Sacco RL, Rundek T, Wright CB. Ultrasound Markers of Carotid Atherosclerosis and Cognition: The Northern Manhattan Study. *Stroke*. 2017;48(7):1855-1861.
2. Willey JZ, **Gardener H***, Caunca MR, Moon YP, Dong C, Cheung YK, Sacco RL, Elkind MS, Wright CB. Leisure-time physical activity associates with cognitive decline: The Northern Manhattan Study. *Neurology*. 2016;86(20):1897-903.
3. **Gardener H**, Wright CB, Dong C, Cheung K, DeRosa J, Nannery M, Stern Y, Elkind MS, Sacco RL. Ideal Cardiovascular Health and Cognitive Aging in the Northern Manhattan Study. *Neurology*. 2016;86(20):1897-903.
4. Wright CB, **Gardener H***, Dong C, Yoshita M, DeCarli C, Sacco RL, Stern Y, Elkind MS. Infectious burden and cognitive decline in the Northern Manhattan Study. *J Am Geriatr Soc*. 2015;63(8):1540-1545.

C.2. MRI markers of vascular damage. A primary area of research focus has been examining the role of vascular risk factors in predicting MRI markers of vascular damage, which may be mediators in the pathways between cardiovascular health indices and both stroke and cognitive function and decline. We have shown that migraine is a risk factor for subclinical brain infarcts imaged using MRI, and that diastolic blood pressure, lipid levels, and adherence to a Mediterranean-style diet are predictive of white matter hyperintensity volume, a risk factor for both stroke and dementia. We have also examined the prevalence and risk factors for cerebral microbleeds in our urban multiethnic cohort. Most recently, in the multi-ethnic NOMAS cohort, we found that having a greater number of ideal cardiovascular health factors is associated with a reduced burden of biomarkers of brain aging, including silent brain infarcts, white matter hyperintensity volume, and brain atrophy.

1. **Gardener H**, Caunca M, Dong C, Cheung YK, Alperin N, Rundek T, Elkind MSV, Wright CB, Sacco RL. Ideal Cardiovascular Health and Biomarkers of Subclinical Brain Aging: The Northern Manhattan Study. *J Am Heart Assoc*. 2018;7.
2. Caunca MR, Del Brutto V, **Gardener H**, Shah N, Dequatre-Ponchelle N, Cheung YK, Elkind MS, Brown TR, Cordonnier C, Sacco RL, Wright CB. Cerebral Microbleeds, Vascular Risk Factors, and Magnetic Resonance Imaging Markers: The Northern Manhattan Study. *J Am Heart Assoc*. 2016;5(9).
3. Monteith T, **Gardener H**, Rundek T, Dong C, Yoshita M, Elkind MSV, DeCarli C, Sacco RL, Wright CB. Migraine, White Matter Hyperintensities, and Subclinical Brain Infarction in a Diverse Community: The NOMAS Study *Stroke*. 2014;45(6):1830-1832.
4. Willey JZ, **Gardener H**, Moon MY, Sacco RL, Elkind MSV, Wright CB. Lipid profile components and subclinical cerebrovascular disease in the Northern Manhattan Study. *Cerebrovascular Diseases*. 2014;37(6):423-430.

C.3. Epidemiology of stroke. Over the past 11 years I have pursued research in stroke epidemiology. I have examined novel and traditional risk factors for stroke and vascular-related death in a multi-ethnic population-based study with an emphasis on understanding race/ethnic disparities. In particular, a primary research interest is the role of dietary factors in the etiology of vascular outcomes. Other novel vascular risk factors that I have examined in a multiethnic population-based sample include migraine, adiponectin and HOMA insulin resistance.

1. Monteith TS, **Gardener H**, Rundek T, Elkind MS, Sacco RL. Migraine and risk of stroke in older adults: Northern Manhattan Study. *Neurology*. 2015;85(8):715-721.
2. **Gardener H**, Goldberg R, Mendez AJ, Wright CB, Rundek T, Elkind MSV, Sacco RL. Adiponectin and risk of vascular events in the Northern Manhattan Study. *Atherosclerosis*. 2013;226(2):483-489.
3. Rundek T, **Gardener H**, Xu Q, Goldberg RB, Wright CB, Boden-Albala B, Disla N, Paik MC, Elkind MSV, Sacco RL. Insulin resistance and risk of ischemic stroke among non-diabetic individuals from the Northern Manhattan Study. *Archives of Neurology*. 2010;67(10):1195-1200.
4. Sacco RL, Khatri M, Rundek T, Xu Q, **Gardener H**, Boden-Albala B, Di Tullio M, Homma S, Elkind MSV, Paik MC. Improving global vascular risk prediction with behavioral and anthropometric factors: the multi-ethnic Northern Manhattan Cohort Study. *Journal of the American College of Cardiology*. 2009;54(24):2303-2311.

C.4. Disparities in stroke care and outcomes after stroke. Over the past four years I have investigated race/ethnic, sex, and geographic disparities in acute stroke care in Florida and Puerto Rico, and how they relate to disparities in outcomes after stroke. In addition, I have studied short-term outcomes in patients with mild and rapidly improving stroke symptoms using Get With The Guidelines-Stroke data.

5. **Gardener H**, Pepe PE, Rundek T, Wang K, Dong C, Ciliberti M, Gutierrez C, Gandia A, Antevy P, Hodges W, Mueller-Kronast N, Sand C, Romano JG, Sacco RL. The Need to Prioritize Education of the Public Regarding Stroke Symptoms and Faster Activation of the 9-1-1 System: Findings from the Florida-Puerto Rico CReSD Stroke Registry. *Prehosp Emerg Care*. 2018:1-23.
6. Asdaghi N, Wang K, Ciliberti-Vargas MA, Gutierrez CM, Koch S, **Gardener H**, Dong C, Rose DZ, Garcia EJ, Burgin WS, Zevallos JC, Rundek T, Sacco RL, Romano JG; FL-PR CReSD Investigators and Collaborators. Predictors of Thrombolysis Administration in Mild Stroke: Florida-Puerto Rico Collaboration to Reduce Stroke Disparities. *Stroke*. 2018;49(3):638-645.
7. Sacco RL, **Gardener H**, Wang K, Dong C, Ciliberti-Vargas MA, Gutierrez CM, Asdaghi N, Burgin WS, Carrasquillo O, Garcia-Rivera EJ, Nobo U, Oluwole S, Rose DZ, Waters MF, Zevallos JC, Robichaux M, Waddy SP, Romano JG, Rundek T; FL-PR CReSD Investigators and Collaborators. Racial-Ethnic Disparities in Acute Stroke Care in the Florida-Puerto Rico Collaboration to Reduce Stroke Disparities Study. *J Am Heart Assoc*. 2017;6(2).
8. Romano JG, Smith EE, Liang L, **Gardener H**, Campo-Bustillo I, Khatri P, Bhatt DL, Fonarow GC, Sacco RL, Schwamm LH. Distinct Short-Term Outcomes in Patients With Mild Versus Rapidly Improving Stroke Not Treated With Thrombolytics. *Stroke*. 2016;47(5):1278-85.

C.5. Epidemiology of atherosclerosis and imaging markers of carotid disease. A primary research focus has been examining the associations of vascular risk factors with carotid atherosclerosis phenotypes to better understand their impact on clinical and subclinical vascular disease. I have studied the role of genetics in the etiology of carotid atherosclerosis. I have examined the relationship between two important and distinct measures of carotid atherosclerosis measured using B-mode ultrasound – carotid intima-media thickness and carotid plaque – and have explored multiple ways to quantify plaque burden including total plaque area. In addition to

diet, modifiable vascular risk factors for carotid atherosclerosis phenotypes that I have published include cigarette smoking, soluble RAGE levels, lipid levels, homocysteine, and adiponectin.

1. Tiozzo E, **Gardener H**, Hudson BI, Dong C, Della-Morte D, Crisby M, Goldberg RB, Elkind MS, Cheung YK, Wright CB, Sacco RL, Desvarieux M, Rundek T. Subfractions of High-Density Lipoprotein-Cholesterol and Carotid Intima-Media Thickness: The Northern Manhattan Study. *Stroke*. 2016;47(6):1508-13.
2. Yang D, Iyer S, **Gardener H**, Della-Morte D, Crisby M, Dong C, Cheung K, Mora-McLaughlin C, Wright CB, Elkind MS, Sacco RL, Rundek T. Cigarette smoking and carotid plaque echodensity in the Northern Manhattan Study. *Cerebrovasc Dis*. 2015;40(3-4):136-143.
3. Alsulaimani S, **Gardener H**, Elkind MSV, Cheung K, Sacco RL, Rundek T. Elevated homocysteine and carotid plaque area and densitometry in the Northern Manhattan Study. *Stroke*. 2013;44(2):457-461.
4. **Gardener H**, Sjoberg C, Crisby M, Goldberg R, Mendez A, Wright CB, Elkind MSV, Sacco RL, Rundek T. Adiponectin and carotid intima-media thickness in the Northern Manhattan Study. *Stroke*. 2012;43(4):1123-1125.

C.6. Nutritional epidemiology of vascular diseases. A primary research interest is the role of dietary factors in the etiology of vascular outcomes. Specifically, I have published on the role coffee and tea, soft drinks, sodium, potassium, and egg consumption as well as adherence to a Mediterranean-style diet in relation clinical vascular events and subclinical markers of vascular damage.

1. Willey J, **Gardener H**, Cespedes S, Cheung YK, Sacco RL, Elkind MSV. Dietary Sodium to Potassium Ratio and Risk of Stroke in a Multiethnic Urban Population: The Northern Manhattan Study. *Stroke*. 2017;48(11):2979-2983.
2. **Gardener H**, Wright CB, Cabral D, Scarmeas N, Gu Y, Cheung K, Elkind MS, Sacco RL, Rundek T. Mediterranean diet and carotid atherosclerosis in the Northern Manhattan Study. *Atherosclerosis*. 2014;234(2):303-310.
3. **Gardener H**, Scarmeas N, Gu Y, Boden-Albala B, Elkind MSV, Sacco RL, DeCarli C, Wright CB. Mediterranean diet and white matter hyperintensity volume in the Northern Manhattan Study. *Archives of Neurology*. 2012;69(2):251-256.
4. **Gardener H**, Wright CB, Gu Y, Demmer RT, Boden-Albala B, Elkind MSV, Sacco RL, Scarmeas N. A Mediterranean-style diet and the risk of ischemic stroke, myocardial infarction, and vascular death: The Northern Manhattan Study. *American Journal of Clinical Nutrition*. 2011;94(6):1458-1464.

*Shared first authorship

Link to my full list of publications:

<http://www.ncbi.nlm.nih.gov/pubmed/?term=Gardener+h>

D. Research Support

R01 NS 029993 (PI: Sacco)

02/01/03 - 07/31/20

NIH/NINDS

Stroke Incidence and Risk Factors in a Tri-Ethnic Region

The goals of this project are to determine the effects of risk factors for stroke, MI, and vascular death, as well as evaluate predictors of cognitive impairment and the importance of subclinical MRI findings in a prospective cohort study of 3300 persons from 3 race-ethnic groups from Northern Manhattan.

U54 NINDS SPIRP U54NS081763 (PI: Sacco)

01/01-12/31/17

NIH/NINDS

Stroke Prevention/Intervention Research Program in Hispanics (& supplement FL-PR CReSD-W)

The goal of this project is to develop high-impact stroke disparities interventions and research projects that have the ability to reduce stroke disparities in the two distinct Hispanic groups in Miami and Puerto Rico using effective and culturally appropriate methods.

Genentech (PI: Romano)

12/14/11 – 10/30/20

Coordinating Center: University of Miami

Mild and Rapidly Improving Stroke Study (MaRISS) This research project encompasses two phases, a *retrospective* analysis of the existing entire Get With The Guidelines-Stroke Registry to determine prevalence and short-term outcomes among patients with mild and rapidly improving stroke symptoms and a *prospective* study in 100 select GWTG hospitals to elucidate the long-term outcomes of patients that suffered mild or rapidly improving stroke.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Joyce Gomes-Osman

eRA COMMONS USER NAME (credential, e.g., agency login): JOYCEGOMES-OSMAN

POSITION TITLE: Assistant Professor, Departments of Physical Therapy and Neurology
Faculty, Transcranial Magnetic Stimulation Intensive Course, Berenson-Allen
Center for Non-invasive Brain Stimulation, Beth Israel Deaconess Medical
Center, Harvard Medical School.

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Escola Bahiana de Medicina e Saude Publica, Salvador, Bahia, Brazil	B.S.	06/07	Physical Therapy
University of Miami Miller School of Medicine, FL, USA	Ph.D.	09/13	Motor Control Physiology
Harvard Medical School, Boston, MA, USA	Post Doctoral Fellowship	09/15	Non-Invasive Brain Stimulation Neurology

A. Personal Statement

I am a rehabilitation scientist with expertise in clinical research that harnesses neuroplasticity through interventions such as neuromodulation and exercise to promote functional and cognitive improvements in different neurologic populations. I am the Director of the Neuromotor Plasticity Laboratory, and an Assistant Professor of Clinical Physical Therapy and Neurology at the University of Miami Miller School of Medicine (UMMSM). Additionally, I am Faculty at the Transcranial Magnetic Stimulation Intensive Course, Berenson-Allen Center for Non-invasive Brain Stimulation, Beth Israel Deaconess Medical Center, Harvard Medical School. My early clinical studies have been directed at using transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS) to characterize neuroplasticity and to augment rehabilitation targeting functional hand use after spinal cord injury. In addition to my interest in physical health, my work in recent years has focused on better understanding how to use exercise to promote neuroplasticity for improving cognitive brain health for aging individuals. The research study proposed in this KL2 application will investigate the mechanisms underlying cognitive benefits after an 8-week aerobic exercise intervention in adults aged 55+ years by combining the use of a non-invasive assessment of synaptic neuroplasticity by TMS and the examination of potential effect modifications by genetic factors. In addition, this KL2 Award will allow me to advance my academic career by obtaining training and mentorship from a distinct and cross-disciplinary group of established researchers at UMMSM and Harvard, combining the fields of clinical and translational research in older adults, genetics, neurophysiology and cognition. The successful completion of the research and training aims will allow me to approach my long-term goal of developing exercise interventions that can be individually tailored to promote cognitive brain health in aging adults, which will be the focus of a future K or R proposal. Given the stage of my clinical and research training, my research field and interests, and strong support from my mentorship team and the Chairs of Physical Therapy and Neurology, I believe I am an excellent candidate for this KL2 award.

B. Positions and Honors

Positions and Employment

- 2017- Assistant Professor (secondary appointment), Department of Neurology, University of Miami Miller School of Medicine.
- 2016- Member, Center on Aging, University of Miami Miller School of Medicine.
- 2014- Member, Evelyn F. McKnight Brain Institute University of Miami Miller, School of Medicine.
- 2014- Assistant Professor, Department of Physical Therapy, University of Miami Miller School of Medicine.
- 2013- Faculty, Transcranial Magnetic Stimulation Intensive Course, Berenson-Allen Center for Non-invasive Brain Stimulation. Beth Israel Deaconess Medical Center, Harvard Medical School.
- 2013-2015 Postdoctoral Research Fellow, Berenson-Allen Center for Noninvasive Brain Stimulation, Beth Israel Deaconess Medical Center, Harvard Medical School.
- 2010-2013 Research Support Specialist, The Miami Project to Cure Paralysis, University of Miami Miller School of Medicine.
- 2007-2010 Research Associate, the Miami Project to Cure Paralysis, University of Miami Miller School of Medicine.

Honors

- 2018 Dr. Gomes-Osman was selected to participate in the prestigious Training for Grantsmanship in Rehabilitation Research (TIGRR) that took place January 9 to 13, 2017 at the Wild Dunes Resort in Charleston (Isle of Palms) South Carolina, hosted by the Medical University of South Carolina. The TIGRR Workshop is funded by NIH/NICHHD grant number T15HD074546.
- 2007 Humberto de Castro Lima Award by the Bahiana School of Medicine and Public Health-Salvador, Brazil as Outstanding Student in the year of 2007.
- 2005 Fundacao de Amparo a Pesquisa do Estado da Bahia (FAPESB) Scholarship for Young Scientists. First non-MD student to be awarded this scholarship by the State of Bahia [Brazil] Foundation for Research

Other Experience and Professional Memberships

- 2018- Reviewer, *Experimental Gerontology*
- 2017- Reviewer, *Frontiers in Aging Neuroscience*
- 2016- Reviewer, *Scientific Reports*
- 2016- Reviewer, *Topics in Spinal Cord Injury Rehabilitation*
- 2016- Reviewer, *Experimental Brain Research*
- 2015- Reviewer, *Journal of Neuroscience*
- 2015- Reviewer, *The Lancet Neurology*
- 2015- Reviewer, *Annals of Neurology*
- 2015- Reviewer, *Frontiers in Psychology*
- 2015- Reviewer, *Lancet Neurology*
- 2014- Reviewer, *European Journal of Neuroscience*
- 2010- Member, American Physical Therapy Association
- 2010- Member, Society for Neuroscience
- 2009- Reviewer, *Journal of Neurologic Physical Therapy*

C. Contribution to Science

C1. Investigating dose of exercise needed to promote cognitive improvements in older adults, and determining consistency of cognitive improvements following exercise. My recent major contribution to the field and relevant to this proposal was a systematic review and regression analysis of 98 randomized clinical trials proposing exercise to improve cognition in older adults with and without cognitive impairments. This study aimed at describing various exercise dose measures, assessing their relationship with improved cognitive performance, and identifying consistent patterns of reported effects on cognition. I found that among various aspects of dose (session duration, weekly minutes, frequency, total weeks, total hours), only total hours was statistically tied to improved cognitive outcomes, and the most stable and consistent cognitive

improvements were seen in the cognitive domains of executive function and processing speed/attention. Furthermore, I found that while the majority of available evidence supports aerobic exercise, other exercise types such as resistance training and low-intensity yoga were also seen to improve cognitive performance in older adults. This study advances the field by producing practical, evidence-based dose parameters of exercise to improve cognitive function. I served as primary and corresponding author on this publications, which was selected for a media release and widely publicized in the media.

1. **Gomes-Osman J**, Cabral D, Morris TP, McInerney K, Oliveira A, Rundek T, and Pascual-Leone A. Exercise for cognitive brain cognitive health in aging: a systematic review for an evaluation of dose. *Neurology: Clinical Practice*; 2018; 1-9.

C2. Characterizing TMS Neuroplasticity and genetic differences in response of aerobic exercise on cognitive performance in middle-aged sedentary adults. In my post-doctoral work, I assessed the feasibility and safety of evaluating the effects of a month-long exercise intervention on cognitive performance, a TMS Measure of Neuroplasticity, and brain derived neurotrophic factor (BDNF) Met carrier status in young sedentary adults. I found cognitive improvements in executive function following 4 weeks of regular aerobic exercise. In addition, neuroplasticity appeared to differ according to BDNF allelic status. This work contributes to the literature by introducing an innovative neuroplasticity assessment and exploring genetic factors that may be useful in further elucidating exercise-mediated improvements in cognitive performance. This was the first study proposing TMS to assess neuroplasticity related to exercise-mediated cognitive improvements in humans and I served as first author.

1. **Gomes-Osman J**, Cabral D, Hinchman C, Jannati A, Morris TP, Pascual-Leone A. The effects of exercise on cognitive function and brain plasticity – a feasibility trial. *Restorative Neurology and Neuroscience*; 2017; 547-556.

C3. Determining stability of TMS measures and developing guidelines to improve internal consistency in TMS studies. In my earlier work I observed inter-individual variability in TMS outcomes, leading to my interest in improving the reproducibility of this technique during my post-doctoral work. I worked in a team on a study to calculate the internal consistency in different TMS measures (single-pulse TMS, paired-pulse TMS, TMS Plasticity), and determine the minimum number of pulses to achieve an accurate estimation of the mean and 95% confidence interval for these measures. This work adds to the literature by providing guidelines to achieve reliable measurements using TMS, and has the potential to decrease the variability often seen with TMS measures across the literature. I served as a co-author in this study.

1. Chang WH, Fried PJ, Saxena S, Jannati A, **Gomes-Osman J**, Kim YH, Pascual-Leone A; Optimal number of pulses as outcome measures of neuronavigated transcranial magnetic stimulation; *Clinical Neurophysiology*; 2016; 2892-2897.

C4. Transcranial magnetic stimulation (TMS), transcranial direct current stimulation (tDCS) and exercise promote neuroplasticity that supports unimanual and bimanual fine motor performance. My doctoral work focused on comparing non-invasive brain stimulation protocols for harnessing plasticity to augment motor function, both in neurologically healthy individuals and individuals with chronic incomplete tetraplegia. I found that TMS and tDCS applied to the primary motor cortex individually augmented the effects of neurorehabilitation exercise programs designed to improve fine motor hand function, both in neurologically healthy individuals and individuals with tetraplegia. This body of work provides evidence that TMS and tDCS can be used to improve the results of rehabilitation programs aimed at improving fine motor control of the hand. I served as primary author on these publications.

1. **Gomes-Osman J**, Field-Fote EC; Improvements in hand function in adults with chronic tetraplegia following a multi-day 10Hz rTMS intervention combined with repetitive task practice; *Journal of Neurologic Physical Therapy*; 2015; 23-30.
2. **Gomes-Osman J**, Field-Fote EC; Bihemispheric Anodal Corticomotor Stimulation Using Transcranial Direct Current Stimulation Improves Bimanual Typing Task Performance; *J Motor Behavior*; 2013; 361-367.
3. **Gomes-Osman J**, Tibbett JA, Poe BP, Field-Fote E. Priming for Improved Hand Strength in Persons with Chronic Tetraplegia: A Comparison of Priming-augmented Functional Task Practice, Priming Alone, and Conventional Exercise Training. *Frontiers in Neurology*; 2016; 1-13.

4. **Gomes-Osman J**, Field-Fote EC; Cortical versus afferent stimulation as an adjunct to functional task practice training: a randomized, comparative pilot feasibility study in people with cervical spinal cord injury; **Clinical Rehabilitation**; 2015; 771-782.

C5. Characterizing the influence of neuromodulation on neuroplasticity after acute peripheral nerve injury. My pre-doctoral work measured neuroplasticity in the form of axonal sprouting in a mouse model of sciatic crush lesion. I contributed to the validation of the sciatic static index for mice, a widely used and highly cited functional measure of sciatic nerve injury. In addition, I contributed to studies demonstrating that clinically available neurostimulation approaches such as TENS and low-frequency pulsed electromagnetic fields impair peripheral regeneration when applied in the cute stage after a crush lesion to the sciatic nerve in mice. I served as a co-author in these studies.

1. Baptista AF, Goes BT, Menezes D, Gomes FC, Zugaib J, Stipursky J, **Gomes JR**, Oliveira JT, Vannier-Santos MA, Martinez AM; PEMF fails to enhance nerve regeneration after sciatic nerve crush lesion. **Journal of the Peripheral Nervous System**; 2009; 285-293.
2. Baptista AF, **Gomes JR**, Oliveira JT, Santos SM, Vannier-Santos MA, Martinez AMB; High and low frequency transcutaneous electrical nerve stimulation delay sciatic nerve regeneration in the mouse. **Journal of Neuroscience Methods**; 2008; 71-80.
3. Baptista AF, **Gomes JR**, Oliveira JT, Santos SM, Vannier-Santos MA, Martinez AMB; A new approach to assess function after sciatic nerve lesion in the mouse-Adaptation of the sciatic static index. **Journal of Neuroscience Methods**; 2007; 259-264.

Complete List of Published Work in My Bibliography:

<http://www.ncbi.nlm.nih.gov/pubmed/?term=Joyce+Gomes>

<http://www.ncbi.nlm.nih.gov/pubmed/?term=Gomes-Osman>

1. Morris TP, Costa-Miserachs D, Rodriguez-Rajo P, Finestres J, Bernabeu M, **Gomes-Osman J**, Pascual-Leone A, Tormos-Muñoz JM. Feasibility of Aerobic Exercise in the Subacute Phase of Recovery from Traumatic Brain Injury: A Case Series. **Journal of Neurologic Physical Therapy**; 2018; in press.
2. **Gomes-Osman J**, Indahlastari A, Fried PJ, Cabral DLF, Rice J, Nissim NR, Aksu S, McLaren ME and Woods AJ. Non-invasive Brain Stimulation: Probing Intracortical Circuits and Improving Cognition in the Aging Brain. **Frontiers in Aging Neuroscience**; 2018; 1-25.
3. **Gomes-Osman J**, Cabral D, Morris TP, McInerney K, Oliveira A, Rundek T, and Pascual-Leone A. Exercise for cognitive brain cognitive health in aging: a systematic review for an evaluation of dose. **Neurology: Clinical Practice**; 2018; 1-9.
4. Spagnuolo G, Farias CDCM, da Silva BA, Ovando, AC, **Gomes-Osman J**, Swarowsky A. Are functional mobility tests responsive to group conventional physical therapy intervention in individuals with Parkinson's disease? **Neurorehabilitation**; 2018; 465-472.
5. **Gomes-Osman J**, Cabral D, Hinchman C, Jannati A, Morris TP, Pascual-Leone A. The effects of exercise on cognitive function and brain plasticity – a feasibility trial. **Restorative Neurology and Neuroscience**; 2017; 547-556.
6. **Gomes-Osman J**, Tibbett JA, Poe BP, Field-Fote E. Priming for Improved Hand Strength in Persons with Chronic Tetraplegia: A Comparison of Priming-augmented Functional Task Practice, Priming Alone, and Conventional Exercise Training. **Frontiers in Neurology**; 2016; 1-13.
7. Morris T, **Gomes-Osman J**, Costa-Miserach D, Pascual-Leone A. The Role of Physical Exercise in Cognitive Recovery After Traumatic Brain Injury: A Systematic Review. **Restorative Neurology and Neuroscience**; 2016; 977-988.
8. Chang WH, Fried PJ, Saxena S, Jannati A, **Gomes-Osman J**, Kim YH, Pascual-Leone A; Optimal number of pulses as outcome measures of neuronavigated transcranial magnetic stimulation; **Clinical Neurophysiology**; 2016; 2892-2897.
9. **Gomes-Osman J**, Cortes M, Guest J, Pascual-Leone A; A Systematic Review of Experimental Strategies Aimed at Improving Motor Function after Acute and Chronic Spinal Cord Injury. **Journal of Neurotrauma**; 2016; 425-438.

10. **Gomes-Osman J**, Field-Fote EC; Improvements in hand function in adults with chronic tetraplegia following a multi-day 10Hz rTMS intervention combined with repetitive task practice; *Journal of Neurologic Physical Therapy*; 2015; 23-30.
11. **Gomes-Osman J**, Field-Fote EC; Cortical versus afferent stimulation as an adjunct to functional task practice training: a randomized, comparative pilot feasibility study in people with cervical spinal cord injury; *Clinical Rehabilitation*; 2015; 771-782.
12. **Gomes-Osman J**, Field-Fote EC; Bihemispheric Anodal Corticomotor Stimulation Using Transcranial Direct Current Stimulation Improves Bimanual Typing Task Performance; *J Motor Behavior*; 2013; 361-367.
13. Baptista AF, Goes BT, Menezes D, Gomes FC, Zugaib J, Stipursky J, **Gomes JR**, Oliveira JT, Vannier-Santos MA, Martinez AM; PEMF fails to enhance nerve regeneration after sciatic nerve crush lesion. *Journal of the Peripheral Nervous System*; 2009; 285-293.
14. Baptista AF, **Gomes JR**, Oliveira JT, Santos SM, Vannier-Santos MA, Martinez AMB; High and low frequency transcutaneous electrical nerve stimulation delay sciatic nerve regeneration in the mouse. *Journal of Neuroscience Methods*; 2008; 71-80.
15. Baptista AF, **Gomes JR**, Oliveira JT, Santos SM, Vannier-Santos MA, Martinez AMB; A new approach to assess function after sciatic nerve lesion in the mouse-Adaptation of the sciatic static index. *Journal of Neuroscience Methods*; 2007; 259-264.

D. Research Support

Current

2017 **National Institutes of Health (NIH) R01 5R01AG053163-02.** A personalized health behavior system to promote well-being in older adults. This project consists in adapting an existing mobile application to promote increased participation in physical exercise, from middle-aged adults to the older adult population. **Role: Consultant (Exercise intervention development).** Grant amount \$579,139.

2017-2018 **Evelyn F. McKnight Brain Institute Internal Pilot Grant.** Aerobic exercise to influence mechanisms of brain plasticity and cognition in healthy aging. This project consists in the assessment of a 4-week aerobic exercise intervention on neuroplasticity and cognitive performance in healthy older individuals without cognitive impairments. **Role: Principal Investigator.** Grant amount \$10,000.

Past

2016-2017 **Foundation to Support Research in the State of Alagoas, Brazil (Fundacao de Amparo a Pesquisa do Estado do Alagoas- FAPEAL).** The use of exercise as a potential tool for brain health in healthy older adults and individuals with MCI: a systematic review aimed at identifying dose-related exercise recommendations. This project consists in a systematic review of randomized controlled trials proposing exercise to influence cognitive performance to assess the methodological quality, describe dose parameters of exercise, and outline evidence-based dose-specific recommendations. Fellowship for Danylo Cabral. **Role: Principal Investigator.** Grant amount: \$1,600.

2007-2012 **National Institutes of Health (NIH) R01 HD053854.** Improving Arm and Hand Function in Individuals with SCI. This project consisted of a comparison of different approaches to improve upper extremity function in individuals with tetraplegia using repetitive task practice and peripherally applied electrical stimulation. Principal Investigator: Edelle Field-Fote, PT, PhD. **Role: Project Coordinator.**

2010-2011 **National Institutes of Health (NIH) R01 HD053854-03S1.** Improving Arm and Hand Function in Individuals with SCI. This project consisted of a comparison of different approaches to improve upper extremity function in individuals with tetraplegia using repetitive task practice and repetitive transcranial magnetic stimulation. Principal Investigator: Edelle Field-Fote, PT, PhD. **Role: Project Coordinator**

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: **Jiang, Hong, MD PhD**

eRA COMMONS USER NAME (credential, e.g., agency login): HongJiang

POSITION TITLE: Clinical Assistant Professor

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	START DATE MM/YYYY	END DATE MM/YYYY	FIELD OF STUDY
Zhejiang Medical University, Hangzhou, Zhejiang	MD	09/1983	07/1988	Medicine
Zhejiang Medical University, Hangzhou, Zhejiang	MS	09/1990	07/1993	Neurology
University of Hong Kong, Hong Kong	PHD	09/1998	07/2001	Neuroscience
Zhejiang Medical University, Hangzhou, Zhejiang	Other training	09/1988	07/1990	Internship (Internal Medicine)
University of Rochester, Rochester, New York	Postdoctoral Fellow	09/2001	07/2005	Neuroscience
Rochester General Hospital, Rochester, New York	Other training	09/2005	07/2006	Intership (Internal Medicine)
Jackson Memorial Hospital/University of Miami, Miami, FL	Resident	09/2007	07/2010	Neurology
Bascom Palmer Eye Institute, University of Miami, Miami, FL	Fellow	09/2010	07/2011	Neuro-Ophthalmology

A. Personal Statement

As a neurologically trained neuroophthalmologist, I have a broad background in both basic and clinical research. I am a member of McKnight Brain Institute at the University of Miami and have been participating in various clinical trials on neurologic disorders. Working with the exceptional and experienced scientists and engineering team at the Bascom Palmer Eye Institute, I have been involved in advanced structural and functional ophthalmic imaging for more than 7 years in studying aging, multiple sclerosis and dementia. My work has been reflected in my recent publications as the corresponding author in the field of retinal and conjunctival functional imaging. The further developments of the retinal function imager (RFI) and optical coherence tomography angiograph (OCTA) image processing approach indicate that our team is well capable of conducting the proposed study. In summary, my expertise and experience make me well equipped and qualified for working on this proposed project.

1. **Jiang H**, Wei Y, Shi Y, Wright C, Sun X, Gregori G, Zheng F, Vanner EA, Lam BL, Rundek T, Wang J. Altered retinal microvasculature in mild cognitive impairment and Alzheimer's disease. Journal of neuro-ophthalmology. Epub ahead of print. PubMed PMID: [29040211](#).
2. **Jiang H**, Liu Y, Wei Y, Shi Y, Wright C, Sun X, Rundek T, Baumel B, Landman J and Wang J. Impaired retinal microcirculation in patients with Alzheimer's disease. PLOS one, 2018;e0192154. PubMed PMID: [29309463](#).
3. Wei Y, **Jiang H**, Shi Y, Qu D, Gregori G, Zheng F, Rundek T, Wang J. Age-Related Alterations in the Retinal Microvasculature, Microcirculation, and Microstructure. Invest Ophthalmol Vis Sci. 2017 Jul 1;58(9):3804-3817. PubMed PMID: [28744554](#); PubMed Central PMCID: [PMC5527847](#).

4. **Jiang H**, Delgado S, Liu C, Rammohan KW, DeBuc DC, Lam BL, Wang J. In Vivo Characterization of Retinal Microvascular Network in Multiple Sclerosis. *Ophthalmology*. 2016 Feb;123(2):437-8. PubMed PMID: [26299696](#); PubMed Central PMCID: [PMC4724448](#).

B. Positions and Honors

Positions and Employment

- 1990 - 1997 Neurologist, Second Affiliated Hospital of Zhejiang Medical University, Hangzhou
- 2011 - 2012 Clinical Instructor, Neuro-ophthalmology and Neurology, Bascom Palmer Eye Institute, University of Miami, Miami, FL
- 2012 - Clinical Assistant Professor, Neuro-ophthalmology & Neurology, Bascom Palmer Eye Institute & Dept. of Neurology, University of Miami, Miami, FL

Other Experience and Professional Memberships

- 2001 - Member, American Academy Of Neurology
- 2010 - Member, Association for Research in Vision and Ophthalmology
- 2010 - Member, American Association of Ophthalmology
- 2012 - Member, Member of American Heart Association
- 2012 - Fellow, North American Neuro-Ophthalmology Society
- 2017 - member, American Medical Association

Honors

- 1997 Lady Ivy Wu Fellowship , University of Hong Kong
- 1999 Travel Grant, International Federation of Parkinson's disease Foundations
- 2000 Young Investigator Award for Best Oral Presentation, Queen Mary Hospital
- 2000 Travel and Conference Award , Dr. Lo Kwee Seong Education Foundation
- 2008 Travel Award, Florida Society of Neurology
- 2011 ARVO Travel Grant, National Eye Institute

C. Contribution to Science

1. I initiated the development of automatic segmentation of the retinal microvascular network obtained using Retinal Function Imager (RFI) and Optic Coherence Tomography Angiography (OCTA) for studying retinal microvascular changes in multiple sclerosis, AD, diabetics and cerebral small vessel diseases.
 - a. **Jiang H**, Wei Y, Shi Y, Wright C, Sun X, Gregori G, Zheng F, Vanner EA, Lam BL, Rundek T, Wang J. Altered retinal microvasculature in mild cognitive impairment and Alzheimer's disease. *Journal of neuro-ophthalmology*. Epub ahead of print. PubMed PMID: [29040211](#).
 - b. Wei Y, **Jiang H**, Shi Y, Qu D, Gregori G, Zheng F, Rundek T, Wang J. Age-Related Alterations in the Retinal Microvasculature, Microcirculation, and Microstructure. *Invest Ophthalmol Vis Sci*. 2017 Jul 1;58(9):3804-3817. PubMed PMID: [28744554](#); PubMed Central PMCID: [PMC5527847](#).
 - c. **Jiang H**, Delgado S, Liu C, Rammohan KW, DeBuc DC, Lam BL, Wang J. In Vivo Characterization of Retinal Microvascular Network in Multiple Sclerosis. *Ophthalmology*. 2016 Feb;123(2):437-8. PubMed PMID: [26299696](#); PubMed Central PMCID: [PMC4724448](#).
 - d. **Jiang H**, DeBuc DC, Rundek T, Lam BL, Wright CB, Shen M, Tao A, Wang J. Automated segmentation and fractal analysis of high-resolution non-invasive capillary perfusion maps of the human retina. *Microvasc Res*. 2013 Sep;89:172-5. PubMed PMID: [23806780](#); PubMed Central PMCID: [PMC3773708](#).
2. To image microvasculature on the conjunctiva for studying cerebral small vessel diseases, a system called functional slit-lamp biomicroscope (FSLB) was developed. This novel system enables easily imaging the conjunctival microvascular network and small vessel blood flow velocity.

- a. Xu Z, **Jiang H**, Tao A, Wu S, Yan W, Yuan J, Liu C, DeBuc DC, Wang J. Measurement variability of the bulbar conjunctival microvasculature in healthy subjects using functional slit lamp biomicroscopy (FSLB). *Microvasc Res.* 2015 Sep;101:15-9. PubMed PMID: [26092682](#); PubMed Central PMCID: [PMC4537817](#).
 - b. Wang L, Yuan J, **Jiang H**, Yan W, Cintrón-Colón HR, Perez VL, DeBuc DC, Feuer WJ, Wang J. Vessel Sampling and Blood Flow Velocity Distribution With Vessel Diameter for Characterizing the Human Bulbar Conjunctival Microvasculature. *Eye Contact Lens.* 2016 Mar;42(2):135-40. PubMed PMID: [25839347](#); PubMed Central PMCID: [PMC4591084](#).
 - c. **Jiang H**, Zhong J, DeBuc DC, Tao A, Xu Z, Lam BL, Liu C, Wang J. Functional slit lamp biomicroscopy for imaging bulbar conjunctival microvasculature in contact lens wearers. *Microvasc Res.* 2014 Mar;92:62-71. PubMed PMID: [24444784](#); PubMed Central PMCID: [PMC3960300](#).
 - d. **Jiang H**, Ye Y, DeBuc DC, Lam BL, Rundek T, Tao A, Shao Y, Wang J. Human conjunctival microvasculature assessed with a retinal function imager (RFI). *Microvasc Res.* 2013 Jan;85:134-7. PubMed PMID: [23084966](#); PubMed Central PMCID: [PMC3534915](#).
3. To study retinal degeneration in neurological diseases such as multiple sclerosis, I contributed to the development of slit-lamp based ultra-high resolution OCT for imaging the retina. My contribution was to run the clinical validation and report the test results. Our segmentation software can manually segment 9 retinal sub-layers. Recently adapted Orion software enables automatic segmentation of 6 maps of retinal sub-layers.
- a. **Jiang H**, Delgado S, Tan J, Liu C, Rammohan KW, DeBuc DC, Lam BL, Feuer WJ, Wang J. Impaired retinal microcirculation in multiple sclerosis. *Mult Scler.* 2016 Dec;22(14):1812-1820. PubMed PMID: [26903007](#); PubMed Central PMCID: [PMC4993688](#).
 - b. **Jiang H**, Delgado S, Liu C, Rammohan KW, DeBuc DC, Lam BL, Wang J. In Vivo Characterization of Retinal Microvascular Network in Multiple Sclerosis. *Ophthalmology.* 2016 Feb;123(2):437-8. PubMed PMID: [26299696](#); PubMed Central PMCID: [PMC4724448](#).
 - c. Wang Y, **Jiang H**, Shen M, Lam BL, DeBuc DC, Ye Y, Li M, Tao A, Shao Y, Wang J. Quantitative analysis of the intraretinal layers and optic nerve head using ultra-high resolution optical coherence tomography. *J Biomed Opt.* 2012 Jun;17(6):066013. PubMed PMID: [22734769](#); PubMed Central PMCID: [PMC3381522](#).
 - d. **Jiang H**, Abukhalil F, Shen M, Gregori G, Lam BL, Wang Y, Wang J. Slit-lamp-adapted ultra-high resolution OCT for imaging the posterior segment of the eye. *Ophthalmic Surg Lasers Imaging.* 2012 Jan-Feb;43(1):76-81. PubMed PMID: [22251848](#).

Complete List of Published Work in My Bibliography:

<https://www.ncbi.nlm.nih.gov/myncbi/1buofoatUF5Q8/bibliography/48052483/public/>

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

NMSS, National Multiple Sclerosis Society	Jiang (PI)	04/01/16-03/31/19
The Role of retinal microvascular impairment on Neurodegeneration in Multiple Sclerosis		
The goal of this study is to determine the role of retinal microvascular impairment on neurodegeneration in MS.		
Role: PI,		
SUN_UM_1, Sun Yat-sen University Collaboration Award	Wang (PI)	10/01/15-09/30/20
Clinical applications of advanced ophthalmic imaging		
The goal of this study is to develop and apply advance ophthalmic imaging for clinical research in ophthalmology.		
Role: Co-Investigator		
Daybreak, Eli Lilly (pharmaceutical company)	Baumel (PI)	07/01/16-03/31/21

A Randomized, Double-Blind, Placebo-Controlled and Delayed-Start Study of LY3314814 in Mild Alzheimer's Disease Dementia

Role: Co-Investigator

Completed Research Support

NANOS Pilot 2015, North American Neuro-Ophthalmology Society Jiang (PI) 04/15/15-10/15/16

Retinal microvascular alteration as a possible biomarker in Alzheimer's disease

The purpose of this project is to characterize the retinal microvascular dysfunction and optical properties of Retinal nerve fiber layer in AD patients.

Role: PI

UM RSA 2015-41, University of Miami

Jiang (PI) 12/01/14-12/31/15

Ocular microvascular biomarkers in Alzheimer's disease

This project is a clinical trial for further studying tear dynamics after treatment with Restasis in dry eye patients.

Role: PI

R01EY020607S, NIH supplemental award

Cabrera DeBuc (PI) 02/01/12-01/31/14

Advanced imaging for diabetic retinopathy

This award (R01 supplement for 2 years) provides support under the Research Supplements to Promote Diversity in Health-Related Research Program to Dr. Jiang who studies retinal neurodegenerative diseases by using the unique prototype of UHR-OCT with added oximetry capability and the Retinal Function Imager (RFI).

Role: Co-Investigator

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Bonnie E. Levin, Ph.D.		POSITION TITLE Professor of Neurology and Psychology	
eRA COMMONS USER NAME bonnie_levin			
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Georgetown University	BS	1974	Psychology
Temple University	Ph.D.	1983	Psychology

A. Personal Statement

My role is to direct and implement all cognitive and behavioral assessments carried out in the Division of Neuropsychology, Department of Neurology at the University of Miami Miller School of Medicine. Currently, I hold the Bernard and Alexandria Schoninger Professorship in Neurology. I am the founder and Director of the Division of Neuropsychology and direct the Neuropsychology and Clinical Neuroscience Teaching Program. I supervise the clinical activities of PhD graduate students in the Child Clinical, Adult Clinical and Behavioral Medicine tracks. I have taught the graduate level course Foundations of Neuropsychology for over 25 years. I have had a long history of collaborations with numerous research teams in neurology, psychology and radiology, and participated in multiple projects examining cognitive, behavioral and imaging changes associated with normal aging and neurodegenerative disease. I am currently the site PI of the cognitive core on a study examining cognitive and behavioral changes among the oldest old funded by the Mcknight Brain Research Institute as well as the PI of the UM Mcknight Frailty Project and recently funded Susceptibility to Deception in the Aged grant. I am also a co-investigator on the NIH-funded population based Northern Manhattan Study, in which I am a member of the neuropsychology team and the dementia adjudication consensus panel. I am a co-investigator on the Bugher AHA grant and a Dept of Defense study examining brain metabolites underlying pain associated with traumatic injury. Currently I am the director of clinical outcomes on the Scythian Bioscience Project, a study examining the role of cannabinoids in TBI. My broad research expertise in cognitive, behavioral and socioemotional aging neuroscience over the lifespan and early biomarkers of behavioral and cognitive decline in neurodegenerative disease, as well as my experience as the director of a large clinical neuroscience lab, gives me necessary qualifications, expertise, administrative and leadership skills to direct the cognitive outcomes on the Mcknight frailty and cognitive core of the MBAR studies.

These peer reviewed publications highlight my experience and qualifications for this project:

1. Headley, A., De Leon-Benedetti, A., Dong, C., **Levin, B.**, Loewenstein, D., Camargo C., Rundek, T., Zetterberg, H., Blennow, K., Wright, C., Sun, X. and AD Neuroimaging Initiative. Neurogranin as a Predictor of Memory and Executive Function Decline in MCI patients. *Neurology* (in press)
2. Sun X, Dong C, **Levin B**, et al. APOE ε4 carriers may undergo synaptic damage conferring risk of Alzheimer's disease. *Alzheimers Dement*. 2016;12(11):1159-1166.
3. **Levin BE**, Llabre MM, Dong C, Elkind MS, Stern Y, Rundek T, Sacco RL, Wright CB. Modeling metabolic syndrome and its association with cognition: the northern Manhattan study. *J Int Neuropsychol Soc*. 2014 Nov;20(10):951-60.
4. Maudsley A, Govind V, **Levin B**, Saigal G, Harris LT, Sheriff S. Distributions of MR Diffusion and Spectroscopy Measures with Traumatic Brain Injury. *J Neurotrauma*. 2014 Oct 21. PMID: 25333480
5. Banerjee N, Getz S, & **Levin, BE**. Neurosensory, neuropsychological and psychiatric co-morbidities in mild TBI. In M. Hoffer & C. Balaban (Eds.), *Neurosensory Disorders in Mild Traumatic Brain Injury*, 2018, Cambridge, MA: Academic Press

Recent 2018-9 abstracts relevant to the proposed application:

Kaur, S., Banerjee, N., Miranda, M., Slugh, M., Sun-Suslow, N., McInerney, K., Sun, X., Ramos, A., Rundek, T., Sacco, R., Levin, B., Sleep quality, frailty and cognitive dysfunction in non-demented middle aged to older adults. To be presented at the 47th Annual meeting of the International Neuropsychological Society 2019, New York, New York.

Banerjee N, Hoffer M, Kiderman A, Hotz G, Getz S, Levin BE. Antisaccade abnormalities predict recovery on the Trail Making Test in mild TBI patients. Presented at the 3rd Joint Symposium of the International and National Neurotrauma Societies and AANS/CNS Section on Neurotrauma and Critical Care meeting, Aug 2018 Toronto, Ontario, Canada.

Gaztanaga W, Sarno M, Kaur S, Banerjee N, Bure-Reyes A, Miranda M, Slugh M, & Levin BE. Do sedatives impair cognition and behavior in Parkinson's disease? 16th American Academy of Clinical Neuropsychology annual meeting, June 2018 San Diego, CA.

Banerjee, N., McInerney, K. F., Getz, S. J., Sun-Suslow, N., Gomes-Osman, J., Bure-Reyes, A., Sarno, M., Dong, C., Sun, X., Rundek, T., Levin, B.E. (2018, March). *The Relationship between Fatigue and Executive Function in Aging Adults*. 8th International Conference on Frailty and Sarcopenia Research, Miami, FL. February, 2018.

Getz, S. J., McInerney, K. F., Banerjee, N. S., Gomes-Osman, J., Sun-Suslow, S., Merritt, S. Gaztanaga, W., Bure-Reyes, A., Sarno, M., Dong, C., Sun, C., Rundek, T., Levin, B. (2018, March). *Low Emotional Reserve as a Risk Factor for the Frailty Syndrome Independent of Gender*. 8th International Conference on Frailty and Sarcopenia Research, Miami, FL.

McInerney, K. F., Gomes-Osman, J., Banerjee, N. S., Getz, S. J., Sun-Suslow, S., Bure-Reyes, A., Sarno, M., Merritt, S., Gaztanaga, W., Dong, C., Sun, X., Rundek, T., Levin, B. (2018, March). *A Comparison of Frailty Criteria in Hispanic/Latino and Non-Hispanic/Latino Older Adults in South Florida*. 8th International Conference on Frailty and Sarcopenia Research, Miami, FL.

Getz, S. J., McInerney, K. F., Sun-Suslow, S., Banerjee, N. S., Bure-Reyes, A., Sarno, M., Levin, B. *Low Emotional Reserve as a Risk Factor for the Frailty Syndrome*. 46th annual meeting of the International Neuropsychological Society, Feb 2018 Washington, DC.

Sun-Suslow, S., Getz, S. J., McInerney, K. F., Banerjee, N. S., Bure-Reyes, A., Sarno, M., Levin, B. *The Association between Indicators of Physical Frailty Syndrome and Cognition*. 46th annual meeting of the International Neuropsychological Society, Feb 2018. Washington, DC.

Sarno, M., Bure-Reyes, A., Banerjee, N., Getz, S., McInerney, K., Sun-Suslow, N., Pinjala, M., Luca, C., Moore, H., Singer, C., & Levin, B. *Is Age of Onset Related to Cognition and Mood in Essential Tremor?* 46th annual meeting of the International Neuropsychological Society, Feb 2018, Washington, DC.

Banerjee, N., Sun-Suslow, N., Getz, S. J., Sarno, M., Bure-Reyes, A., Pinjala, M., Luca, C., Levin, B.E. (2018, February). *Age-related Differences in the Association between Cardiometabolic Risk Factors and Cognition in Parkinson's Disease*. 46th annual meeting of the International Neuropsychological Society, Feb 2018, Washington, DC.

B. Positions and Honors

POSITIONS AND EMPLOYMENT

Academic Appointments

1979-1980	Fellow in Psychology, Department of Psychiatry, Harvard Medical School, Boston, MA
1979-1980	Intern, Clinical Pediatric Neuropsychology, Children's Hospital Center, Boston, MA.
1980	Extern, Boston Veteran's Administration Hospital, Boston, MA
1981-1982	Instructor, Department of Neurology, University of Miami
1981	Director, Division of Neuropsychology, Department of Neurology, University of Miami
1986-1992	Assistant Professor, Department of Neurology, University of Miami
1992-2011	Associate Professor (with tenure), Department of Neurology, University of Miami Miller School of Medicine

Honors

Cum Laude, Georgetown University; Psi Chi Honor Society 1974

Fellow, Mahoney Residential College

International Neuropsychology Society (INS) Program Chair-1997

INS Board of Governors 1998-2001

NINDS Study Section Member NSD-K, 2001-2005

NINDS AD hoc Reviewer-NSD-A 2001, 2002

NINDS Special Emphasis Panels 7/1998, 8/1999, 12/1999, 5/2000, 8/2000, 10/2000, 12/2001, 6/2001, 10/2001, 8/2002, 12/2002, 1/2004, 8/2004, 12/2004, 2/2005, 1/2006, 10/2006, 11/2006, 11/2006, 6/2007, (6/24 & 6/29) 3/2008, 4/2008.

NINDS Ad hoc reviewer, NSD-K, 2006 - 2008

Alzheimer Association Medical and Scientific Council Reviewer, 1999, 2002

Consultant: University of Miami Brain Endowment Bank, Department of Neurology; Clinical

Neuroscience Unit, UM Department of Neurology

Member, National Acute Brain Injury Study: Hypothermia II: Data Safety of Monitoring Board

Pediatrics; UM Sleep Center, Department of Neurology.

Professional Advisory Board: Epilepsy Foundation of South Florida

Editorial Boards: Neuropsychology, Journal of International Neuropsychology Society,

Neuropsychology Review, Aging, Neuropsychology and Cognition

Alexandria and Bernard Schoninger Endowed Professorship in Neurology, 2009

C. Contributions to Science

C.1. Over the past 30 years, I have focused on cognitive and behavioral changes over the life course. My research projects are largely in the field of aging, examining age related cognitive decline and early biomarkers of behavioral and cognitive decline in normal aging and neurodegenerative disease. As the Schoninger Professor of Neurology, I oversee the Division of Neuropsychology, a major training and research site that evaluates over 300 patients a year examining age related cognitive change as well as pathological behavioral alterations associated with degenerative disease. I have published extensively on cognitive change across the lifespan.

1. Kelley, R.E., Chang, JY, Scheinman, NJ, **Levin, BE**, Duncan, RC, Shih-Chang, L: Transcranial doppler ultrasonographic assessment of cerebral artery flow velocity during cognitive activity. *Stroke*, 1992; 23:9-14.
2. Tomer, R, **Levin, BE**, Differential affects of aging in two verbal fluency tasks. *Perceptual and Motor Skills*, 1993; 76: 465-466
3. **Levin, BE**, Katzen, H.L., Klein, B., Llabre, M. Cognitive decline affects subject attrition in longitudinal research. *Journal of Clinical and Experimental Neuropsychology*. 2000, 22 (5), 580-586.
4. Grossman A, Levin B, Katzen H, Lechner S. PTSD symptoms and onset of neurologic disease in elderly trauma survivors. *Journal of Clinical and Experimental Neuropsychology* 2004; 26(5): 698-705.

C.2. Our group was among the earliest investigators to document and describe non-motor changes in Parkinson's disease. I have also examined how gait and other lateralized motor changes are linked to cognitive and behavioral symptoms and PD progression. These studies reflect my longstanding interest in gait, movement and cognition.

1. **Levin, BE**, Llabre, MM, Weiner, WJ: Cognitive impairments associated with early Parkinson's disease. *Neurology*, 1989, 39:557-561.
2. **Levin, BE**, Llabre, MM, Weiner, WJ, Brown, MC: Visuospatial decline in Parkinson's disease. *Neurology*, 1991; 41:365-369.
3. Tomer, R, **Levin, BE**, Weiner, WJ: Side of motor onset influences cognition in Parkinson's disease. *Annals of Neurology*, 1993; 34:579-584.
4. Katzen, H, **Levin, BE**, Llabre, M: Age of onset influences cognition in Parkinson's disease. *Journal of International Neuropsychological Society*, 1998, 4, 285-290.

C.3. I am currently involved in several studies examining the relationship between MRS metabolites and cognitive changes in normative aging, TBI, ALS and Parkinson's disease. These studies utilize a unique whole brain analysis that permits a study of a large fraction of the brain volume, including the cortical mantle. My role as the neuropsychologist on these projects is to identify sensitive outcome measures and to work with my collaborators linking the behavioral presentation associated a traumatic injury or neurologic illness with distributions of proton magnetic resonance spectroscopy (MRS) observed metabolites throughout the whole brain.

1. **Levin BE**, Katzen, HL, Maudsley, A, Post, J, Myerson, C, Govind, G, Nahab, F, Scanlon, B, Mittel. A Whole-brain proton MR spectroscopic imaging in Parkinson's disease. *Journal of Neuroimaging*, 2014, 24, 39-44

2. Maudsley, A, Govind, V, **Levin, BE**, Saigal, G, Harris, L, Sheriff, S Distributions of MR Diffusion and Spectroscopy Measures with Traumatic Brain Injury. J. Neurotrauma. 2015; 32 (14): 1056-1063
 3. Widerstrom-Noga, E, Govind, VB, Adcock, J, **Levin, BE**, Maudsley, A Subacute Pain after TBI is associated with lower insular N-acetyl-aspartate concentrations. J Neurotrauma, 2016; 33(14):1380-9
- Complete List of Published Work at NCBI:
[http://www.ncbi.nlm.nih.gov/pubmed/?term=\(%22levin%2C%20bonnie%22%5BAll%20Fields%5D\)&cmd=DetailsSearch](http://www.ncbi.nlm.nih.gov/pubmed/?term=(%22levin%2C%20bonnie%22%5BAll%20Fields%5D)&cmd=DetailsSearch)

D. Research Support **Ongoing Research Support**

Scythian Bioscience

The Effects of Cannabinoids on TBI

08/01/2016-7/30/2021

(\$16,000,0000)

B. Levin, Co-Investigator, Director of Clinical Trials

This study will examine the inflammatory properties of cannabinoids and determine whether they can be used as a therapeutic intervention in traumatic brain injury

7 R01 NS 029993 (PI, Sacco) NIH/NINDS

Stroke Incidence and Risk Factors in a TriEthnic Region

02/01/03-03/31/21

1.20 calendar

(B. Levin, Co-Investigator)

The goals of this project are to determine the effects of risk factors for stroke, MI, and vascular death, as well as evaluate predictors of cognitive impairment and the importance of subclinical MRI findings in a prospective cohort study of 3300 persons from 3 race-ethnic groups from Northern Manhattan.

09/28/12-09/27/15

1.20 calendar

National Multiple Sclerosis

Fast Forward a Randomized Double Blind Placebo Controlled (PI: Ortega; B. Levin, Co-Investigator)

To evaluate the therapeutics effects of caprylic triglyceride administered once a day for 90 days on cognitive impairment in subjects with multiple sclerosis.

\$169,003

AHA/ASA 14BFSC1759000 (PI: Sacco)

AHA (B. Levin, Co-Investigator)

Bugher Center Foundation Center of Excellence in Stroke Award

This award will conduct two projects evaluating the effects of physical activity and cognitive training on animals and stroke survivors on cognitive recovery

04/01/14 – 03/31/18

0.6 calendar

\$234,667

DoD/CDMRP/USAMRMC (PI: Widerstrom-Noga)

(B. Levin, Co-Investigator)

Utility of MRS Brain Biomarkers of Pain Phenotypes after TBI

Goals are to evaluate advanced metabolic imaging methods for injury assessment and prognosis following mild and moderate traumatic brain injury.

11/2015-10/2018

.84 calendar

\$977,099 (direct)

Prior Research Support

NINDS 1 UO1 NS052478-01A2 (Adelson)

Pediatric Traumatic Brain Injury Consortium: Hypothermia

This is a multicenter clinical trial to determine the efficacy of early induced moderate hypothermia after severe TBI in a pediatric sample. Subject mortality at 3 months is the primary measure of outcome. Secondary outcome measures included functional assessment and performance based neuropsychological measures. Role: Study Principal Investigator of the Outcome Center.

7/30/07 – 6/30/2011

NIH/NINDS 2U01NS38529-07A1 (Benavente/ Romano, site PI)

Secondary Prevention of Small, Subcortical Strokes (SPS3)

NIH/NINDS R01 NS055107 (Maudsley)

Volumetric MRSI Evaluation of Traumatic Brain Injury

Goals are to evaluate advanced metabolic imaging methods for injury assessment and prognosis following mild and moderate traumatic brain injury.

6/1/2006 – 12/31/2012

NIH/NINDS R01 NS060874 (Govind)

Brain Metabolic Imaging in Amyotrophic Lateral Sclerosis

The major goal of this project is to examine the efficacy of whole-brain proton MRSI and DTI methods for evaluating cerebral pathological changes in ALS.

1/1/2009 – 8/31/2012

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Miguel A. Perez-Pinzon, PhD, FAHA		POSITION TITLE Professor	
eRA COMMONS USER NAME mperezpinzon			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
University of Panama	B.Sc.	1983	Biology
University of Miami (RSMAS)	M.Sc.	1987	Marine Biology
University of Miami (RSMAS/Neurology)	PhD	1991	Neuroscience
New York University	Postdoc	1992	Neurophysiology
Stanford University	Postdoc	1993	Neuroscience

A. Personal Statement

Although I have been working on cerebral hypoxia/ischemia since 1987, my independent group at the University of Miami was established in 1995 and in the last two decades has been studying cerebral ischemia. I direct the Cerebral Vascular Disease Research Center at the University of Miami since 2005, which was established approximately 45 years ago by Dr. Pertiz Scheinberg (first Chair of Neurology at UM). Many seminal investigators of the field directed or were part of this center (e.g., Kyuya Kogure, Mordecai Globus, Dalton Dietrich). Dr. Myron Ginsberg led the center for 22 years until 2005. I am a Professor of Neurology and Neuroscience and I am Vice-Chair of Basic Sciences in the Department of Neurology. My main research expertise is in the area of cerebral ischemia, which results from cardiac arrest or stroke. My research focuses on the areas of synaptic, cognitive, vascular and mitochondrial dysfunction that ensue following cerebral ischemia. Over the last 20 years, my laboratory has investigated the signaling pathways that lead to neuroprotection against cerebral ischemia. A major emphasis has been our work in cardiac arrest and its devastating effect on hippocampal pathology. Our goal is to develop new therapies for pre- and post-treatment in cardiac arrest patients. Our center uses a large number of techniques that include imaging, electrophysiology, behavior, stereotaxic surgeries, and molecular biology techniques.

B. Positions and Honors.**PROFESSIONAL APPOINTMENTS**

1995 – 2001 Assistant Professor, Department of Neurology, University of Miami School of Medicine.
1999 – 2006 Co-Director of Cerebral Vascular Disease Center, University of Miami School of Medicine, Miami, FL (Dr. Ginsberg, Director)
2001 – 2006 Associate Professor, Department of Neurology, University of Miami School of Medicine.
2005 – present Director of Cerebral Vascular Disease Center, University of Miami, Miller School of Medicine, Miami, FL
2006 – present Professor, Department of Neurology, University of Miami Miller School of Medicine, Miami, FL
2007 – 2010 Associate Chair for Basic Science, Department of Neurology, University of Miami Miller School of Medicine, Miami, FL
2010 – present Vice-Chair for Basic Science, Department of Neurology, University of Miami Miller School of Medicine, Miami, FL

AWARDS AND OTHER PROFESSIONAL ACTIVITIES:

1982, 1983 Fellowships (2), Smithsonian Tropical Research Institute (STRI). Panama
1986 Fellowship, Fishing and Conservation Trust. Miami, FL
1989 - present Member of Society for Neuroscience (1989), International Society on Oxygen Transport to Tissues (1996), International Society of Cerebral Blood Flow and Metabolism (1995),

- American Association for the Advancement of Science (1996) and American Heart Association (2000)
- 1991 Koczy Fellowship, (Graduate student of the year) for excellence in graduate research and education, Rosenstiel School of Marine and Atmospheric Science, Univ of Miami, Miami, FL
- 1991 Invited speaker at the Society for Experimental Biology in Birmingham, U.K.
- 2000 – 03 NIH-NINDS BDCN-3 Study Section reviewer
- 2000 Invited speaker at the Pharmacology of Cerebral Ischemia Symposium. Marburg, Germany.
- 2002 Grass Traveling Scientist for the Alaska Chapter of the Society for Neuroscience. Society for Neuroscience
- 2004 – 08 Brain 2 American Heart Association Grant Reviewer
- 2006 – 10 NIH-NINDS BINP Study Section
- 2014 NIH-NINDS BINP Study Section Ad-hoc member
- 2007 – 08 International Stroke Conference Program Committee: Co-Chair–Experimental Mechanisms and Models.
- 2008 – 10 International Stroke Conference Program Committee: Chair–Experimental Mechanisms and Models.
- 2009 Associate Editor for the journal: Translational Stroke Research
- 2010 Assistant Editor for the journal: Stroke
- 2010 Elected as Fellow of the American Heart Association/American Stroke Association (FAHA)
- 2012-13 Co-Chair of the Program Committee for the International Society of Cerebral Blood Flow and Metabolism (Brain 13), Shanghai, China
- 2014 Member of the Program Committee for the International Society of Cerebral Blood Flow and Metabolism (Brain 15), Vancouver, Canada
- 2016-18 Vice-Chair of the Program Committee for the International Stroke Conference.
- 2018-20 Chair of the Program Committee for the International Stroke Conference.

C. Contribution to Science

1. A major area of research in my group is to define the pathological mechanisms in the brain that ensue following cardiac arrest. We have targeted multiple aspects of the pathology that include synaptic dysfunction, cognitive impairments and cerebral blood flow derangements. We have shown that PKC ϵ activation provides neuroprotection while activation of δ PKC is detrimental to the ischemic brain. Overall, my studies provide a potential pathway of ischemia-mediated neuroprotection by the regulation of cerebral blood flow from evaluating blood flow dynamics, neuroprotection, and functional neuronal outcomes/firing properties based on electrophysiological studies.
 - a. Cohan, C. H., Neumann, J. T., Dave, K. R., Alekseyenko, A., Binkert, M., Stransky, K., Lin, H. W., Barnes, C. A., Wright, C. B. & Perez-Pinzon, M. A. Effect of cardiac arrest on cognitive impairment and hippocampal plasticity in middle-aged rats. *PLoS One* 10, e0124918, (2015). PMID:25933411
 - b. Lin, H. W., Gresia, V. L., Stradecki, H. M., Alekseyenko, A., Dezfulian, C., Neumann, J. T., Dave, K. R. & Perez-Pinzon, M. A. Protein kinase C delta modulates endothelial nitric oxide synthase after cardiac arrest. *J Cereb Blood Flow Metab* 34, 613-620, (2014). PMID:24447953
 - c. Lin, H. W., Defazio, R. A., Della-Morte, D., Thompson, J. W., Narayanan, S. V., Raval, A. P., Saul, I., Dave, K. R. & Perez-Pinzon, M. A. Derangements of post-ischemic cerebral blood flow by protein kinase C delta. *Neuroscience* 171, 566-576, (2010). PMID:20813167
 - d. Raval, A. P., Dave, K. R., Prado, R., Katz, L. M., Busto, R., Sick, T. J., Ginsberg, M. D., Mochly-Rosen, D. & Perez-Pinzon, M. A. Protein kinase C delta cleavage initiates an aberrant signal transduction pathway after cardiac arrest and oxygen glucose deprivation. *J Cereb Blood Flow Metab* 25, 730-741, (2005). PMID:15716854
2. My group has been studying mitochondrial dysfunction for approx 20 years. In the late 1990's we carried out several studies that defined the effect of anoxia/ischemia and reperfusion on mitochondrial electron carrier hyperoxidation, including NADH. We also published simultaneously with the Pak Chan's group in

1999, the first study demonstrating cytochrome c release from mitochondria following cerebral anoxia/ischemia. For the last 15 years, my group has done seminal work on the signaling pathways that lead to mitochondrial dysfunction and apoptosis and on signaling pathways that lead to ischemic neuroprotection.

- a. Morris-Blanco, K. C., Dave, K. R., Saul, I., Koronowski, K. B., Stradecki, H. M. & Perez-Pinzon, M. A. Protein Kinase C Epsilon Promotes Cerebral Ischemic Tolerance Via Modulation of Mitochondrial Sirt5. *Sci. Rep.* **20**;6:29790 (2016). PMID: 27435822
 - b. Morris-Blanco, K. C., Cohan, C. H., Neumann, J. T., Sick, T. J. & Perez-Pinzon, M. A. Protein kinase C epsilon regulates mitochondrial pools of Nampt and NAD following resveratrol and ischemic preconditioning in the rat cortex. *J Cereb Blood Flow Metab* **34**, 1024-1032, (2014). PMID:24667915
 - c. Thompson, J. W., Dave, K. R., Saul, I., Narayanan, S. V. & Perez-Pinzon, M. A. Epsilon PKC increases brain mitochondrial SIRT1 protein levels via heat shock protein 90 following ischemic preconditioning in rats. *PLoS One* **8**, e75753, (2013). PMID:24058702
 - d. Dave, K. R., DeFazio, R. A., Raval, A. P., Torraco, A., Saul, I., Barrientos, A. & Perez-Pinzon, M. A. Ischemic preconditioning targets the respiration of synaptic mitochondria via protein kinase C epsilon. *J Neurosci* **28**, 4172-4182, (2008). PMID:18417696
3. My group has also been a leader in the field of ischemic preconditioning. We have been studying compounds such as resveratrol and certain PKC isoforms to pharmacologically precondition *in vivo* and *in vitro* to lessen ischemia-induced neuronal damage. We sought to identify novel preconditioning pathways to alleviate ischemia, so therapies can be developed based on this mechanistic approach.
- a. Koronowski, K. B., Dave, K. R., Saul, I., Camarena, V., Thompson, J. W., Neumann, J. T., Young, J. I. & Perez-Pinzon, M. A. Resveratrol Preconditioning Induces a Novel Extended Window of Ischemic Tolerance in the Mouse Brain. *Stroke* **46**, 2293-2298, (2015). PMID:26159789
 - b. Neumann, J. T., Thompson, J. W., Raval, A. P., Cohan, C. H., Koronowski, K. B. & Perez-Pinzon, M. A. Increased BDNF protein expression after ischemic or PKC epsilon preconditioning promotes electrophysiologic changes that lead to neuroprotection. *J Cereb Blood Flow Metab* **35**, 121-130, (2015). PMID:25370861
 - c. Narayanan, S. V., Dave, K. R., Saul, I. & Perez-Pinzon, M. A. Resveratrol Preconditioning Protects Against Cerebral Ischemic Injury via Nuclear Erythroid 2-Related Factor 2. *Stroke* **46**, 1626-1632, (2015). PMID:25908459
 - d. Raval, A. P., Dave, K. R., Mochly-Rosen, D., Sick, T. J. & Perez-Pinzon, M. A. Epsilon PKC is required for the induction of tolerance by ischemic and NMDA-mediated preconditioning in the organotypic hippocampal slice. *J Neurosci* **23**, 384-391, (2003). PMID:12533598

Complete List of Published Work in MyBibliography:

<https://www.ncbi.nlm.nih.gov/myncbi/browse/collection/40678659/?sort=date&direction=descending>

D. Research Support.

Active

R01 NS45676-08 **Perez-Pinzon (PI)** 6/1/07-5/31/15

NIH/NINDS

Mechanisms of Neuroprotection against Cardiac Arrest

The major goal of this project is to study the mechanisms of synaptic and vascular dysfunction and putative neuroprotective agents following cardiac arrest.

Non-cost extension

R01 NS34773-15 **Perez-Pinzon (PI)** 6/1/15-5/31/20

NIH/NINDS

Ischemic Preconditioning: Mechanisms of Neuroprotection

The major goal of this project is to study the signaling pathways that lead to ischemic preconditioning neuroprotection

American Heart Association/ASA-Bugher Foundation (14BFSC17690007). Sacco R. (PI) 4/1/14-3/31/18
Physical and Cognitive Training to Enhance Post-Stroke Outcomes. **Project 2 (PI – Perez-Pinzon):** Enriched Environment, Exercise And Neurotherapeutics To Enhance Functional Recovery Following A Stroke

1R21NS098896-01 **Perez-Pinzon (PI)** 7/1/16-6/30/18
NIH/NINDS

Decellularized Extracellular Matrix Biomaterials As Therapy To Ameliorate Cerebral Ischemia Damage
The goals of the project are for the University of Miami to help build stroke research capabilities at INDICASAT AIP, Panama that will ultimately help foster stronger collaboration between the two institutes and to evaluate therapeutic potential of decellularized extracellular matrix biomaterials against cerebral ischemic damage.

BIOGRAPHICAL SKETCH

NAME: Milena Pinto

eRA COMMONS USER NAME (credential, e.g., agency login): Pintom1n

POSITION TITLE: Research Assistant Professor

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date MM/YYYY	FIELD OF STUDY
• Universita' degli studi di Trieste, Italy	M.Sc.	04/2005	Medical Biotechnology
• International School for Advanced Studies (SISSA) Trieste, Italy	Ph.D.	11/2009	Neurobiology
• University of Miami, Miller School of Medicine, Miami, USA	Postdoc	04/2015	Neurobiology

A. Personal Statement

I have more than ten years of research experience on neurodegenerative disorders, in particular on Parkinson's and Alzheimer's disease. During my Masters and PhD studies, I extensively worked on drug-induced and genetically modified animal models of neurodegeneration as well as on neuronal cellular models and primary cultures. For my postdoctoral training, I have been involved in understanding the possible neuronal-specific role of mitochondrial dysfunctions and mitochondrial DNA deletions and depletion in mouse models of neurodegenerative disorders, in particular of Parkinson's and Alzheimer's diseases. I mastered techniques in the study of motor and behavior disorders in mouse models and I focused my research in the neurodegeneration associated with Alzheimer's and aging. I recently accepted an appointment as research assistant professor at the University of Miami to establish a program in Alzheimer's Disease.

B. Positions and Honors.**PROFESSIONAL APPOINTMENTS****Mar 2017-present** Research Assistant Professor at Neurology department, University of Miami**Apr 2015-Mar 2017** Sr. Research Associate at Neurology department, University of Miami**Apr 2010-Apr 2015** Postdoctoral Associate at Neurology department, University of Miami**Nov 2009-Apr 2010** Temporary Research Fellow, SISSA, Trieste, Italy**HONORS**

Nov-2014 ISSNAF Award for young Investigators, Special Mention, Bio-Medicine and Cognitive Sciences

April-2013 UMDf, Mitochondrial Medicine 2013 Abstract Cash Award

March-2013 Medical Faculty Association Travel Award from the Margaret Whelan foundation

C. Contribution to Science

1. I became involved in the study of neurodegenerative diseases during my Ph.D. at the International School for Advanced Studies (SISSA) in Trieste, Italy, under the supervision of Dr. Stefano Gustincich. In my first years I was involved in the study of the role of PARK7/DJ-1 gene, whose mutations are associated to autosomal recessive early onset forms of Parkinson's disease (PD). We studied two DJ-1 missense mutations that cause misfolding of the protein, degradation or accumulation into insoluble cytoplasmic aggregates. By yeast-two hybrid screening, we identified two novel DJ-1 interactors (TRAF6 and TTRAP) that bound more strongly the mutated forms than the wild type form of DJ1, and we analyzed in vitro their role in physiologic and pathologic conditions.

Moreover, we discovered that both the proteins were present in the Lewy Bodies (neuropathological hallmarks of PD) of post mortem brains of PD patients, identifying them as new players not only in rare genetic cases of PD but also in the more common sporadic cases.

A. Zucchelli S, Vilotti S, Calligaris R, Lavina ZS, Biagioli M, Foti R, De Maso L, **Pinto M**, Gorza M, Speretta E, Casseler C, Tell G, Del Sal G, Gustincich S.

Aggresome-forming TTRAP mediates pro-apoptotic properties of Parkinson's disease-associated DJ-1 missense mutations.

Cell Death and Differentiation 2009 Mar;16(3):428-38 [PMID 19023331]

B. Zucchelli S., Codrich M, Marcuzzi F, **Pinto M**, Vilotti S., Biagioli M, Ferrer I, Gustincich S.

TRAF6 promotes atypical ubiquitination of mutant DJ-1 and alpha-synuclein and is localized to Lewy bodies in sporadic Parkinson's disease brains.

Hum Mol Genet. 2010 Jul 14 [PMID: 20634198]

C. Vilotti S, Codrich M, Dal Ferro M, **Pinto M**, Ferrer I, Collavin L, Gustincich S, Zucchelli S.

Parkinson's disease DJ-1 L166P alters rRNA biogenesis by exclusion of TTRAP from the nucleolus and sequestration into cytoplasmic aggregates via TRAF6.

PLoS One. 2012;7(4):e35051 [PMID: 22532838]

2. During my PhD I also studied the expression profile of A9 neurons of *substantia nigra*, a subpopulation of dopaminergic neurons that degenerate in patients affected by Parkinson's disease. This research project led to the discovery that these particular neurons express alpha and beta chains of hemoglobin, a well-known protein with essential role in binding and delivering oxygen, carbon dioxide and nitric oxide. This particular finding opened a new line of research since hemoglobin has a non-oxygen-carrying function as an antioxidant and a regulator of iron metabolism, both essential mechanisms involved in the pathogenesis of Parkinson's disease. These findings helped other researchers to look into the role of this protein in brain metabolism, finding correlations with Alzheimer's disease, Parkinson's disease and dementia with Lewy bodies. Moreover, Hemoglobin-derived peptides have been studied as novel type of bioactive signaling molecules. We also discovered that 46% of genes that encode for subunits of mitochondrial complex I-V were induced in stable cell lines overexpressing hemoglobin chains, suggesting a link between hemoglobin expression and mitochondrial biogenesis/function.

A. **Milena Pinto**(*), Marta Biagioli (*), Daniela Cesselli, Marta Zaninello, Dejan Lazarevic, Roberto Simone, Christina Vlachouli, Charles Plessy, Nicolas Bertin, Antonio Beltrami, Kazuto Kobayashi, Vittorio Gallo, Isidro Ferrer, Claudio Santoro, Stefano Rivella, Carlo Alberto Beltrami, Piero Carninci, Elio Raviola and Stefano Gustincich. (*) co-authorship

Unexpected expression of α - and β -globin in mesencephalic dopaminergic neurons and glial cells
PNAS, 2009 Sep. vol.106 no.36 [PMID: 19717439]

3. As a result of this work in Italy, I was recruited to join the Neurology Department of the University of Miami, Miller School of Medicine as a Postdoctoral Associate. I joined Dr. Carlos Moraes laboratory to expand my knowledge and research in the study of the role of mitochondria in neurodegenerative diseases. Neuronal OXPHOS deficiency, in fact, has been associated with a variety of late-onset progressive neurodegenerative diseases, including Parkinson's disease and Alzheimer's disease. Almost all the animal models of PD available at that time were created by knocking out or knocking in mutated forms of the genes involved in the rare genetic forms of PD. In order to create a model resembling the more common sporadic forms of PD, we decided to induce mitochondrial defects in different neuronal subpopulations, mimicking the mitochondrial function decline that occurs naturally with aging. We induced OXPHOS deficiency in neurons by inducing mitochondrial DNA depletion, or by knocking out mitochondrial Complex IV, one of the complexes that is deficient in PD patients. By inducing mtDNA depletion in neurons we discovered that the striatum is particularly sensitive to defects in OXPHOS and these results helped explain how mitochondrial dysfunctions alone can lead to a preferential elimination of certain neuronal populations *in vivo*. We then created and compared two different mouse models of PD, one mimicking the pathology slow progression that occurs in sporadic PD cases, the other more similar to late stages of the disease. Because mitochondrial dysfunctions have been closely associated with PD, the creation of this new mouse models provided important clues to the pathophysiology of the disease. The PD mouse models have been widely received and accepted in the field and can provide also a valuable tool to test new mitochondrial therapies in the treatment of this disease.
- A. Alicia Pickrell, Hirokazu Fukui, Xiao Wang, **Milena Pinto**, and Carlos Moraes
The Striatum is Highly Susceptible to Mitochondrial Oxidative Phosphorylation Dysfunctions
J Neurosci. 2011 Jul 6;31(27):9895-904 [PMID: 21734281]
- B. **Milena Pinto(*)**, Alicia Pickrell(*), Aline Hida, Carlos Moraes (*) **co-authorship**
Striatal dysfunctions associated with mtDNA damage in dopaminergic neurons of a mouse model of PD
J Neurosci. 2011 Nov 30;31(48):17649-58 [PMID: 22131425]
- C. **Pinto M**, Nissanka N, Peralta S, Brambilla R, Diaz F, Moraes CT.
Pioglitazone ameliorates the phenotype of a novel Parkinson's disease mouse model by reducing neuroinflammation.
Mol Neurodegener. 2016 Apr 2;11(1):25 [PMID: 27038906]
- D. **Pinto M**, Nissanka N, Moraes CT.
Lack of Parkin Anticipates the Phenotype and Affects Mitochondrial Morphology and mtDNA Levels in a Mouse Model of Parkinson's Disease.
J Neurosci. 2018 Jan 24;38(4):1042-1053. [PMID: 29222404]
4. Even though my main line of research is focused on neurodegenerative disorders, my contribution has also been essential in other fields where mitochondrial dysfunctions play an important role, like aging, age-related cachexia, and mitochondrial diseases (Leber's hereditary optic neuropathy plus dystonia), as shown in recent publications in Human Molecular Genetics, Nature Medicine, and Cell Death and Differentiation.
- A. Bacman SR, Williams SL, **Pinto M**, Peralta S, Moraes CT.
Specific elimination of mutant mitochondrial genomes in patient-derived cells by mitoTALENs.
Nat Med. 2013 Sep;19(9) [PMID: 23913125]
- B. Wang X, Pickrell AM, Rossi SG, **Pinto M**, Dillon LM, Hida A, Rotundo RL, Moraes CT.
Transient systemic mtDNA damage leads to muscle wasting by reducing the satellite cell pool.
Hum Mol Genet. 2013 Oct 1;22(19):3976-86 [PMID: 23760083]

C. **Milena Pinto**(*), Alicia M Pickrell(*), Xiao Wang(*), Sandra R Bacman, Aixin Yu, Aline Hida, Lloye M Dillon, Paul D Morton, Thomas R Malek, Siôn L Williams and Carlos T Moraes (*) **co-authorship**.

Transient mitochondrial DNA double strand breaks in mice cause accelerated aging phenotypes in a ROS-dependent but p53/p21-independent manner.

Cell Death and Differentiation 2016, December 2; doi: 10.1038/cdd.2016.123

D. Bacman SR, Kauppila JHK, Pereira CV, Nissanka N, Miranda M, **Pinto M**, Williams SL, Larsson NG, Stewart JB, Moraes CT.

MitoTALEN reduces mutant mtDNA load and restores tRNA^{Ala} levels in a mouse model of heteroplasmic mtDNA mutation. Nat Med. 2018 Nov;24(11):1696-1700 [PMID: 30250143]

5. Since mtDNA damage and the generation of reactive oxygen species have been associated with and implicated in the development and progression of Alzheimer's disease, we studied how mtDNA damage affects reactive oxygen species and amyloid beta pathology in vivo. We generated an Alzheimer's disease mouse model expressing an inducible mitochondrial-targeted endonuclease (Mito-PstI) in the central nervous system that cleaves mtDNA causing mtDNA depletion, which leads to a partial oxidative phosphorylation defect when expressed during a short period in adulthood. We found that a mild mitochondrial dysfunction in adult neurons decreased plaque pathology by altering the cleavage pathway of amyloid precursor protein without increasing oxidative stress in the brain. These data suggest that mtDNA damage is not a primary cause of Ab accumulation.

A. **Pinto M**, Pickrell AM, Fukui H, Moraes CT.

Mitochondrial DNA damage in a mouse model of Alzheimer's disease decreases amyloid beta plaque formation.

Neurobiol Aging. 2013 Oct;34(10):2399-407 [PMID: 23702344]

Complete List of Published Work in MyBibliography:

<http://www.ncbi.nlm.nih.gov/sites/myncbi/milena.pinto.1/bibliography/50578890/public/?sort=date&direction=ascending>.

D. Research Support

Post-doctoral fellowships:

Parkinson's Disease Foundation

"The role of Parkin in the clearance of defective mitochondria with deleted mtDNA. A new mouse model of Parkinson's disease."

July/2013 – July/2014

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Ramos, Alberto Rafael

eRA COMMONS USER NAME (credential, e.g., agency login): ARAMOS1

POSITION TITLE: Associate Professor of Neurology

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	END DATE MM/YYYY	FIELD OF STUDY
University of Puerto Rico, Rio Piedras, PR	BS	06/1999	Natural Sciences
U Central del Caribe, School of Medicine, Bayamon, PR	MD	05/2003	Medicine
Jackson Memorial Hospital-U. of Miami, Miami, Florida	Residency	06/2007	Neurology
Jackson Memorial Hospital-U. of Miami, Miami, Florida	Fellowship	06/2008	Sleep Medicine
Miller School of Medicine, U of Miami, Miami, Florida	MSPH	06/2012	Epidemiology
Miller School of Medicine, U. of Miami, Miami, Florida	MS	05/2018	Translational Research

A. Personal Statement

Dr. Alberto Ramos is Associate Professor of Clinical Neurology and Research Director of the Sleep Disorders program at the University of Miami, Miller School of Medicine. Dr. Ramos's research is aimed at the intersection between sleep disorders, cerebrovascular disease and neurocognitive aging in population based studies. Dr. Ramos completed a diversity supplement grant from the NIH/NINDS, aimed to determine the sleep disorders associated to stroke risk factors and cognitive decline in the Northern Manhattan Study. He is also an investigator of the Hispanic Community Health Study/Study of Latinos (HCHS/SOL); where He serve as primary consultant for Sleep Research at the Miami field site. Dr. Ramos is supported by NIH/NIA to evaluate sleep phenotypes, neurocognitive decline and incident dementia in HCHS/SOL. He is also supported by NIH/NLBI to determine the sleep phenotypes that predict cardiovascular disease in HCHS/SOL. He was the site-PI for the Sueño study-*Sleep as a Risk Factor for Disease in HCHS/SOL* – Field Center at the University of Miami. This NHLBI ancillary study evaluated the determinants of abnormal sleep patterns with actigraphy and their effect on cardiometabolic diseases. Dr. Ramos was also the principal investigator of an HCHS/SOL ancillary study evaluating sleep apnea and cerebral hemodynamics as an early marker of cerebrovascular risk at the Miami field site.

1. **Ramos AR**, Dib SI, Wright CB. Vascular Dementia. *Curr Transl Geriatr Exp Gerontol Rep.* 2013 Sep 1;2(3):188-195. PubMed PMID: [26213642](#); PubMed Central PMCID: [PMC4513364](#).
2. **Ramos AR**, Dong C, Rundek T, Elkind MS, Boden-Albala B, Sacco RL, Wright CB. Sleep duration is associated with white matter hyperintensity volume in older adults: the Northern Manhattan Study. *J Sleep Res.* 2014 Oct;23(5):524-30. PubMed PMID: [25040435](#); PubMed Central PMCID: [PMC4177451](#).
3. **Ramos AR**, Jin Z, Rundek T, Russo C, Homma S, Elkind MS, Sacco RL, Di Tullio MR. Relation between long sleep and left ventricular mass (from a multiethnic elderly cohort). *Am J Cardiol.* 2013 Aug 15; 112(4):599-603. PubMed PMID: [23711813](#); PubMed Central PMCID: [PMC3770129](#).

B. Positions and Honors**Positions and Employment**

2006 - 2007 Administrative Chief Resident, Neurology Residency Program, U of Miami, Miami, FL

- 2007 - 2009 Neurology Staff Physician, Miami VA Hospital, Miami, FL
- 2009 - 2010 Instructor, Miller school of Medicine, University of Miami, Miami, FL
- 2010 - 2016 Assistant Professor of Neurology, Miller School of Medicine, U. of Miami, Miami, FL
- 2010 - Research Director Sleep Medicine Program, Miller School of Medicine, U. of Miami, Miami, FL
- 2013 - 2018 Associate Graduate Faculty, College of Engineering & Computer Science, Florida Atlantic University, Boca Raton, FL
- 2016 - Associate Professor of Neurology, Miller School of Medicine, U. of Miami, Miami, FL

Other Experience and Professional Memberships

- 2008 - Member, American Academy of Sleep Medicine
- 2008 - Member, American Academy of Neurology
- 2015 - Collaborator, Evelyn McKnight Brain Institute, Miller School of Medicine
- 2016 - Clinical Research Subcommittee member , American Academy of Neurology
- 2017 - Topic Editor, Frontiers of Neurology, Sleep and Chronobiology Section
- 2017 - 2018 Vice Chair, Young Investigator Research Forum, American Academy of Sleep Medicine
- 2018 – Chair, Young Investigator Research Forum, American Academy of Sleep Medicine
- 2018 Representative, Dept. of Neurology, Faculty Council, Miler School of Medicine

Honors

- 2003 Cum Laude, U. Central Del Caribe, School of Medicine
- 2003 Alpha Omega Alpha, U. Central Del Caribe, School of Medicine
- 2007 Clinical Neuroscience Prize, Neurology Residency Program, U. of Miami
- 2008 Faculty Development Award, American Neurological Association
- 2013 - 2014 Scholar, Program to Increase Diversity among Individuals Engaged in Health-Related Research (PRIDE), NHLBI
- 2013 Fellow, American Academy of Sleep Medicine
- 2015 Diversity Leadership Development Program, American Academy of Neurology
- 2015-2016 Peer Mentor , PRIDE, NHLBI/NYU
- 2015 Travel Award, U13 Conference Series: Sleep, Circadian Rhythms, and Aging: Supported by the National Institutes of Aging and the American Geriatric Society

C. Contribution to Science

4. **Sleep and neurocognitive aging.** During *Dr. Ramos mentored research award*, we evaluated the associations between OSA and neurocognitive function in over 8,000 Latinos from HCHS/SOL. OSA was cross-sectionally associated with worse neurocognitive function, particularly among *females* (cf males), in the neurocognitive domains of memory, language and executive function. The association was stronger in younger (45-54 years), rather than older females (65-74 years). We also performed a cross-sectional evaluation of sleep duration and neurocognitive function in HCHS/SOL. We found curvilinear (inverted U-shaped) associations between self-reports of sleep duration and neurocognitive function. That is, participants with average (7.8 hours \pm 1.7 hours) self-reported sleep duration had better neurocognitive scores, compared to the extremes of sleep duration. In addition, Dr. Ramos's work from the multi-ethnic cohort of the Northern Manhattan study showed that self-reported symptoms of OSA (i.e. snoring, daytime sleepiness) led to worse neurocognitive performance and predicted *decline* in executive function.
 - a. **Ramos AR**, Tarraf W, Rundek T, Redline S, Wohlgemuth WK, Loredó JS, Sacco RL, Lee DJ, Arens R, Lazalde P, Choca JP, Mosley T Jr, González HM. Obstructive sleep apnea and neurocognitive function in a Hispanic/Latino population. *Neurology*. 2015 Jan 27;84(4):391-8. PubMed PMID: [25540308](https://pubmed.ncbi.nlm.nih.gov/25540308/); PubMed Central PMCID: [PMC4336004](https://pubmed.ncbi.nlm.nih.gov/PMC4336004/)
 - b. **Ramos AR**, Tarraf W, Daviglius M, Davis S, Gallo LC, Mossavar-Rahmani Y, Penedo FJ, Redline S, Rundek T, Sacco RL, Sotres-Alvarez D, Wright CB, Zee PC, González HM. Sleep Duration and Neurocognitive Function in the Hispanic Community Health Study/Study of Latinos.

Sleep. 2016 Oct 1;39(10):1843-1851. PubMed PMID: [27450689](#); PubMed Central PMCID: [PMC5020366](#).

c. **Ramos AR**, Gardener H, Rundek T, Elkind MS, Boden-Albala B, Dong C, Cheung YK, Stern Y, Sacco RL, Wright CB. Sleep disturbances and cognitive decline in the Northern Manhattan Study. *Neurology*. 2016 Oct 4;87(14):1511-1516. PubMed PMID: [27590286](#); PubMed Central PMCID: [PMC5075974](#).

d. **Ramos AR**, Dong C, Elkind MS, Boden-Albala B, Sacco RL, Rundek T, Wright CB. Association between sleep duration and the mini-mental score: the Northern Manhattan study. *J Clin Sleep Med*. 2013 Jul 15;9(7):669-73. PubMed PMID: [23853560](#); PubMed Central PMCID: [PMC3671331](#).

5. **Sleep and cerebrovascular risk:** As part of his *mentored research grant*, Dr. Ramos evaluated impaired cerebral hemodynamics, which associate with stroke and worse cognition, using transcranial Doppler ultrasound at the HCHS/SOL Miami field site (*accepted for publication*). Regression models adjusting for covariates showed impaired cerebral hemodynamics associated to OSA in the basilar artery, while short sleep was associated with increased vascular resistance in the middle cerebral artery. These measures of cerebral hemodynamics indicate disturbances in cerebral vascular blood flow and brain vascular resistance that justify further investigation into the pathophysiology of sleep disorders into cerebrovascular disease, especially with MRI. In HCHS/SOL, we have also observed strong associations between actigraphic sleep habits with prevalent hypertension a known contributor to cerebral small vessel disease, which adversely related to neurocognitive decline.

a. Yang D, Rundek T, Patel S, Cabral D, Redline S, Testai F, Jianwen Cai, Zee P, **Ramos A**. Cerebral hemodynamics in sleep apnea and actigraphy-determined sleep duration in a sample of the Hispanic community health study: study of Latinos. *Sleep Medicine* **40**, e275-e276 (2017)

b. **Ramos AR**, Weng J, Wallace DM, Petrov MR, Wohlgemuth WK, Sotres-Alvarez D, Loredó JS, Reid KJ, Zee PC, Mossavar-Rahmani Y, Patel SR. Sleep Patterns and Hypertension Using Actigraphy in the Hispanic Community Health Study/Study of Latinos. *Chest*. 2018 Jan;153(1):87-93. PubMed PMID: [28970105](#); PubMed Central PMCID: [PMC5812757](#).

c. Chen J, Patel SR, Redline S, Durazo-Arvizu R, Garside DB, Reid KJ, Lash J, Sotres-Alvarez D, Gallo LC, Petrov ME, Perreira KM, Talavera GA, **Ramos AR**, Zee P, Daviglius ML. Weekly Sleep Trajectories and their Associations with Obesity and Hypertension in the Hispanic/Latino Population. *Sleep*. 2018 Jul 25. doi: 10.1093/sleep/zsy150. PMID:30053253

d. **Ramos AR**, Cabral D, Lee DJ, Sacco RL, Rundek T. Cerebrovascular pulsatility in patients with sleep-disordered breathing. *Sleep Breath*. 2013 May; 17(2):723-6. PubMed PMID: [22773271](#); PubMed Central PMCID: [PMC3619007](#).

6. **Sleep disorders and health disparities.** The long term goal of my research program is to alleviate the sleep health disparities and improve health outcomes in minority populations. I aim to determine the factors associated to health disparities in Hispanic/Latinos and non-Hispanic blacks. Our work showed that Hispanic/Latinos have greater frequency of sleep symptoms, compared to non-Hispanic whites; and these sleep symptoms and abnormal sleep patterns are strongly associated to vascular risk factors (Hypertension) and may precede ischemic stroke and cerebrovascular disease.

a. Dudley KA, Weng J, Sotres-Alvarez D, Simonelli G, Cespedes Feliciano E, Ramirez M, **Ramos AR**, Loredó JS, Reid KJ, Mossavar-Rahmani Y, Zee PC, Chirinos DA, Gallo LC, Wang R, Patel SR. Actigraphic Sleep Patterns of U.S. Hispanics: The Hispanic Community Health Study/Study of Latinos. *Sleep*. 2017 Feb 1;40(2)PubMed PMID: [28364514](#).

b. Cade BE, Chen H, Stilp AM, Gleason KJ, Sofer T, Ancoli-Israel S, Arens R, Bell GI, Below JE, Bjornes AC, Chun S, Conomos MP, Evans DS, Johnson WC, Frazier-Wood AC, Lane JM, Larkin EK, Loredó JS, Post WS, **Ramos AR**, Rice K, Rotter JI, Shah NA, Stone KL, Taylor KD, Thornton TA, Tranah GJ, Wang C, Zee PC, Hanis CL, Sunyaev SR, Patel SR, Laurie CC, Zhu X, Saxena R, Lin X, Redline S. Genetic Associations with Obstructive Sleep Apnea Traits in Hispanic/Latino Americans. *Am J Respir Crit Care Med*. 2016 Oct 1;194(7):886-897. PubMed PMID: [26977737](#); PubMed Central PMCID: [PMC5074655](#).

- c. **Ramos AR**, Guillian D, Dib SI, Koch S. Race/ethnic differences in obstructive sleep apnea risk in patients with acute ischemic strokes in south Florida. *Sleep Breath*. 2014 Mar;18(1):165-8. PubMed PMID: [23771345](#).
- d. Redline S, Sotres-Alvarez D, Loreda J, Hall M, Patel SR, **Ramos A**, Shah N, Ries A, Arens R, Barnhart J, Youngblood M, Zee P, Daviglius ML. Sleep-disordered breathing in Hispanic/Latino individuals of diverse backgrounds. *The Hispanic Community Health Study/Study of Latinos*. *Am J Respir Crit Care Med*. 2014 Feb 1;189(3):335-44. PubMed PMID: [24392863](#); PubMed Central PMCID: [PMC3977733](#).

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

R21 AG056952-01

Ramos, Alberto Rafael (PI) 08/01/17-05/31/19 3.12 Cal Months

Title: Exploring Sleep in Neurocognitive Aging and Alzheimer's Research (eSANAR)

This study provides the framework for future SOL studies on sleep and ADRD in Latinos. Evaluating the severity of baseline sleep apnea, levels of hypoxemia, apnea duration, sleep duration and sleep fragmentation, provides an opportunity to refine the sleep phenotypes associated to early neurocognitive decline and mild cognitive impairment and Alzheimer's disease and related dementias. **Role: Principal Investigator (PI)**

Scythian Biosciences

Title: The Effects of Cannabinoids on brain injury (Hotz) 8/1/2016-7/30/2021 0.6 Cal Months
Study to address the effects of combining CBD (a cannabinoid derivative), and an NMDA antagonist for the treatment of traumatic brain injury (TBI) and sleep. **Role: Co-Investigator, Director for Clinical Trials**

Scientific Advisory Committee Pilot Study Award, Miller School of Medicine, University of Miami

Ramos, Alberto Rafael (PI) 02/01/18-01/01/19

Title: Elucidating the link between sleep apnea and dementia using multimodal MRI and cognitive testing.

This pilot study compares MRI brain regions, total volumetric blood flow to the brain, and regional cerebral perfusion; in addition to differences in attention, memory, executive function, and processing speed across different sleep apnea phenotypes, before and after treatment with positive airway pressure. **Role: PI**

Boehringer Ingelheim. Chaturvety/Ramos (PI)

05/2016-12/2019

Title: Arrhythmia Detection In Obstructive Sleep apnea (ADIOS)

The goal of the study is to evaluate cardiac arrhythmias and use anticoagulants as a novel therapy for stroke prevention in patients with newly diagnosed obstructive sleep apnea. **Role: PI**

OVERLAP: None

PENDING

R21 (Ramos)

10/01/17 – 09/30/22

2.76 Cal Months

NIH/NHLBI

Sleep Apnea Phenotypes in Latinos (SLEPT). This study will help develop risk-stratification strategies for sleep apnea and inform future intervention studies in cardiovascular risk and sleep apnea; providing a step towards personalized medicine in sleep. This study would contribute to reducing health disparities among diverse Latinos, who are burdened by increased risk for cardiovascular disease and a high prevalence of sleep apnea.

Role: Principal Investigator

R01 (Brown - Epidemiology)

04/01/18-03/31/21

3.0 Cal Months

NIH

Neighborhood Greenness and Cardiovascular Disease among Hispanics in HCHS/SOL Study

The objective is to examine the healthcare built environment in relation to health, and increasing physical activity and improving sleep as opportunities through built environment policy. **Role: Co-Investigator**

Completed Research Support

KL2 TR000461-02/03

Szapocznik, Jose (PI)

06/27/12-05/31/16

Miami Clinical and Translational Science Institute

The goal of this study is to evaluate the cerebral hemodynamic as an early marker of cerebrovascular risk in participants with sleep apnea compared to controls. 75% effort. *Mentor: Tatjana Rundek, MD, PhD.*

Role: Scholar

L60 MD005231-01-04

Ramos, Alberto Rafael (PI)

07/01/12-06/30/16

Sleep apnea, cerebral blood flow and cognition. Loan repayment program from the National Institutes of Health/National Institute of Minority Health and Health Disparities to evaluate associations between sleep apnea, sleep disturbances, cerebral blood flow and cognitive function in Latinos.

Role: Principal Investigator

R01: HL098297 Patel (PI)

07/2011-04/2014

Sueño: Sleep patterns as a risk factor in the Hispanic Community Health Study. The goal of the study was to determine the cardiovascular consequences of abnormal sleep patterns with actigraphy in Hispanic/Latinos.

Role: Site PI/Co-investigator, 10% effort time.

R37 (Javits Award): 2R01 (NS 29993), Sacco (PI)

06/2009-05/2012

Stroke Incidence and Risk Factors in a Tri-Ethnic Region Agency. Supplements to Promote Diversity in Health-Related Research. The goal of the study was to investigate the associations between sleep symptoms and sub-clinical vascular disease in a 3298 community subjects.

Role: Scholar, 50% effort time. *Mentor: Ralph Sacco, MD, MS*

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Ami P. Raval		POSITION TITLE Research Associate Professor	
eRA COMMONS USER NAME (credential, e.g., agency login) ARAVAL			
EDUCATION/TRAINING (<i>Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.</i>)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
M.S. University of Baroda, India	B. Sc	1989	Zoology, Botany, Chemistry
M.S. University of Baroda, India	M.Sc	1991	Zoology
M.S. University of Baroda, India	Ph.D	1995	Zoology (Physiology of reproduction)
University of Miami, USA	Post-doc	2000-2003	Neurophysiology
University of Miami, USA	MSPH	2010-2012	Epidemiology

A. Personal Statement

I have numerous years of experience in the field of cerebral ischemia and mitochondrial biology. My ongoing research focuses on elucidating the mechanism(s) by which the female sex hormone- estrogen - decreases the risk of cerebral ischemia in females utilizing *in vivo* and *in vitro* cerebral ischemia models in rats, and analysis of mitochondrial function. While working to earn my PhD, I studied the effects of endogenous variations of female sex hormones on non-reproductive tissues; this knowledge helped me to design studies to understand the mechanism of ischemic brain protection by estrogen. My post-doctoral training with Dr. Miguel A. Perez-Pinzon, a prominent neuroscientist and a pioneer in field of ischemic preconditioning and center PI of present application, laid a strong foundation for me in the basics essential for understanding ischemic neurodegeneration. I continued to study the mechanism of neuronal death following cerebral ischemia that is a consequence of cardiac arrest or stroke, and I am well versed in various *in vivo* and *in vitro* models of cerebral ischemia as well as in imaging, electrophysiology, and behavior and molecular biology techniques. I have also successfully trained and supervised post-doctoral fellows, students, and technicians to perform ischemia models and the aforementioned techniques. I am also part of the University of Miami's undergraduate neuroscience program, and I am involved in education of premedical and medical students.

**B. Positions and Honors:
Professional Experience:**

- Lecturer: Zoology, M. S. University of Baroda, Gujarat, India. 1994 - 2000
- Assistant scientist: University of Miami, U.S.A. 2003 –2006
- Research Assistant Professor: University of Miami, U.S.A. 2006 - 2018
- American Heart Association- Innovative grant study section reviewer Fall 2014 - Present
- American Heart Association- Brain 2 study section reviewer Spring 2015 - Present
- Animal resource committee member 2009- present
- Institutional Scientific advisory committee grants Ad-hoc reviewer 2012-Present
- Facilitator for MD-MPH Problem base learning at University of Miami 2014-Present
- NIH-Neuroendocrinology, Neuroimmunology, Rhythms and Sleep Study Section Ad-hoc member 2017

Scholarship and Awards:

- Fellowship awarded by Gujarat Government of India for Ph.D. studies from 1991 to 1994.
- Awarded Young Scientist award on "Effect of sex hormones on Salivary gland" by ICMR, New Delhi.
- Awarded American Heart Association (Florida/Puerto Rico) Post-doctoral Fellowship 7/2002 to 6/2004. (AHA identification number- 0225227B)
- Best poster 2009 at Celebrating Excellence in Women's Health Research, University of Miami, Miami

Membership in Professional Societies:

- Society for Neuroscience (SFN)
- Society for Cerebral Blood Flow & Metabolism
- American Heart Association (AHA)
- Organization for the Study of Sex Differences (OSSD)
- Society for Reproductive Biology and Comparative Endocrinology (SRBCE)

C. Contribution to Science

Note: * represents equal contribution; ** Corresponding author Google h-index = 25

1. Studies from my laboratory simulating the conditions of nicotine exposure produced by cigarette smoking and the oral contraceptive (OC) regimen of women in female rats provides evidence that the severity of ischemic hippocampal damage is far greater in female rats simultaneously exposed to OC than to nicotine alone. These studies also demonstrated that the concurrent exposure of OC and nicotine reduces endogenous 17β -estradiol levels and inhibits ER- β signaling in the brains of female rats. My study demonstrated that concurrent exposure to nicotine and OC impaired ER- β -mediate mitochondrial respiration at the complex-IV level due to lower protein levels of its catalytic subunits in the hippocampus of female rats.

- a. d'Adesky ND, de Rivero Vaccari JP, Bhattacharya P, Schatz M, Perez-Pinzon MA, Bramlett HM, **Raval AP****. Nicotine Alters Estrogen Receptor-Beta-Regulated Inflammasome Activity and Exacerbates Ischemic Brain Damage in Female Rats. *Int J Mol Sci.* 2018; 19(5)
- b. **Raval AP****, Borges-Garcia R, Diaz F, Sick TJ and Bramlett H. Oral contraceptives and nicotine synergistically exacerbate cerebral ischemic injury in the female brain. *Translational Stroke Research* 2013 4:402–412
- c. **Raval AP****, Sick JT, Gonzalez GJ, Defazio RA, Dong C and Sick TJ. Chronic nicotine exposure inhibits estrogen-mediated synaptic functions in hippocampus of female rats. *Neuroscience Letters* 2012; 517(1):41-6
- d. **Raval AP****, Hirsch N, Dave KR, Yavagal DR, Bramlett H, Saul I. Nicotine and estrogen synergistically exacerbate cerebral ischemic injury. *Neuroscience* 2011; 181:216-25.
- e. **Raval AP****. Nicotine addiction causes unique detrimental effects on female brain. *Journal of Addictive Diseases. Review.* 2011; 30:149–158

2. Mitochondrial dysfunction is a major factor involved in ischemic neuronal death. My early publications directly addressed the fact that protein kinase C subtype epsilon (PKC ϵ) translocates to mitochondria following sub-lethal ischemic insult, and improved mitochondrial function and resistance to cerebral ischemic damage. My work also demonstrated that the activation of PKC ϵ agonist phosphorylates the mitochondrial K⁺_{ATP} channel subunit Kir6.2, which is involved in opening of potassium channels. The neuroprotection conferred by ischemic preconditioning was lost in the presence of K⁺_{ATP} - channel antagonists. Overall, my work provided initial evidence that PKC ϵ activation and its interaction with mitochondrial targets confer stability to mitochondrial functions during subsequent ischemic stress, thus reducing ischemic damage.

- a. **Raval AP**, Dave KR, Mochly-Rosen D, Sick TJ, Perez-Pinzon MA. ϵ PKC is required for the induction of tolerance by ischemic and NMDA – mediated preconditioning in the organotypic hippocampal slice. *J Neuroscience.* 2003; 23(2): 384-91.
- b. **Raval AP****, Dave KR, DeFazio RA, Perez-Pinzon MA. EpsilonPKC phosphorylates the mitochondrial K(+) (ATP) channel during induction of ischemic preconditioning in the rat hippocampus. *Brain Res.* 2007; 1184:345-53. (PMCID: 2577914)
- c. Dave KR, DeFazio RA, **Raval AP**, Torraco A, Saul I, Barrientos A, Perez-Pinzon MA. Ischemic preconditioning targets the respiration of synaptic mitochondria via protein kinase C epsilon. *J Neurosci.* 2008; 28(16):4172-82. (PMCID: 2678917)
- d. Pérez-Pinzón MA, Dave KR, **Raval AP**. Role of reactive oxygen species and protein kinase C in ischemic tolerance in brain. *Antioxidants and redox signaling* 2005; Vol 7(9 & 10): 1150-57.

3. Another focus of my research is investigating the mechanism by which female sex hormone(s) provide ischemic brain protection. Studies from my lab demonstrate that either a single bolus or repetitive periodic 17 β -estradiol treatments prior to ischemic episode reduces ischemic brain damage in ovariectomized rats. Periodic E₂ pretreatment protects hippocampal neurons through the activation of estrogen receptor subtype beta (ER- β) and silencing of hippocampal ER- β ameliorated 17 β -estradiol-induced ischemic protection. My study also demonstrated that the activation of ER- β regulates mitochondrial function in the brain, and maintains mitochondrial function after cerebral ischemia. My research underscores that ER- β activation is a key mechanism to prevent ischemic neuronal death. My study was the first one to show that the silencing of hippocampal ER- β lowers protein levels of mitochondria-encoded complex IV subunits; it also implicates a role for ER- β in protein expression of the mitochondrial oxidative phosphorylation system.

- a. **Raval AP****, Dave KR, Saul I, Gonzalez GJ, Diaz F. Synergistic inhibitory effect of nicotine plus oral contraceptive on mitochondrial complex-IV is mediated by estrogen receptor- β in female rats. J Neurochemistry 2012; 121(1):157-67.
- b. **Raval AP****, Borges-Garcia R, Moreno WJ, Perez-Pinzon MA and Bramlett H. Periodic 17 β -estradiol pretreatment protects rat brain from cerebral ischemic damage via estrogen receptor- β . Plos One 2013;8(4):e60716
- c. **Raval AP****, Saul I, Dave KR, DeFazio RA, Perez-Pinzon MA, Bramlett H. Pretreatment with a single estradiol-17 β bolus activates CREB and protects CA1 neurons against global cerebral ischemia. Neuroscience. 2009; 160:307–18. (PMCID: 2711690)
- d. **Raval AP****, Bramlett H, Perez-Pinzon MA. Estrogen preconditioning protects the hippocampal CA1 against ischemia. Neuroscience. 2006; 141(4):1721-30.

4. It is known that cerebral ischemia activates the innate immune response, and a key component of the innate immune response is the inflammasome. Recent study from my laboratory demonstrated that the ER- β activation regulates inflammasome activation and protects the brain from global ischemic damage in reproductively senescent female rats.

- a. de Rivero Vaccari JP, Patel HH, Brand III FJ, Perez-Pinzon MA, Bramlett H and **Raval AP**. Estrogen receptor beta signaling alters cellular inflammasomes activity after global cerebral ischemia in reproductively senescence female rats. J Neurochemistry 2016 Feb;136(3):492-6.

Complete List of Published Work in My Bibliography:

<http://www.ncbi.nlm.nih.gov/pubmed/?term=raval+ap>

D. Active Support

NIH-NINDS 1/8/ 17 - 31/7/ 2022

Mitochondria and cerebral ischemia: Intracellular Signaling

Principal Investigator: Dr. Pérez-Pinzón

Role: Co-investigator, 15% efforts

Florida Department of Health#7JK01

03/1/17- 2/29/2020

Whole body vibrations improves stroke outcome in nicotine-exposed rats

The major goal of this project is to study the effects whole body vibration on post-stroke frailty in nicotine exposed female rats. There is no scientific overlap with current application.

Principal Investigator: Dr. Helen Bramlett

Role: CO-PI (50% effort)

American Heart Association- Grant-in-aid

AHA # 16GRNT31300011

07/1/16- 6/30/2019

Nicotine alters brain oxidative metabolism and exacerbates ischemic brain damage

The major goal of this project is to study the effects of chronic nicotine usage on brain metabolism in adolescent and young female rats. There is no scientific overlap with current application.

Role: PI, 20% efforts

NIH/NINDS

Grant #3R01NS034773-16S1

07/1/16- 6/30/2017

Ischemic Preconditioning: Mechanisms of Neuroprotection

This project is an administrative supplement for research on sex/gender differences in ischemic preconditioning.

PI: Dr. Miguel A. Perez-Pinzon

Role: Co-investigator, 10% efforts

Department of Neurology's 2016 Pilot Research Support Program

01/1/16-6/31/17

Mechanism of neuroprotection against cerebral ischemia

Role: PI, no % efforts

Completed Research Support:

United Mitochondrial Disease Foundation

07/1/14-6/30/16

Modulation of GSK3 activity and enhancement of glycolysis to maintain neuronal survival in complex IV deficient mice

PI: Dr. Francisca Diaz

Role: Co-investigator (5% effort)

University of Florida Southeast Center for Integrated Metabolomics

07/1/14-7/30/15

Pilot and Feasibility Projects

Nicotine alters brain oxidative metabolism

Role: PI, no % efforts

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: **Tatjana Rundek, MD PhD**

eRA COMMONS USER NAME (credential, e.g., agency login): **TR89XX**

POSITION TITLE: Professor of Neurology, Executive Vice Chair of Research and Faculty Affairs, Director of Clinical Translational Research Division, University of Miami Miller School of Medicine

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
University of Zagreb, Croatia	B.S.	1979-1983	Applied Mathematics
Medical School University of Zagreb, Croatia	M.D.	1984-1989	Medicine
Medical School University of Zagreb, Croatia	M.S.	1989-1991	Epidemiology/Bioinformatics
Ludwig-Maximillan University, Munich, Germany	Ph.D.	1991-1995	Neuroscience
Medical School University of Zagreb, Croatia	Residency	1991-1994	Neurology
Grossharden Spital Munich, Germany	Fellowship	1994-1995	Stroke
Columbia University, New York, NY	Fellowship/MS	1998-2000	Stroke/Neuroepidemiology

A. Personal Statement

I was named Scientific Director of the Evelyn F. McKnight Brain Institute in January 2018 and Evelyn F. McKnight Chair for Learning and Memory in Aging in October, 2018. I served as an interim Scientific Director after Dr. Wright left the University of Miami (UM) in 2016. Since my relocation from Columbia University to UM in 2008, I have been dedicated to the research and education mission of our McKnight Brain Institute. As a Vice Chair and Director of the Clinical Translational Research Division in Neurology, and a PI of NIH/NINDS R01 grants and Co-I of several R01s I have been performing research on vascular factors affecting stroke and cognitive decline and providing research environment and training in neuroscience, vascular neurology and epidemiology for many graduate and post-graduate trainees and junior faculty. I am also a program Director of a Miller School of Medicine MS degree in Clinical Translational Investigations. I serve as a Training Director of the NINDS StrokeNet and NeuroNEXT (1 trainee/year) and Miami AHA Bugher Stroke Center (2 trainees/year). I was awarded a NINDS K24 training grant that provided me with the protected time for research and mentorship. In addition, I am a director of the Neurology Residents and Fellows Clinician Researcher Program, a 3-year program aimed to provide research and career development mentorship. In the past 10 years, I have mentored over 20 trainees at various stages of their career, 20 completed their MD, PhD, MS or MPH degrees during my mentorship and obtained NIH grants or other awards. I was awarded a 3-year AHA Mentor grant to mentor 3 trainees nationally for 3 years. I have been a productive investigator with over 380 publications and have extensive research collaborations with various national and international research teams, such as investigators from Columbia University on large NIH-funded population based studies (NOMAS, INVEST, CABLE, PHPT, eMERGE) and Albert Einstein in the Bronx on Einstein Aging Study. I am a collaborator and site investigator of the large international stroke genetic, MR imaging, and atherosclerosis projects and consortia (NINDS SiGN, ISGC, PROG-IMT, ELSA).

These peer-reviewed publications highlight my experience and qualifications:

1. **Rundek T**, Della-Morte D, Gardener H, Dong C, Markert MS, Gutierrez J, et al. Relationship between carotid arterial properties and cerebral white matter hyperintensities. *Neurology*. 2017;88(21):2036-42.
2. Wei Y, Jiang H, Shi Y, Qu D, Gregori G, **Rundek T**, Wang J. Age-Related Alterations in the Retinal Microvasculature, Microcirculation, and Microstructure. *Invest Ophthalmol Vis Sci*. 2017;58(9):3804-17.
3. Luca CC, **Rundek T**. Parkinsonism, small vessel disease, and white matter disease: Is there a link? *Neurology*. 2015;85(18):1532-3.
4. **Rundek T**, Bennett DA. Cognitive leisure activities, but not watching TV, for future brain benefits. *Neurology* 2006; 66(6): 794-5.

B. Positions and Honors

POSITIONS AND EMPLOYMENT

Academic Appointments:

1994-96	Assistant Professor of Neurology	Dept. of Neurology, University of Zagreb, Croatia
1996-98	Associate Professor of Neurology	Dept. of Neurology, University of Zagreb, Croatia
2002-07	Assistant Professor of Neurology	Columbia University, New York, NY
2007-11	Associate Professor of Neurology	Miller School of Medicine, U Miami, Miami, FL
2011-	Professor of Neurology (with tenure)	Miller School of Medicine, U Miami, Miami, FL
2017-	Scientific Director, McKnight Brain Institute; Evelyn F. McKnight Chair for Learning and Memory in Aging	Miller School of Medicine, U Miami, Miami, FL

Hospital Appointments:

1994-00	Stroke Attending	Department of Neurology, University of Zagreb, Croatia
2002-07	Director&Attending,Vascular Laboratory	Columbia University Medical Center, New York, NY
2007-	Director, Clinical Translational Division	Miller School of Medicine, U Miami, Miami, FL
2010-	Vice Chair, Clinical Translational	Miller School of Medicine, U Miami, Miami, FL
2014-	Director, MS Clinical Translational	Miller School of Medicine, U Miami, Miami, FL

Honors

1995	Humbolt Award, Neurosonology Laboratory, University of Ulm, Germany
1996	George Soros Scholarship, Neurology Seminars, University of Krems, Austria
1997-99	Fulbright Award and Scholarship, Neurological Institute, Columbia University, New York, NY
2006	Nassau Women Physicians Foundation Award for Stroke Research in Women; Long Island, NY
2009-14	President, the Neurosonology Community of Practice, American Institute of Ultrasound in Medicine
2012-	Member, the Board of the Directors, Intersocietal Accreditation Committee (IAC)-Vascular
2012-	Consulting Editor of <i>Stroke</i>
2013-	Editorial Board Member of <i>Neurology</i> , <i>Cerebrovascular Disease</i> , <i>Journal of Ultrasound in Medicine</i>
2014-	Member, the Clinical Standards Committee, American Institute of Ultrasound in Medicine (AIUM)
2015-	Secretary, the Executive Committee, Intersocietal Accreditation Committee (IAC)-Vascular
2015-	Reviewer, NIH section ZHL1 CT-K (C1)1 – LRP
2015	The American Heart Association Core Vitae Award for Stroke

C. Contribution to science

C.1. Neuroepidemiology. Over the past 20 years I have pursued research in neuroepidemiology. The central findings from this research include the discovery of novel stroke risk factors (e.g., insulin resistance, sleep duration, homocysteine, adiponectin, oral infection). Some of these reports were among the first in the literature. We conducted the largest investigation of the role of PFO in stroke and migraine. Our group was the first to report that atorvastatin reduces the serum coenzyme Q10 levels linking it to muscle pain. More recently I have been investigating neurocognitive functions in large longitudinal studies including Einstein Aging Study, HCHS-SOL, and NOMAS. I am a strong believer in team science and many of my research products are the results of multiple collaborations with international research teams and institutions.

1. **Rundek T**, Elkind MS, Di Tullio MR, Carrera E, Jin Z, Sacco RL, Homma S. Patent Foramen Ovale and Migraine. A Cross-Sectional Study from the Northern Manhattan Study. **Circulation**. 2008;118:1419-24.
2. Fleisher R, Lipton ML, Noskin O, **Rundek T**, Lipton R, Derby CA. White Matter Structural Integrity and Trans-Cranial Doppler Blood Flow Pulsatility in Normal Aging. *Magn Reson Imaging*. 2017 Nov 1
3. **Rundek T**, Naini A, Sacco RL, Coates K, DiMauro S. Atorvastatin decreases the coenzyme Q10 level in the blood of patients at risk for cardiovascular disease and stroke. *Arch Neurol*. 2004; 61:889-92.
4. Ramos AR, Tarraf W, **Rundek T**, Redline S, Wohlgemuth WK, Loreda JS, Sacco RL, Lee DJ, Arens R, Lazalde P, Choca JP, Mosley T Jr, González HM. Obstructive sleep apnea and neurocognitive function in a Hispanic/Latino population. *Neurology*. 2015;84(4):391-8.

C.2. Extracranial and intracranial imaging markers of carotid disease. Vascular imaging has been my primary tool to investigate atherosclerosis. I have been in the field of ultrasound for over 25 years. I was trained in ultrasound technologies by the inventor of transcranial Doppler (TCD) Dr. Rune Aaslid in early 80's and have

been a part of an international brain hemodynamic research group since. I coauthored the first consensus document on carotid ultrasound imaging. I have been a part of large international collaborations on the progression of subclinical atherosclerosis (PROG-IMT, USE-IMT). I have applied arterial vessel wall principles to improve arterial compliance using a new technique of integrated power Doppler and changes of vessel wall diameter during cardiac cycle. In addition, I have helped advancing the field of brain circulation investigations using TCD to vascular cognitive impairment, memory loss and dementia. I have been an active member of IAC (Intersocietal Accreditation Committee) Board of Directors, the largest US accreditation body that sets the standards for performance of clinical ultrasound, CT/MRI, PET, and cardiac Echo. I have been an advocate for advancing quality and access to clinical ultrasound in medicine for vascular and cognitive disorders.

1. **Rundek T**, Blanton SH, Bartels S, Dong C, Raval A, Demmer RT, Cabral D, Elkind MS, Sacco RL, Desvarieux M. Traditional risk factors are not major contributors to the variance in carotid intima-media thickness. **Stroke**. 2013;44:2101-8.
2. **Rundek T**, Arif H, Boden-Albala B, Elkind MS, Paik MC, Sacco RLS. Carotid plaque, a subclinical precursor of vascular events: the Northern Manhattan Study. **Neurology** 2008; 70:1200-7.
3. Suemoto CK, Santos IS, Bittencourt MS, Pereira AC, Goulart AC, **Rundek T**, Passos VM, Lotufo P, Benseñor IM. Subclinical carotid artery atherosclerosis and performance on cognitive tests in middle-aged adults: Baseline results from the ELSA-Brasil. *Atherosclerosis*. 2015;243(2):510-5.
4. Beecham A, Dong C, Wright CB, Dueker N, Brickman AM, Wang L, DeCarli C, Blanton SH, **Rundek T**, Mayeux R, Sacco RL. Genome-wide scan in Hispanics highlights candidate loci for brain white matter hyperintensities. *Neurol Genet*. 2017;3(5):e185.
5. Wei Y, Jiang H, Shi Y, Qu D, Gregori G, Zheng F, **Rundek T**, Wang J. Age-Related Alterations in the Retinal Microvasculature, Microcirculation, and Microstructure. *Invest Ophthalmol Vis Sci*. 2017;58(9):3804-17.

C.3. Genetic contribution to atherosclerosis and stroke. I have been investigating genetic contribution to carotid disease for the past 10 years as PI of 2 NINDS R01 grants and a NINDS K24 award, co-PI of family study of atherosclerosis and site PI of the NINDS SiGN (ischemic Stroke Genetic Network). In one of my investigations I have take the approach of extreme phenotypes by investigating genetic profile of individuals with a lot of risk factors but less atherosclerosis than expected as well as those with little to no risk factors but a lot of atherosclerosis. These investigations are now contributing novel findings on genetic and environmental determinants of atherosclerosis and stroke for targeted vascular therapies and prevention of CVD and stroke. I have also investigated family of sirtuin genes that are playing a central role in aging and caloric restriction that can be targets for anti-aging medical interventions.

1. **Rundek T**, Elkind MS, Pittman J, Boden-Albala B, Martin S, Humphries SE, Hank Juo SH, Sacco RL. Carotid Intima-Media Thickness is Associated with Allelic Variants of Stromelysin-1, Interleukin-6 and Hepatic Lipase Genes: The Northern Manhattan Prospective Cohort Study. **Stroke** 2002, 333:1420-3.
2. Dong C, Della-Morte D, Beecham A, Wang L, Cabral D, Blanton SH, Sacco RL, **Rundek T**. Genetic variants in LEKR1 and GALNT10 modulate sex-difference in carotid intima-media thickness: A genome-wide interaction study. *Atherosclerosis*. 2015;240(2):462-7.
3. Traylor M, Zhang CR, Adib-Samii P, Devan WJ, Parsons OE, Lanfranconi S, Gregory S, Cloonan L, Falcone GJ, Radmanesh F, Fitzpatrick K, Kanakis A, Barrick TR, Moynihan B, Lewis CM, Boncoraglio GB, Lemmens R, Thijs V, Sudlow C, Wardlaw J, Rothwell PM, Meschia JF, Worrall BB, Levi C, Bevan S, Furie KL, Dichgans M, Rosand J, Markus HS, **Rundek T**, Rost N; International Stroke Genetics Consortium. Genome-wide meta-analysis of cerebral white matter hyperintensities in patients with stroke. *Neurology*. 2016;86(2):146-53.
4. Della-Morte D, Ricordi C, **Rundek T**. The fountain of youth: role of sirtuins in aging and regenerative medicine. *Regen Med*. 2013;8(6):681-3.
5. Della-Morte D, Dong C, Beecham A, Wang L, Cabral D, Markert MS, Blanton SH, Sacco RL, **Rundek T**. Relationship between sirtuin and mitochondrial uncoupling protein genes and carotid artery stiffness. *Transl Res*. 2015;165(2):358-9.

Complete List of Published Work in MyBibliography:

<https://www.ncbi.nlm.nih.gov/pubmed?term=rundek>

<https://www.ncbi.nlm.nih.gov/sites/myncbi/tatjana.rundek.1/bibliography/40707409/public/?sort=date&direction=ascending>

D. Research Support

List of selected ongoing and completed research projects for the past three years:

- NIH/NINDS R01 NS 40807 Rundek, Sacco (Multi-PI) 05/01/02-09/30/17
Family Study of Stroke Risk and Carotid Atherosclerosis
The major goal of this study is to evaluate heritability and genetic linkage of novel vascular risk factors such as carotid intima-media thickness among the families of high-risk Caribbean Hispanics.
Role: PI
- NIN/NIHHD MR R01MD012467 Sacco/ Rundek/ Romano (Multi-PI) 09/26/17 – 06/30/22
Disparities in Transition of Care after Acute Stroke Hospitalization: The Transition of Care Disparity Study
Aims: To define race/ethnic and sex disparities in transitions of care from hospital to home after stroke, identify modifiable factors, and develop initiatives to reduce disparities and improve outcomes after stroke
Role: PI
- NIH/NINDS R37 NS 029993-11 Sacco (PI) 02/01/03-01/31/20
Stroke Incidence and Risk Factors in a Tri-Ethnic Region
The major goals of this project are to determine the effect of vascular risk factors on cognitive impairment and subclinical MRI findings in a prospective cohort study from 3 race-ethnic groups from Northern Manhattan.
Role: Co-Investigator
- NIH/NIDCR R01 DE 13094 Desvarieux (PI) 06/15/06-05/31/22
Oral Infections, Carotid Atherosclerosis and Stroke (INVEST)
This cohort study will examine the effect of chronic periodontal disease and inflammation as a risk factor for stroke and carotid atheroma progression.
Role: Co-Investigator
- NIH/NINDS U10 NS 077423 Benatar, Sacco (PIs) 09/30/11-08/31/18
University of Miami: Network of Excellence in Neuroscience Clinical Trials (NeuroNEXT)
The goals of this proposal are to enhance quality and efficiency of NIH trial implementation at the University of Miami and to leverage existing institutional strengths to enhance NeuroNEXT consortium activities.
Role: Co-Investigator
- NIH/NIA P01 AG003949 Lipton, Derby (PIs) 07/1/11-06/30/20
The Albert Einstein Study Program Project in Aging
This is a Cerebral Hemodynamics Study of Aging of the AES program project aimed to study the vascular mechanisms of normal aging, MCI and dementia using TCD challenge test.
Role: PI of TCD Core
- NIH/NINDS U54 NINDS SPIRP U54NS081763 Sacco (PI) 01/01/13-12/31/17
Stroke Prevention/Intervention Research Program in Hispanics
The goal is to develop high-impact stroke disparities interventions with the ability to reduce stroke disparities in distinct Hispanic groups in Miami and Puerto Rico using effective and culturally appropriate methods
Role: PI of Core C and PI of Supplement- Stroke Outcome in Women
- NIH/NINDS U10 NS086528 Romano (PI) 09/30/13-07/31/18
Miami Regional Coordinating Center for NINDS Stroke Trials Network
PI: J Romano; T. Rundek, Training Director
The major goal of this award is to function effectively as a Regional Coordinating Center for the NINDS stroke trials and to enhance quality and efficiency of NINDS stroke trial implementation at the Miami site.
Role: Training Director
- NIH/NINDS R01 NS084288-01A1 Romano (PI) 04/01/14-03/31/19
Mechanisms of Early Recurrence in Intracranial Atherosclerotic Disease (MyRIAD)
The objective of this proposal is to determine the mechanisms and predictors of stroke in patients with symptomatic Intracranial Atherosclerotic Disease.
Role: Co- Investigator

NIH/NHLBI N01-HC65234	Schneiderman (PI)	06/01/14-05/31/19
Hispanic Community Health Study-Study of Latinos (HCHS-SOL) Miami Field Center		
The HCHS/SOL is a multi-center epidemiologic study designed to determine the role of acculturation in disease prevalence and to identify health risk factors in Hispanics/Latinos.		
Role: Adjudication Core investigator		
AHA14BFSC17690000	Sacco (PI)	04/01/14-03/31/18
AHA-ASA/Bugher Foundation Center of Excellence in Stroke Collaborative Research		
This initiative supports a collaboration of basic, clinical and population research and training in stroke prevention and recovery after a stroke including the areas of repair, regeneration, and rehabilitation.		
Role: Training Director		
AHA 15MM26340000	Rundek (PI)	07/01/15-06/30/18
NCRP Winter 2015 Mentor / AHA Mentee Award		
This awards supports Dr. Rundek's mentorship activities for 2 AHA fellows (from John Hopkins & UT Huston).		
Role: PI		
ARISTA-USA CV185-564	Rundek (PI)	01/04/17-3/31/20
BMS		
Disparities in Stroke Outcomes and Care Delivery in Patients with Atrial Fibrillation: FLiPER-AF Study		
This study will examine race-ethnic and sex disparities in health care delivered to stroke patients with AF and their outcomes after acute stroke hospitalization.		
Role: PI		
NIH/NCATS UL1TR000460	Sacco (PI)	06/1/2012-05/30/18
UM Clinical Translation Science Institute		
The Miami CTSI advances culturalized health sciences that embrace our majority racial/ethnic communities. Fundamental to accomplishing our mission is the orchestration of new and existing research, services and resources that foster excellence in translational research, promote interdisciplinarity, elevate research ethics, build research partnerships in community, and establish strong multidisciplinary graduate research programs.		
Role: co-PI of Educational Core		
<u>Prior Research Support</u>		
NIH/NINDS K24 NS 062737	Rundek (PI)	09/30/09-08/31/17
Genetic Determinants of Extreme Phenotypes of Subclinical Atherosclerosis		
Role: PI		
NIH/NINDS R01 NS 065114	Rundek (PI)	07/01/10-06/30/17
Novel Factors for Unexplained Phenotypes of Subclinical Carotid Atherosclerosis		
Role: PI		
NIH/NINDS U01 U01 NS 069208	Kittner (PI)	04/01/10-3/31/16
The NINDS International Stroke Genetics Consortium Study: Ischemic Stroke Genetics		
PI: S. Kittner, U Maryland; T. Rundek, Site PI		
Role: Site PI		
NIH/NHLBI R01 HL108623-01A1	Wright (PI)	12/01/12-11/30/16
FGF-23 and the Risk of Stroke and Cognitive Decline		
Role: Co-Investigator		
KN01 James & King Biomedical Research	Dong (PI)	09/01/11-08/31/14
Gene-Smoking Interactions and Atherosclerosis		
Role: Co-Investigator		

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Ralph Lewis Sacco, MD MS

eRA COMMONS USER NAME (credential, e.g., agency login): SACCORL

POSITION TITLE: Chairman and Professor of Neurology, Public Health Sciences, Human Genetics, and Neurosurgery

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Cornell University, College of Engineering	B.S. Distinction	1975-79	BioElectrical Engineering
Boston University, School of Medicine	M.D. cum laude	1979-83	Medicine
Columbia University, School of Public Health	M.S.	1987-89	Epidemiology
Neurological Institute, Presbyterian Hospital	Residency	1984-87	Neurology
Columbia College of Physicians & Surgeons	Fellow	1987-89	Cerebrovascular Disease

A. Personal Statement

I serve as Executive Director for the Evelyn F. McKnight Brain Institute at the University of Miami. I am currently Professor and Chairman of Neurology at the Miller School of Medicine, Director of the UM-Clinical Translational Science Institute, and Senior Associate Dean for Clinical and Translation Science. I have an extensive research track record in stroke, vascular cognitive impairment, clinical trials and disparities research. As Executive Director of the McKnight Brain Institute I am committed to expanding translational research in cognitive aging. I am PI for several large-scale collaborative research programs such as the Northern Manhattan Study (NINDS-funded community-based, epidemiologic cohort study researching the determinants of cognitive impairment and stroke among an elderly, multi-ethnic, urban northern Manhattan population). This study has provided essential data on stroke disparities, as well as the impact of novel risk factors including inflammatory biomarkers and infectious burden. As the NOMAS study cohort ages, our focus has expanded to include the vascular contributions to cognitive aging and functional impairment. Further, my disparities related research (PI for the NINDS U54 Stroke Prevention and Intervention Research Program to support the Florida Puerto Rico Stroke Registry, and as PI in the Multi-PI Transition of Care Stroke Disparities Study), seeks to identify disparities and gaps in stroke care, which may limit cognitive recovery and severely affect quality of life after stroke. My work as Center Director for the AHA/ASA Bugher Center Foundation Center of Excellence has produced complementary clinical and basic science studies to enhance cognitive recovery and quality of life after stroke. I also have an extensive record of accomplishments in clinical trials currently functioning as Co-PI for the Miami Regional Coordinating Center for NINDS and Co-chair of the Steering Committee for RE-SPECT ESUS. These experiences have collectively provided me the knowledge and motivation to carry out and direct brain health research that is translational and of clinical relevance. I have published extensively with over 600 peer-reviewed articles and over 120 invited articles in the areas of stroke prevention, treatment, epidemiology, risk factors, vascular cognitive impairment, and human genetics. I have most recently been elected to the National Academy of Medicine and previously received numerous awards including, the Feinberg Award of Excellence in Clinical Stroke, the Wepfer Award, the Chairman's Award from the American Heart Association, and the NINDS Javits Award in Neuroscience. I have helped train numerous fellows in stroke and epidemiology and was co-director of a T32 entitled Neuro-epidemiology Training Program to train neurologists in epidemiology, as well as to mentor MD, PhD, and graduate students. I am fully committed to a clinical translational research agenda within my department and institution and have enhanced this mission through recruitments of academic faculty and the support of research infrastructure for training the next generation of translational scientists. As former president of the American Heart Association and current president of the American Academy of Neurology, I am fully committed to advancing scientific collaborations and building partnerships for clinical and translational brain research.

These four peer reviewed publications highlight my experience and qualifications for this project:

1. **Sacco RL**, Boden-Albala B, Abel G, Lin IF, Elkind M, Hauser WA, Paik MC, Shea S. Race-ethnic disparities in the impact of stroke risk factors: the northern Manhattan stroke study. **Stroke**. 2001; 32:1725-31.
2. **Sacco RL**, DeRosa JT, Haley EC Jr, Levin B, Ordonneau P, Phillips SJ, Rundek T, Snipes RG, Thompson JL; Glycine Antagonist in Neuroprotection Americas Investigators. Glycine antagonist in neuroprotection for patients with acute stroke: GAIN Americas: a randomized controlled trial. **JAMA**. 2001; 285:1719-28.
3. **Sacco RL**, Adams R, Albers G, Alberts MJ, Benavente O, Furie K, Goldstein LB, Gorelick P, Halperin J, Harbaugh R, Johnston SC, Katzan I, Kelly-Hayes M, Kenton EJ, Marks M, Schwamm LH, Tomsick T; American Heart Association/American Stroke Association Council on Stroke; Council on Cardiovascular Radiology and Intervention; American Academy of Neurology. Guidelines for prevention of stroke in patients with ischemic stroke or transient ischemic attack: a statement for healthcare professionals from the American Heart Association/American Stroke Association Council on Stroke: co-sponsored by the Council on Cardiovascular Radiology and Intervention: the American Academy of Neurology affirms the value of this guideline. **Circulation**. 2006; 113:e409-49.
4. **Sacco RL**. Achieving ideal cardiovascular and brain health: opportunity amid crisis: Presidential Address at the American Heart Association 2010 Scientific Sessions. **Circulation**. 2011; 123:2653-7.

B. Positions and Honors

POSITIONS AND EMPLOYMENT

Academic Appointments:

1989-97	Assistant Professor of Neurology & Public Health (Epidemiology) in the Sergievsky Center
1997-02	Associate Professor of Neurology & Public Health (Epidemiology) (with tenure)
2003-07	Professor of Neurology & Epidemiology, Columbia University, College of Physicians and Surgeons, Mailman School of Public Health, and the Sergievsky Center (with tenure)
2007-	Oleberg Family Chair in Neurological Disorders, Miller Professor of Neurology, Public Health Sciences, Neurosurgery, and Human Genetics (with tenure) and Chairman of Neurology, Miller School of Medicine, University of Miami
2016-	Senior Associate Dean of Clinical Research, Miller School of Medicine, University of Miami

Honors:

1982	Alpha Omega Alpha	1998	American Neurological Association
2001	Fellow of the American Heart Association	2004	Fellow of the American Academy of Neurology
2006	AHA/ASA William Feinberg Award	2007	AHA Chairman's Award
2008	NINDS Jacob Javits Award in the Neurosciences	2008	American Association of Physicians
2015	AHA, Gold Heart Award	2015	The Johann Jacob Wepfer Award of the ESC
2015	UM Provost's Award for Scholarly Activity	2016	World Stroke Organization, Global Leadership
2018	Nomination to the National Academy of Medicine		

Other Professional Experience

1997-03	NINDS, Performance Safety & Monitoring Committee, VISP Trial
2004-06	NINDS Neurosciences Training Grant Review Group, Member
2013-16	NINDS, National Advisory Neurological Disorders and Stroke Council
2002-03	NIH, Center for Scientific Review, EDC-3
2003-07	FDA, Peripheral and Central Nervous System Drug Advisory Panel
2005-08	AHA, National Board of Directors; ASA, Chair Stroke Advisory Committee
2010-11	AHA, President, National Board of Directors
1999-05	American Academy of Neurology, Clinical Research Subcommittee, Chair
2005-09	American Academy of Neurology, Board of Directors
2013-15	AAN, Vice President
2015-17	AAN, President-elect
2017-19	AAN, President

C. Contribution to Science

C.1. Health Disparities As Principal Investigator for both a 26-year old community-based, epidemiologic study designed to determine stroke incidence, risk factors, and prognosis in an elderly, multi-ethnic, urban population, as well as a more recent stroke registry, we have been gathering and reviewing essential data on stroke disparities. Through these studies, we have been able to document the greater incidence of stroke among Hispanics and the increased burden of hypertension and diabetes in this ethnic group. My work in the area aims to develop and implement high-impact,

culturally-appropriate interventions and prevention programs aimed at minority racial/ethnic groups, as well as those who are socioeconomically disadvantaged

1. **Sacco RL**, Boden-Albala B, Gan R, Kargman DE, Paik M, Shea S, Hauser WA, and the Northern Manhattan Stroke Study Collaborators. Stroke incidence among white, black and Hispanic residents of an urban community: the Northern Manhattan Stroke Study. *Am J Epidemiol* 1998;147:259-268
2. **Sacco RL**, Boden-Albala B, Abel G, Lin IF, Elkind M, Hauser WA, Paik MC, Shea S. Race-ethnic disparities in the impact of stroke risk factors: The Northern Manhattan Stroke Study. *Stroke* 2001;32:1725-1731
3. Dong C, Rundek T, Wright CB, Anwar Z, Elkind MS, **Sacco RL**. Ideal cardiovascular health predicts lower risks of myocardial infarction, stroke, and vascular death across whites, blacks, and Hispanics: the northern Manhattan study. *Circulation*. 2012; 125:2975-84. PMID: PMC3396556
4. **Sacco RL**, Gardener H, Wang K, Dong C, Ciliberti-Vargas MA, Gutierrez CM, Asdaghi N, Burgin WS, Carrasquillo O, Garcia-Rivera EJ, Nobo U, Oluwole S, Rose DZ, Waters MF, Zevallos JC, Robichaux M, Waddy SP, Romano JG, Rundek T; FL-PR CReSD Investigators and Collaborators.. Racial-Ethnic Disparities in Acute Stroke Care in the Florida-Puerto Rico Collaboration to Reduce Stroke Disparities Study. *J Am Heart Assoc*. 2017 Feb 14;6(2). pii: e004073. doi: 10.1161/JAHA.116.004073. PubMed PMID: 28196814

C.2. Randomized Clinical Trials – I have been involved in the design and conduct of numerous NIH and industry sponsored randomized clinical trials on stroke treatment and prevention. These include serving as PI, co-PI, co-I or on the executive or steering committees of international multi-center trials. Some have included innovative designs and answered important evidence treatment gaps.

1. **Sacco RL**, DeRosa JT, Haley EC Jr, Levin B, Ordonneau P, Phillips SJ, Rundek T, Snipes RG, Thompson JL. Glycine Antagonist in Neuroprotection Americas Investigators. Glycine antagonist in neuroprotection for patients with acute stroke: GAIN Americas: a randomized controlled trial. *JAMA*. 2001; 285:1719-28
2. Mohr JP, Thompson JL, Lazar RM, Levin B, **Sacco RL**, Furie KL, Kistler JP, Albers GW, Pettigrew LC, Adams HP Jr, Jackson CM, Pullicino P; Warfarin-Aspirin Recurrent Stroke Study Group. A comparison of warfarin and aspirin for the prevention of recurrent ischemic stroke. *N Engl J Med*. 2001;15;345:1444-51.
3. Homma S, **Sacco RL**, Di Tullio MR, Sciacca RR, Mohr JP; PFO in Cryptogenic Stroke Study (PICSS) Investigators. Effect of medical treatment in stroke patients with patent foramen ovale: patent foramen ovale in Cryptogenic Stroke Study. *Circulation*. 2002; 105:2625-31.
4. **Sacco RL**, Diener HC, Yusuf S, Cotton D, Ôunpuu S, Lawton WA, Palesch Y, Martin RH, Albers GW, Bath P, Bornstein N, Chan BP, Chen ST, Cunha L, Dahlöf B, De Keyser J, Donnan GA, Estol C, Gorelick P, Gu V, Hermansson K, Hilbrich L, Kaste M, Lu C, Machnig T, Pais P, Roberts R, Skvortsova V, Teal P, Toni D, Vandermaelen C, Voigt T, Weber M, Yoon BW; PRoFESS Study Group.. Aspirin and extended-release dipyridamole versus clopidogrel for recurrent stroke. *N Engl J Med*. 2008; 359:1238-1251. PMID: PMC2714259

C.3. Vascular Determinants of Cognitive Aging. Through the 26-year-old Northern Manhattan Study, which maintains an aging cohort, I have led our multi-disciplinary team towards research which considers a broader definition of brain health. Some resulting studies have focused on characterizing vascular risk factors and their involvement as brain health determinants.

1. Warsch JR, Rundek T, Paik MC, Elkind MS, **Sacco RL**, Wright CB. Association between northern Manhattan study global vascular risk score and successful aging. *J Am Geriatr Soc* 2013 Apr;61(4):519-24.
2. Katan M, Moon YP, Paik MC, **Sacco RL**, Wright CB, Elkind MS. Infectious burden and cognitive function The Northern Manhattan Study. *Neurology*. 2013 Mar 26;80(13):1209-15.
3. **Sacco RL**. Evolution from Stroke Risk Factors to Brain Health Determinants. *Cerebrovascular Diseases*. 2015 Jul 18;40(3-4):102-13.
4. Gardener H, Wright CB, Dong C, Cheung K, DeRosa J, Nannery M, Stern Y, Elkind MS, **Sacco RL**. Ideal cardiovascular health and cognitive aging in the Northern Manhattan Study. *JAHA*. 2016 Mar 1;5(3):e002731.

C.4. Epidemiology of Stroke. Over the past 33 years we have pursued research in stroke epidemiology. The central findings from this research include the elucidation of novel risk stroke factors (e.g., patent foramen ovale, carotid plaque, ideal cardiovascular health, homocysteine, HDL, alcohol, inflammation and infectious burden in stroke prevention) particularly in minority populations. Some of these reports were among the first in the literature.

1. **Sacco RL**, Elkind M, Boden-Albala B, Lin I-F, Kargman DE, Hauser WA, Shea S, Paik M. The protective effect of moderate alcohol consumption on ischemic stroke. *JAMA* 1999;281:53-60
2. **Sacco RL**, Benson RT, Kargman DE, Boden-Albala B, Tuck C, Lin I-F, Cheng JF, Paik MC, Shea S, Berglund L. High-density lipoprotein cholesterol and ischemic stroke in the elderly. *JAMA* 2001;285:2729-35
3. **Sacco RL**, Anand K, Lee HS, Boden-Albala B, Stabler S, Allen R, Paik MC. Homocysteine and the Risk of Ischemic Stroke in a Triethnic Cohort. The Northern Manhattan Study. *Stroke* 2004;35:2263-9
4. **Sacco RL**, Khatri M, Rundek T, Xu Q PhD, Gardener H, Boden-Albala B, Di Tullio M, Homma S, Elkind MSV, Paik MC. Improving Global Vascular Risk Prediction with Behavioral and Anthropometric Factors: The Multi-ethnic Northern Manhattan Cohort Study. *J Am Coll Cardiol* 2009;54:2303-11

C.5. Evidence-based Treatment Recommendations, Scientific Statements and Honorary Lectures – I have participated as lead author or collaborator on numerous highly-cited evidence-based recommendations from the AHA/ASA NSA, and IOM, as well as Scientific Statements that have been important to the field of stroke and cardiovascular diseases. I have also been a collaborator on numerous consortium including the Global Burden of Disease reports, Stroke Genetics Consortia, CHARGE, and other meta-analyses.

1. **Sacco RL**, Adams R, Albers G, Alberts MJ, Benavente O, Furie K, Goldstein LB, Gorelick P, Halperin J, Harbaugh R, Johnston SC, Katzan I, Kelly-Hayes M, Kenton EJ, Marks M, Schwamm LH, Tomsick T. Guidelines for prevention of stroke in patients with ischemic stroke or transient ischemic attack: a statement for healthcare professionals from the American Heart Association/American Stroke Association Council on Stroke. **Stroke**. 2006 Feb 37(2):577-617 PMID: 16432246 and *Circulation*. 2006; 113:e409-49
2. **Sacco RL**. The 2006 William Feinberg lecture: shifting the paradigm from stroke to global vascular risk estimation. *Stroke*. 2007; 38:1980-7.
3. **Sacco RL**. Achieving ideal cardiovascular and brain health: opportunity amid crisis: Presidential Address at the American Heart Association 2010 Scientific Sessions. *Circulation*. 2011;123:2653-7.
4. **Sacco RL**, Frieden TR, Blakeman DE, Jauch EC, Mohl S. What the million hearts initiative means for stroke: a presidential advisory from the American Heart Association/American Stroke Association. *Stroke*. 2012; 43:924-8.

Complete List of Published Work in My Bibliography:

<http://www.ncbi.nlm.nih.gov/pubmed/?term=sacco+rl>

D. Research Support

List of selected ongoing and completed research projects for the past three years:

Ongoing Research Support

R01NS 29993	Sacco (PI)	01/01/93-07/31/20
Stroke Incidence and Risk Factors in a Tri-Ethnic Region		
Aims: To determine the effects of risk factors including subclinical carotid and brain disease on the risk of stroke, MI, and vascular death in a prospective cohort of 3299 stroke-free community subjects from Northern Manhattan.		
Role: PI		
2R01NS240807	Rundek/Blanton (Multi-PI)	05/01/02-03/31/23
Family Study of Stroke Risk and Carotid Atherosclerosis		
Aims: The major goals of this project are to determine the genetic determinants of carotid IMT and plaque among high-risk Caribbean Hispanic families of the NOMAS.		
Role: Co-I		
U242NS107376	Benatar	07/01/18-06/30/23
University of Miami: Network of Excellence in Neuroscience Clinical Trials (NEXT)		
Aims: The goals of this proposal are to function effectively as a Neuro-NEXT NINDS consortium trial site		
Role: Co-I		
UL1TR002736	Sacco (PI)	06/28/18-05/31/23
KL2TR002737		06/28/18-05/32/23
UM Clinical Translation Science Institute		
To propel scientific discovery and its translation into evidence-based practice and community health, the Miami CTSI advances culturalized health sciences that embrace our majority racial/ethnic communities. Fundamental to accomplishing our mission is the orchestration of new and existing research, services and resources that foster excellence in translational research, promote interdisciplinarity, elevate research ethics, build research partnerships in community, and establish strong multidisciplinary graduate research programs.		
Role: PI		
U54 (NS 081763) (NCE)	Sacco (PI)	01/01/13-03/31/19
Hispanic Stroke Prevention Intervention Research Program		
Aims: The major goals of this project are to create the Florida Puerto Rico Stroke Registry to identify and reduce stroke disparities in acute stroke and secondary prevention		
Role: PI		

U24NS107267 Romano (PI) 08/01/18-07/31/23
Florida Regional Coordinating Center for NINDS Stroke-NET
Aims: The goals of the Miami RCC are to implement high-quality research clinical trials that address acute stroke treatment, prevention and recovery.
Role: Co-PI

1U01NS086872 Broderick (PI) 10/01/13-07/31/18
NSTN National Clinical Coordinating Center Stroke NET
Aims: The goals for the National Clinical Coordinating Center for the NINDS Stroke Network are to coordinate NINDS-funded trials in stroke prevention, acute therapy, and rehabilitation.
Role: Prevention, Co-chair and Co-I

R01NS083784 di Tullio (PI) 04/01/14-01/31/19
Prevalence and predictors of asymptomatic atrial fibrillation in the community
Aim: To expand knowledge of atrial fibrillation/other arrhythmias in the elderly and their relationship with stroke and other vascular events in addition to identifying high risk candidates for arrhythmia development whom might best benefit from intervention.
Role: Co-I

14BFSC17590000 (NCE) Sacco (PI) 04/01/14-03/31/19
American Heart Association/ASA-Bugher Foundation
University of Miami ASA/Bugher Foundation Center of Excellence in Stroke Collaborative
The intent of this initiative is to support a collaboration of basic, clinical and population researchers from different specialties whose collective efforts will lead to new approaches, not only to improve the prevention of stroke, but to also expand upon the previous Bugher Stroke initiatives by inviting research on recovery after a stroke; including the areas of repair, regeneration, neuro-plasticity and rehabilitation.
Role: PI

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Anita Seixas Dias Saporta

eRA COMMONS USER NAME (credential, e.g., agency login):

POSITION TITLE: Postdoctoral Research Associate

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Universidade Federal Fluminense (Rio de Janeiro, Brazil)	MD	09/2002	Medicine
Universidade do Estado do Rio de Janeiro (Rio de Janeiro, Brazil)	N/A	02/2004	Pediatric Residency
Instituto Fernandes Figueira (Rio de Janeiro, Brazil)	N/A	02/2006	Pediatric Neurology (Clinical Fellowship)
Wayne State University (MI, USA)	N/A	07/2009	Neuroimaging Research - Child Neurology (Post-doc)
Wayne State University (MI, USA)	N/A	07/2010	Neurogenetics Research - Inherited Neuropathies (Post-doc)
University of California in San Francisco (CA, USA)	N/A	05/2012	Neuroimaging Research - Neonatal Neurology (Post-doc)
University of Miami	N/A	Current	Neuroimaging Research - Clinical and Translational Research, Cognitive disorders and Epilepsy (Post-doc)

A. Personal Statement

I am highly motivated to pursue an academic carrier and, under the mentoring of Dr. Rundek, I am currently a research fellow at the University of Miami Evelyn F. McKnight Brain Institute.

My previous research work includes brain neuroimaging from the neonatal period to adulthood and utilizing multiple imaging modalities to analyze brain function and structure (PET, MRI, DTI, MRS). I also have experience with large database management and development of clinical tools. Since my clinical training in child neurology in Rio de Janeiro, Brazil, I developed an interest in the normal and pathological development of the brain, behavior and cognition. This interest brought me to pursue training and research projects in neuroimaging in reference centers including the PET Center at Wayne State University (Detroit, MI) and the Neonatal Brain Disorders Lab at UCSF (San Francisco, CA), and more recently at University of Miami.

Ultimately, I believe my previous experience and the opportunity to collaborate with the present project will help me follow my main career goal which is to identify clinical and neuroimaging phenotypical correlations in neurological disorders throughout the human's brain lifespan.

B. Positions and Honors

- 1996 - 2002 School of Medicine - Fluminense Federal University (UFF), Rio de Janeiro, Brazil
- 2002 MD Graduation
- 2003 - 2004 Pediatric Residency Program, State University of Rio de Janeiro (UERJ), Brazil
- 2005 - 2006 Child Neurology Fellowship, Fernandes Figueira Institute – FIOCRUZ (Reference center for autistic disorders, epilepsy, and neurogenetics)
- 2006 Board Certification in Pediatrics - Brazilian Pediatric Society
- 2007 – 2009 Post-doctoral Fellow in Neuroimaging – Translational Imaging Center / Children's Hospital of Michigan / Pediatric department - Wayne State University (Supervisor: Harry T. Chugani)
- 2009 – 2010 Post-doctoral Fellow in Neurogenetics – Charcot-Marie-Tooth North American Network / Neurology department - Wayne State University (Supervisor: Michael E. Shy)
- 2010 – 2012 Post-doctoral Fellow in the Neonatal Brain Disorders Lab, Department of Neurology - University of California, San Francisco (Supervisor: Donna M. Ferriero)
- 2014 Board Certification in Child Neurology – Brazilian Pediatric Society
- 2017 - to date Post-doctoral Research Fellow in Neuroimaging – Epilepsy Division, Neurology Department - University of Miami (Supervisor: Andres Kanner)
- June 2018 to date: McKnight Brain Institute Research Fellow at University of Miami

C. Contributions to Science

1. My early publications focused in identifying neuroimaging anatomical correlations in a diverse spectrum of neurological disorders. We identified, using Diffusion Tensor imaging (DTI), abnormal frontal lobe tracts in children with socio-emotional deprivation, thought to be related to defective fiber pruning and the reason for the behavior and cognitive abnormalities found in these children. We also demonstrated that the phenotypical variation in language development in children with congenital bilateral perisylvian syndrome is associated with the presence or absence of the Arcuate Fasciculus, a major language tract detectable by DTI. We also used multimodalities of neuroimaging, including Positron Emission Tomography (PET) and DTI, to study Tourette Syndrome. We identified the presence of asymmetric synthesis of serotonin in basal ganglia in addition to microstructural abnormalities of the cortico-striato-thalamo-cortical circuit, providing an anatomical basis for future therapy development efforts.

- a. Behen ME, Muzik O, Saporta AS, Wilson BJ, Pai D, Hua J, et al. Abnormal fronto-striatal connectivity in children with histories of early deprivation: A diffusion tensor imaging study. *Brain Imaging Behav.* 2009;3(3):292-7.
- b. Alkonyi B, Juhasz C, Muzik O, Asano E, Saporta A, Shah A, et al. Quantitative brain surface mapping of an electrophysiologic/metabolic mismatch in human neocortical epilepsy. *Epilepsy Res.* 2009;87(1):77-87.

- c. Saporta AS, Chugani HT, Juhasz C, Makki MI, Muzik O, Wilson BJ, et al. Multimodality neuroimaging in Tourette syndrome: alpha-[11C] methyl-L-tryptophan positron emission tomography and diffusion tensor imaging studies. *J Child Neurol.* 2010;25(3):336-42.
- d. Saporta AS, Kumar A, Govindan RM, Sundaram SK, Chugani HT. Arcuate fasciculus and speech in congenital bilateral perisylvian syndrome. *Pediatr Neurol.* 2011;44(4):270-4.

2. Next, my research focused on the most common cause of inherited peripheral neuropathies, Charcot-Marie-Tooth disease (CMT). I was responsible for curating a large registry of patients with CMT as part of a natural history and prevalence study. The goal of this project was to design effective strategies for the molecular diagnosis of CMT. The resulting paper in *Annals of Neurology* is a highly cited paper in the field (338 citations) and has had significant impact in the clinical management of patients with CMT.

- a. Saporta AS, Sottile SL, Miller LJ, Feely SM, Siskind CE, Shy ME. Charcot-Marie-Tooth disease subtypes and genetic testing strategies. *Ann Neurol.* 2011;69(1):22-33.
- b. Miller LJ, Saporta AS, Sottile SL, Siskind CE, Feely SM, Shy ME. Strategy for genetic testing in Charcot-Marie-disease. *Acta Myol.* 2011;30(2):109-16.

3. My most recent research contribution was a return to the neuroimaging field and focus on understanding the effects of therapeutic hypothermia in neonatal encephalopathy. Using proton magnetic resonance spectroscopy (H-MRS), We demonstrated that whole body hypothermia reduces disturbances of brain metabolism and preserve its microstructure in the setting of neonatal hypoxic encephalopathy.

- a. Bonifacio SL, Saporta A, Glass HC, Lee P, Glidden DV, Ferriero DM, et al. Therapeutic hypothermia for neonatal encephalopathy results in improved microstructure and metabolism in the deep gray nuclei. *AJNR Am J Neuroradiol.* 2012;33(11):2050-5.

My bibliography:

<https://www.ncbi.nlm.nih.gov/sites/myncbi/1L53O30urrJsd9/bibliography/56618993/public/?sort=date&direction=ascending>

D. Additional Information: Research Support and/or Scholastic Performance

None

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Wang, Jianhua

eRA COMMONS USER NAME (credential, e.g., agency login): jianhuawang

POSITION TITLE: Associate Professor

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)

INSTITUTION AND LOCATION	DEGREE (if applicable)	START DATE MM/YYYY	END DATE MM/YYYY	FIELD OF STUDY
Zhejiang Medical University, Hangzhou, Zhejiang	MD	09/1983	07/1988	Medicine
University of Waterloo, Waterloo, ON	MS	04/1999	06/2000	Vision Science
University of Waterloo, Waterloo, ON	PHD	07/2000	07/2003	Vision Science

A. Personal Statement

I have a broad background in vision research and electronic engineering, especially on advanced ophthalmic imaging and human studies. As an assistant professor at the University of Rochester, I have learnt optics and prototyped time domain optical coherence tomography devices through the joint work with OCT experts. After I moved to Miami, I have been working with other researchers to develop many other prototypes of spectral domain OCT devices. They are ultra-high resolution OCT, ultra-long scan depth OCT, dual-channel OCT, magnetomotive OCT and CMOS camera based ultra-high speed OCT. In recent 5 years, I have worked on vascular imaging of the eye and developed the methods and hardware to image microvasculature on the conjunctiva and retina. Working with a group of clinicians, I focus on microvasculature and microcirculation in the retina as a window of the cerebral vasculature in aging, multiple sclerosis and dementia. As the PI or co-Investigator on many previous industrial- and NIH-funded grants, I worked out the proposed research and published more than 140 papers in top journals. Currently, I am the co-director of scientific experimental imaging laboratory at the Bascom Palmer Eye Institute and managing my own lab. In summary, I have a good record of successful research projects in the area of ophthalmic imaging and clinical research. My expertise and experience make me well equipped and qualified for working in this proposed project.

1. Jiang H, Wei Y, Shi Y, Wright CB, Sun X, Gregori G, Zheng F, Vanner EA, Lam BL, Rundek T, **Wang J**. Altered Macular Microvasculature in Mild Cognitive Impairment and Alzheimer Disease. J Neuroophthalmol. 2017 Oct 16;PubMed PMID: [29040211](#).
2. Wei Y, Jiang H, Shi Y, Qu D, Gregori G, Zheng F, Rundek T, **Wang J**. Age-Related Alterations in the Retinal Microvasculature, Microcirculation, and Microstructure. Invest Ophthalmol Vis Sci. 2017 Jul 1;58(9):3804-3817. PubMed PMID: [28744554](#); PubMed Central PMCID: [PMC5527847](#).
3. Jiang H, Liu Y, Wei Y, Shi Y, Wright C, Sun X, Rundek T, Baumel B, Landman J and **Wang J**. Impaired retinal microcirculation in patients with Alzheimer's disease. PLOS one, 2018;e0192154. PubMed PMID: [29309463](#).
4. Wang L, Jiang H, Grinvald A, Jayadev C and **Wang J**. A mini review of clinical and research applications of the retinal function imager. Curr Eye Res. 2018 Jan8:1-16. PubMed PMID: [29308926](#).

B. Positions and Honors**Positions and Employment**

1988 - 1990	Resident, Department of Ophthalmology, Hangzhou First Hospital, Hangzhou
1991 - 1995	Ophthalmologist, Department of Ophthalmology, Hangzhou First Hospital, Hangzhou
1996 - 1999	Professional Affairs Manager, Johnson & Johnson Vision Products, China, Shanghai
2001 - 2001	Research Associate, University of Waterloo, Waterloo, ON
2003 - 2006	Research Assistant Professor, University of Rochester, Department of Ophthalmology,

- Rochester, NY
- 2006 - 2010 Assistant Professor, Bascom Palmer Eye Institute, University of Miami, Miami, FL
- 2008 - Assistant Professor, Department of Electrical and Computer Engineering, University of Miami, Miami, FL
- 2009 - Scientific Co-director of Experimental Imaging Laboratory, Bascom Palmer Eye Institute, University of Miami, Miami, FL
- 2010 - 2012 Associate Professor, Bascom Palmer Eye Institute, University of Miami, Miami, FL
- 2012 - Associate Professor (Tenured), Bascom Palmer Eye Institute, University of Miami, Miami, FL

Other Experience and Professional Memberships

- 1999 - Member, Association for Research in Vision and Ophthalmology (ARVO)
- 2001 - Fellow, American Association of Optometry (FAAO)
- 2001 - Member, American Association of Ophthalmology (AAO)
- 2002 - Member, Contact Lens Association of Ophthalmologists (CLAO)
- 2003 - Fellow, International Association of Contact Lens Research (IACLE)
- 2005 - Member, International Society of Contact Lens Research (ISCLR)

Honors

- 2000 Irvin M. & Beatrice Borish Student Travel Fellowship Award, American Academy of Optometry
- 2001 Travel award, International Society of Contact Lens Research
- 2003 Best Paper in Session, American Society of Cataract & Refractive Surgery
- 2003 Travel award, International Society of Contact Lens Research
- 2004 Pearson Medal for Creative Research, University of Waterloo

C. Contribution to Science

1. Through my more than 15 years of career development, I significantly contribute the development of optical coherence tomography prototypes for clinical research, especially in the field of anterior segment imaging. Worked with OCT experts, high speed time-domain OCT was developed for imaging tear film and tear dynamics in contact lens wearers and patients with dry eye syndrome. Collaborated with clinicians and engineers, ultra-high resolution OCT devices for imaging the anterior segments were developed for imaging the tear film, epithelium and ocular tumor by conducting clinic research.
 - a. Shao Y, Tao A, Jiang H, Mao X, Zhong J, Shen M, Lu F, Xu Z, Karp CL, Wang J. Age-related changes in the anterior segment biometry during accommodation. Invest Ophthalmol Vis Sci. 2015 Jun;56(6):3522-30. PubMed PMID: [26030106](#); PubMed Central PMCID: [PMC4464043](#).
 - b. Zhu D, Shen M, Jiang H, Li M, Wang MR, Wang Y, Ge L, Qu J, Wang J. Broadband superluminescent diode-based ultrahigh resolution optical coherence tomography for ophthalmic imaging. J Biomed Opt. 2011 Dec;16(12):126006. PubMed PMID: [22191923](#); PubMed Central PMCID: [PMC3247935](#).
 - c. Chen Q, Wang J, Shen M, Cui L, Cai C, Li M, Li K, Lu F. Tear menisci and ocular discomfort during daily contact lens wear in symptomatic wearers. Invest Ophthalmol Vis Sci. 2011 Apr 6;52(5):2175-80. PubMed PMID: [21051728](#).
 - d. Palakuru JR, Wang J, Aquavella JV. Effect of blinking on tear dynamics. Invest Ophthalmol Vis Sci. 2007 Jul;48(7):3032-7. PubMed PMID: [17591869](#).
2. Worked with optics experts, I contributed significantly to long scan depth OCT for imaging the full eyes in studying accommodation and full eye biometry. A unique system consists of two spectral domain OCT devices equipped with wavefront sensor was developed.
 - a. Du C, Shen M, Li M, Zhu D, Wang MR, Wang J. Anterior segment biometry during accommodation imaged with ultralong scan depth optical coherence tomography. Ophthalmology. 2012 Dec;119(12):2479-85. PubMed PMID: [22902211](#); PubMed Central PMCID: [PMC3505244](#).

- b. He JC, Wang J. Measurement of wavefront aberrations and lens deformation in the accommodated eye with optical coherence tomography-equipped wavefront system. *Opt Express*. 2014 Apr 21;22(8):9764-73. PubMed PMID: [24787861](#); PubMed Central PMCID: [PMC4083049](#).
 - c. Shao Y, Tao A, Jiang H, Mao X, Zhong J, Shen M, Lu F, Xu Z, Karp CL, Wang J. Age-related changes in the anterior segment biometry during accommodation. *Invest Ophthalmol Vis Sci*. 2015 Jun;56(6):3522-30. PubMed PMID: [26030106](#); PubMed Central PMCID: [PMC4464043](#).
3. I contribute significantly to image microvasculature on the ocular surface and retina. A system called functional slit-lamp biomicroscope (FSLB) was developed and a patent of single shot for generating conjunctival microvascular network map was filed. This novel system enables easily imaging the conjunctival microvascular network and small vessel blood flow velocity, which can be used to study microvascular response to contact lens wear and changes in dry eye. Worked with vascular experts in neuro-ophthalmology, we developed automatic segmentation of retinal microvascular network obtained using Retinal Function Imager (RFI) for studying retinal microvascular changes in multiple sclerosis, AD, diabetics and cerebral small vessel diseases. In addition, we developed ultra-high resolution OCT for imaging the retina and our segmentation software can segment 9 retinal sub-layers. Recent development of segmentation software enables automatic segmentation of 6 maps of retinal sub-layers. Furthermore, I adapted the RFI for the first time for imaging the conjunctiva by designing a optical adapter.
- a. Jiang H, Delgado S, Tan J, Liu C, Rammohan KW, DeBuc DC, Lam BL, Feuer WJ, Wang J. Impaired retinal microcirculation in multiple sclerosis. *Mult Scler*. 2016 Dec;22(14):1812-1820. PubMed PMID: [26903007](#); PubMed Central PMCID: [PMC4993688](#).
 - b. Xu Z, Jiang H, Tao A, Wu S, Yan W, Yuan J, Liu C, DeBuc DC, Wang J. Measurement variability of the bulbar conjunctival microvasculature in healthy subjects using functional slit lamp biomicroscopy (FSLB). *Microvasc Res*. 2015 Sep;101:15-9. PubMed PMID: [26092682](#); PubMed Central PMCID: [PMC4537817](#).
 - c. Jiang H, Zhong J, DeBuc DC, Tao A, Xu Z, Lam BL, Liu C, Wang J. Functional slit lamp biomicroscopy for imaging bulbar conjunctival microvasculature in contact lens wearers. *Microvasc Res*. 2014 Mar;92:62-71. PubMed PMID: [24444784](#); PubMed Central PMCID: [PMC3960300](#).
 - d. Jiang H, Debuc DC, Rundek T, Lam BL, Wright CB, Shen M, Tao A, Wang J. Automated segmentation and fractal analysis of high-resolution non-invasive capillary perfusion maps of the human retina. *Microvasc Res*. 2013 Sep;89:172-5. PubMed PMID: [23806780](#); PubMed Central PMCID: [PMC3773708](#).
4. I am also the first person who applied molecular imaging in ophthalmic research by using multimodal imaging modalities. Working with biologists, I developed a strategy to use novel spectroscopic and magnetomotive OCT approaches for in vivo detecting cochlin (a protein) in glaucomatous mice. This approach significantly improve our ability to detect and quantify proteins that are predictors of susceptibility (and/or progression or efficacy of treatments) in specific local tissue prior to clinical detection. The breakthrough will be immensely helpful to control various disease states.
- a. Wang J, Wang MR, Jiang H, Shen M, Cui L, Bhattacharya SK. Detection of magnetic particles in live DBA/2J mouse eyes using magnetomotive optical coherence tomography. *Eye Contact Lens*. 2010 Nov;36(6):346-51. PubMed PMID: [21060257](#); PubMed Central PMCID: [PMC3401487](#).
 - b. Goel M, Sienkiewicz AE, Picciani R, Wang J, Lee RK, Bhattacharya SK. Cochlin, intraocular pressure regulation and mechanosensing. *PLoS One*. 2012;7(4):e34309. PubMed PMID: [22496787](#); PubMed Central PMCID: [PMC3319572](#).
 - c. Wang J, Aljohani A, Carreon T, Gregori G, Bhattacharya SK. In vivo quantification of cochlin in glaucomatous DBA/2J mice using optical coherence tomography. *Sci Rep*. 2015 Jun 5;5:11092. PubMed PMID: [26047051](#); PubMed Central PMCID: [PMC4457137](#).

Complete List of Published Work in My Bibliography:

<https://www.ncbi.nlm.nih.gov/sites/myncbi/jianhua.wang.1/bibliography/48035987/public/?sort=date&direction=descending>

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

Sun_UM_1, Sun Yat-sen University collaboration award Wang, Jianhua (PI) 10/01/15-09/30/20
Clinical applications of advanced ophthalmic imaging
The goal of this study is to develop and apply advance ophthalmic imaging for clinical research in ophthalmology.
Role: PI

NMSS, National Multiple Sclerosis Society Hong Jiang (PI) 04/01/16-03/31/19
The Role of retinal microvascular impairment on Neurodegeneration in Multiple Sclerosis
The goal of this study is to determine the role of retinal microvascular impairment on neurodegeneration in MS.
Role: Co-Investigator

Food UM 01, Global Healthcare Focus LLC Wang, Jianhua (PI) 01/01/17-12/31/18
Food supplement Ocufofin on retinal blood flow velocity in patients with vascular retinopathy
The goal of this study is to determine retinal blood flow velocity in patient with vascular retinopathy after taking food supplement Ocufofin for 6 months.
Role: PI

Imaging Research, Bausch & Lomb, CooperVision and Allergan Jianhua Wang (PI) 01/01/06-12/31/20
Advanced ophthalmic imaging research
Unrestricted grants from Bausch & Lomb, CooperVision and Allergan for developing advanced ophthalmology imaging lab and clinical research.
Role: PI

Completed Research Support

JJVC, Johnson & Johnson Vision Product Hong Jiang (PI) 12/01/14-12/31/16
Conjunctival microvascular characterization of contact lens wear
The purpose is to characterize conjunctiva microvascular in contact lens wearer
Role: Co-Investigator

UM SAC 2015-27R1, University of Miami Jianhua Wang (PI) 01/01/15-06/30/16
Conjunctival Microvasculature and its association with tear protein biomarkers in dry eye syndrome
The purpose is to characterize conjunctival microvasculature in dry eye
Role: PI

NANOS, North American Neuro-Ophthalmology Society Hong Jiang (PI) 04/15/15-10/15/16
Retinal microvascular alteration as a possible biomarker in Alzheimer's disease
The purpose of this project is to characterize the retinal microvascular dysfunction and optical properties of Retinal nerve fiber layer in AD patients.
Role: Co-Investigator

R21 EY021012-01 National Eye Institute (NEI) WANG, JIANHUA (PI) 08/05/10-07/31/12
Magnetomotive optical coherence tomography for molecular imaging of the eye
The purpose of this project is to develop magnetomotive OCT for molecular imaging of the eye.
Role: PI

R03 EY016420-02 National Eye Institute (NEI) WANG, JIANHUA (PI) 09/30/05-08/31/08
Characterization of Tear Dynamics
The purpose of this project is to characterize human tear dynamics using custom built optical coherence tomography
Role: PI

Allergan UM Contract, Allergan Jianhua Wang (PI) 07/25/11-12/31/15
Tear dynamics after Restasis treatment in dry eye patients
This project is a clinical trial for further studying tear dynamics after treatment with Restasis in dry eye patients.
Role: PI

R21EY021336-01A1, National Eye Institute (NEI) He, Jichang (PI) 12/01/11-12/01/14
Optical coherence tomography equipped wavefront system for studying accommodation
The purpose of this project is to develop optical coherence tomography equipped wavefront system for studying accommodation
Role: Co-Investigator

1R21 EY019742-01A2, National Eye Institute (NEI) Wang, Michael (PI) 08/01/10-07/31/12
Optical reflectometry for tear film measurement
The purpose of this project is to develop a novel method called optical reflectometry for measuring human tear film in a nanometer scale.
Role: Co-Investigator

R03 EY016420-03 National Eye Institute (NEI) WANG, JIANHUA (PI) 09/30/05-08/31/08
Characterization of Tear Dynamics
The purpose of this project is to characterize human tear dynamics using custom built optical coherence tomography
Role: PI