

EVELYN F. McKNIGHT BRAIN INSTITUTE

**PROGRESS REPORT
JANUARY 1, 2015 TO DECEMBER 31, 2015
JANUARY 15, 2016**

**PRESENTED TO THE
EVELYN F. McKNIGHT BRAIN RESEARCH FOUNDATION
BOARD OF TRUSTEES**

THE UNIVERSITY OF MIAMI LEONARD M. MILLER SCHOOL OF MEDICINE

EVELYN F. McKNIGHT BRAIN INSTITUTE

January 13th, 2016

J. Lee Dockery, M.D.
Michael L. Dockery, M.D.
Nina Ellenbogen Raim, M.D., J.D.
Gene Ryerson, M.D.
Madhav Thambisetty, MD, Ph.D.
Robert 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,

Enclosed you will find an original and five copies of the 2015 Evelyn F. McKnight Brain Institute Progress Report. The report provides an update of our progress in fulfilling the mission of the McKnight Brain Research Foundation this past year at the University of Miami.

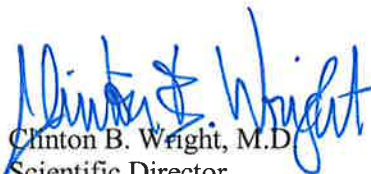
Please let us know if you have any questions about the report or would like further information.
Dr. Sacco: 305-243-7519 and Dr. Wright: 305-243-1664.

We are eager to begin working on our goals and endeavors for 2016 and look forward to a productive year.

Yours Sincerely,



Ralph L. Sacco, M.D., M.S.
Executive Director
Professor and Olemberg Chair of Neurology
Evelyn F. McKnight Brain Institute



Clinton B. Wright, M.D.
Scientific Director
McKnight Endowed Chair for Learning and
Memory in Aging
Evelyn F. McKnight Brain Institute

RLS/CBW/SM/bd

cc: Marsha Kegley
Hank Raatama
Marjorie Neil

1. Summary of Scientific Achievements since Last Report

This past year has been an exciting one at the UM-MBI, and our members and collaborators are energized by new initiatives that have brought investigators together, both at the University of Miami and across McKnight Institutes. Our research portfolio on age-related cognitive changes has continued to grow through extramural funding from the NIH and other sources, while new funding from the MBRF is allowing continued work to standardize neuroimaging and cognitive assessments across MBIs and establish a registry of the oldest old.

In 2015 the McKnight MRI core began to support development of the Brain Aging Registry and work has continued to get the program up and running across MBIs. Through these efforts the cognitive group was reconvened and a proposal was submitted. As a result, the MBRF awarded a two-year \$800,000 block grant to fund the McKnight Inter-Institutional Cognitive Aging Assessment Core, and work began in September to harmonize cognitive assessments across sites. With both the MRI and Cognitive cores funded, MBI investigators were able to develop a complete protocol that is now in the process of regulatory review by IRBs across Institutes.

Clinical and Population-based Research

Members of the UM-MBI have continued to initiate and collaborate on important epidemiologic studies. The Northern Manhattan Study was funded for a fifth five-year cycle with a major shift in focus to age-related cognitive changes and outcomes. Through continued collaboration between the departments of Neurology and Psychology, the Hispanic Communities Health Study (HCHS) Neurocognitive Assessment study was funded by NIA. This five year multi-site grant will allow a second wave of neuropsychological assessments across the four HCHS sites involving several thousand participants. We have continued to enroll participants into our AHA Bugher project examining the effects of aerobic and resistance exercise training on cognition after stroke in humans. We have initiated studies of cortical excitability and plasticity using non-invasive brain stimulation in McKnight Brain Aging Registry participants as well as participants in the AHA Bugher trial. We have begun collaborating on a study of the effects of traumatic brain injury on cognition funded by the Department of Defense. New initiatives involving large epidemiologic studies, including the Multi-ethnic Study of Atherosclerosis (MESA), are planned. In addition, our trainees have been awarded new grants to study sleep and caregiver burden among stroke patients.

Basic and Translational Science

As part our AHA Bugher Center of Excellence, our animal work continues on the effects of an enriched environment and exercise on ischemic damage and cognitive abilities. A new grant funds a novel model of white matter disease with translational potential for vascular cognitive impairment. New animal imaging techniques will explore the effects of diabetes on brain synapses with potential for cognitive studies as part of future grant applications. New NIH funding in 2015 supports our mitochondrial work. These projects now range from yeast models to human tissue.

Educational Programs

Our UM-MBI educational programs have continued to grow in 2015, with increasing effect across a wide audience. In her role as Education Director, Dr. Sun has provided much needed support in designing our seminar series and journal clubs directed at trainees at all levels, and has worked on enhancing the curriculum for medical students and house staff in Neurology. Dr. Levin continues to educate psychology graduate students and Post-Doctoral fellows on age-related memory loss as part of a seminar series and practicum curriculum. Education of caregivers and health professionals has also continued through community outreach in collaboration with Drs. Czaja and Crocco as part of the Miami Area Geriatric Education Center (MAGEC) and the State of Florida Alzheimer Disease Initiative as well as the Center On Aging. On both the clinical and basic research tracks, MBI members and collaborators mentor a wide range of trainees in diverse areas related to the mission of the Institute and several trainees have successfully competed for funding from different sources, both intra-mural and extra-mural.

2. Selected Publications by Institute Members, Collaborators & Trainees (Peer Reviewed)

Abrams AJ, Hufnagel RB, Rebelo A, Zanna C, Patel N, Gonzalez MA, Campeanu IJ, Griffin LB, Groenewald S, Strickland AV, Tao F, Speziani F, Abreu L, Schüle R, Caporali L, La Morgia C, Maresca A, Liguori R, Lodi R, Ahmed ZM, Sund KL, Wang X, Krueger LA, Peng Y, Prada CE, Prows CA, Schorry EK, Antonellis A, Zimmerman HH, Abdul-Rahman OA, Yang Y, Downes SM, Prince J, Fontanesi F, **Barrientos A**, Németh AH, Carelli V, Huang T, Zuchner S, Dallman JE. Mutations in SLC25A46, encoding a UGO1-like protein, cause an optic atrophy spectrum disorder. *Nat Genet.* 2015;47:926-32.

Alperin N, Lee SH, Bagci AM. MRI Measurements of Intracranial Pressure in the Upright Posture: The Effect of the Hydrostatic Pressure Gradient. *J Magn Reson Imaging* 2015;42:1158-63.

Alperin N, Loftus JR, Oliu CJ, Bagci AM, Lee SH, Ertl-Wagner B, Sekula R, Lichtor T, Green AB. Imaging-Based Features of Headaches in Chiari Malformation Type I. *Neurosurgery* 2015;77:96-103.

Arguello T, **Moraes CT**, Cre recombinase activity is inhibited in vivo but not ex vivo by a mutation in the asymmetric spacer region of the distal loxP site. *Genesis* 2015 Sep 1. doi: 10.1002/dvg.22899. [Epub ahead of print].

Bademci G, Foster J 2nd, Mahdieh N, Bonyadi M, Duman D, Cengiz FB, Menendez I, Diaz-Horta O, Shirkavand A, Zeinali S, Subasioglu A, Tokgoz-Yilmaz S, Huesca-Hernandez F, de la Luz Arenas-Sordo M, Dominguez-Aburto J, Hernandez-Zamora E9, Montenegro P, Paredes R, Moreta G, Vinueza R, Villegas F, Mendoza-Benitez S, Guo S, Bozan N, Tos T, Incesulu A, Sennaroglu G, **Blanton SH**, Ozturkmen-Akay H, Yildirim-Baylan M, Tekin M. Comprehensive analysis via exome sequencing uncovers genetic etiology in autosomal recessive nonsyndromic deafness in a large multiethnic cohort. *Genet Med.* 2015 Jul 30. doi: 10.1038/gim.2015.89. [Epub ahead of print]. *PMC Journal-In Process.*

Barrientos A. Mitochondriolus: assembling mitoribosomes. *Oncotarget* 2015;6:16800-1.

Cespedes EM, Dudley KA, Sotres-Alvarez D, Zee PC, Daviglius ML, Shah NA, Talavera GA, Gallo LC, Mattei J, Qi Q, **Ramos AR**, Schneiderman N, Espinoza-Giacinto RA, Patel SR. Joint Associations of Insomnia and Sleep Duration with Prevalent Diabetes: The Hispanic Community Health Study/ Study of Latinos (HCHS/SOL). *J Diabetes.* 2015 doi: 10.1111/1753-0407.12308. PMID:25952169.

Chang YC, **Alperin N***, Bagci AM, Lee SH, Rosa PR, Giovanni G, Lam BL, Relationship between Optic Nerve Protrusion Measured by OCT and MRI and Papilledema Severity. *Invest Ophthalmol Vis Sci.* 2015;5:2297-302. (*co-first author).

Cheung YK, Yu G, Wall MM, **Sacco RL**, Elkind MS, Willey JZ. Patterns of leisure-time physical activity using multivariate finite mixture modeling and cardiovascular risk factors in the Northern Manhattan Study. *Ann Epidemiol.* 2015;25:469-74.

Cohan CH, Neumann JT, **Dave KR**, Alekseyenko A, Binkert M, Stransky K, **Lin HW**, Barnes CA, **Wright CB**, **Perez-Pinzon MA**. Effect of Cardiac Arrest on Cognitive Impairment and Hippocampal Plasticity in Middle-aged Rats. *PLoS One* 2015;10:e0124918.

Czaja SJ. Can technology empower older adults to manage their health? *Generations* 2015;1:46-51.

- Czaja SJ**, Sabbag S, Lee CC, Schulz R, Lang S, Vlahovic T, Jaret AJ, Thurston C. Concerns about aging and caregiving among middle-aged and older Lesbian and Gay Adults. *Aging & Mental Health* 2015 doi:10.1080/13607863.2015.1072795.
- Czaja SJ**, Zarcadoolas C, Vaughon W, Lee CC, Rockoff M, Levy J. The Usability of Electronic Personal Health Record System for an underserved Adult Population. *Human Factors* 2015;3:491-506, DOI: 10.1177/0018720814549238 May.
- de Rivero Vaccari JP, Patel HH, Brand FJ 3rd, **Perez-Pinzon MA**, Bramlett HM, **Raval AP**. Estrogen receptor beta signaling alters cellular inflammasomes activity after global cerebral ischemia in reproductively senescence female rats. *J Neurochem*. 2015 (In press).
- De Silva D, Tu YT, Amunts A, Fontanesi F, **Barrientos A**. Mitochondrial ribosome assembly in health and disease. *Cell Cycle* 2015;14:2226-50.
- Del Brutto OH, Mera RM, Del Brutto VJ, Maestre GE, **Gardener H**, Zambrano M, **Wright CB**. Influence of depression, anxiety and stress on cognitive performance in community-dwelling older adults living in rural Ecuador: results of the Atahualpa Project. *Geriatric Gerontology International* 2015;15:508-14.
- Dhamoon MS, **Dong C**, Elkind MS, **Sacco RL**. Ideal cardiovascular health predicts functional status independently of vascular events: the Northern Manhattan Study. *J Am Heart Assoc*. 2015;4.
- 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;240:462-7. doi: 10.1016/j.atherosclerosis.2015.04.019. PMID: PMC4441583 [Available on 2016-06-01]. PMID: PMC4441583 [Available on 2016-06-01].
- Dong C**, Della-Morte D, Cabral D, Wang L, **Blanton SH**, Seemant C, **Sacco RL**, **Rundek T**. Sirtuin/uncoupling protein gene variants and carotid plaque area and morphology. *Int J Stroke*. 2015 Sep 1. doi: 10.1111/ijss.12623. [Epub ahead of print]. PMC Journal-In Process.
- Dong C**, Nabizadeh N, **Caunca M**, Cheung YK, **Rundek T**, Elkind MS, DeCarli C, **Sacco RL**, Stern Y, **Wright CB**. Cognitive correlates of white matter lesion load and brain atrophy: the Northern Manhattan Study. *Neurology* 2015;85:441-9.
- Cespedes EM, Hu FB, Redline S, Rosner B, Alcantara C, Cai J, Hall MH, Loreda JS, Mossavar-Rahmani Y, **Ramos AR**, Reid KJ, Shah NA, Sotres-Alvarez D, Zee PC, Wang R, Patel SR. Comparison of Self-Reported Sleep Duration with Actigraphy: Results from the Hispanic Community Health Study/Study of Latinos Sueño Ancillary Study. *Am J of Epidemiology*. 2015 (in press).
- Garcia L, Lee A, **Zeki Al Hazzouri A**, Neuhaus J, Epstein M, Haan M. The Impact of Neighborhood Socioeconomic Position on Prevalence of Diabetes and Prediabetes in Older Latinos: The Sacramento Area Latino Study on Aging. *Hisp Health Care Int*. 2015;13:77-85. PMC4470296.
- Gardener H**, **Rundek T**, **Wright CB**, Gu Y, Scarmeas N, Homma S, Russo C, Elkind MS, **Sacco RL**, Di Tullio MR. A Mediterranean-style diet and left ventricular mass (from the Northern Manhattan Study). *Am J Cardiol*. 2015;15:510-4. doi: 10.1016/j.amjcard.2014.11.038.
- Gardener H**, **Wright CB**, **Rundek T**, **Sacco RL**. Brain health and shared risk factors for dementia and stroke. *Nat Rev Neurol*. 2015;11:651-7.

Glazer H, **Dong C**, Yoshita M, **Rundek T**, Elkind, MSV, **Sacco RL**, DeCarli C, Stern Y, **Wright CB**. Subclinical cerebrovascular disease inversely associates with learning ability: The NOMAS Study. *Neurology* 2015;84:2362-2367.

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. *J Neurotrauma* 2015.

Gomes-Osman J, Field-Fote EC. Cortical vs. afferent stimulation as an adjunct to functional task practice training: A randomized, comparative pilot study in people with cervical spinal cord injury. *Clin Rehabil* 2015;29:771-82.

Gomes-Osman J, Field-Fote EC. Improvements in Hand Function in Adults With Chronic Tetraplegia Following a Multiday 10-Hz Repetitive Transcranial Magnetic Stimulation Intervention Combined With Repetitive Task Practice. *J Neurol Phys Ther.* 2015;39:23-30.

Gutierrez J, Cheung K, Bagci A, **Rundek T**, **Alperin N**, **Sacco RL**, **Wright CB**, Elkind MS. Brain Arterial Diameters as a Risk Factor for Vascular Events. *J Am Heart Assoc.* 2015;6:4:e002289. doi: 10.1161/JAHA.115.002289.

Gutierrez J, Elkind MS, Cheung K, **Rundek T**, **Sacco RL**, **Wright CB**. Pulsatile and steady components of blood pressure and subclinical cerebrovascular disease: the Northern Manhattan Study. *J Hypertens.* 2015;33:2115-22. doi: 10.1097/HJH.0000000000000686.

Gutierrez J, Elkind MS, Gomez-Schneider M, DeRosa JT, Cheung K, Bagci A, **Alperin N**, **Sacco RL**, **Wright CB**, **Rundek T**. Compensatory intracranial arterial dilatation in extracranial carotid atherosclerosis: The Northern Manhattan Study. *Int J Stroke.* 2015;10:843-8.

Hashimoto M, Bacman SR, Peralta S, Falk MJ, Chomyn A, Chan DC, Williams SL, **Moraes CT**. MitoTALEN: A General Approach to Reduce Mutant mtDNA Loads and Restore Oxidative Phosphorylation Function in Mitochondrial Diseases. *Molecular therapy: the journal of the American Society of Gene Therapy* 2015;23:1592-1599.

Haussen DC, Rose DZ, Drazin D, Newsome SD, **Gardener H**, Edgell RC, Boulos A, Bernardini G, **Rundek T**, Yavagal DR. Ipsilateral Infarct in Newly Diagnosed Cervical Internal Carotid Artery Atherosclerotic Occlusion. *Interventional Neurology* 2015;3:142-8.

Ivkovic M, Reiss-Zimmermann M, Katzen H, Preuss M, Kovanlikaya I, Heier L, **Alperin N**, Hoffmann KT, Relkin N. MRI assessment of the effects of acetazolamide and external lumbar drainage in idiopathic Normal Pressure Hydrocephalus. *Fluids Barriers CNS* 2015;12:9.

Koronowski KB, **Perez-Pinzon MA**. Sirt1 in cerebral ischemia. *Brain Circulation.* 2015;1:69-78.

Koronowski KB, **Dave KR**, Saul I, Camarena V, Thompson JW, Neumann JT, **Young JI**, **Perez-Pinzon MA**. Resveratrol Preconditioning Induces a Novel Extended Window of Ischemic Tolerance in the Mouse Brain. *Stroke* 2015;46:2293-8.

Lee RHC, Couto e Silva A, Wilkins CS, Valido SE, Klein DD, Wu CY, Neumann JT, **Wright CB**, Guadagni F, Caso V, Santucci M, Della Morte D, **Lin HW**. Neuroprotective effects of sympathetic attenuation in the ischemic brain (2015) (In progress).

Lee RHC, Goyanes Vasquez JJ, Couto e Silva A, Klein DD, Valido SE, Chen JA, Lerner FM, Neumann JT, Wu CY, **Lin HW**. Fatty acid methyl esters as a potential therapy against cerebral ischemia. *Oilseeds & fats Crops and Lipids.* 2015 (In press).

Lee RHC, Wilkins CS, Couto e Silva A, Valido SE, Klein DD, Wu CY, **Lin HW**. Characterization of methyl palmitate in the brain (2015) (In progress).

Maniyar FH, Sprenger T, **Monteith T**, Schankin CJ, Goadsby PJ. The premonitory phase of migraine-- what can we learn from it? *Headache*. 2015;5:609-20.

Materson BJ, **Wright CB**. Goal blood pressure for cognition-impaired patients: let's treat the patients-- not the numbers. *J Am Soc Hypertens*. 2015;9:504-6. doi: 10.1016/j.jash.2015.04.005. Epub 2015 May 1.

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;32:1056-1063.

Minen MT, **Monteith T**, Strauss LD, Starling A. New Investigator and Trainee Task Force Survey on the Recruitment and Retention of Headache Specialists. *Headache* 2015;8:1092-101.

Monteith TS, Gardener H, Rundek T, Elkind MS, Sacco RL. Migraine and risk of stroke in older adults: Northern Manhattan Study. *Neurology* 2015;85:715-21.

Moraes CT, Oliveira DB, Campos AC, Bosso PA, Lima HN, Stewien KE, Gilio AE, Vieira SE, Botosso VF, Durigon EL. Genetic variability in G2 and F2 region between biological clones of human respiratory syncytial virus with or without host immune selection pressure. *Memorias do Instituto Oswaldo Cruz* 2015;110:138-141.

Mossavar-Rahmani Y, Jung M, Patel SR, Sotres-Alvarez D, Arens R, **Ramos A**, Redline S, Rock CL, Van Horn L. Eating behavior by sleep duration in the Hispanic Community Health Study/Study of Latinos. *Appetite* 2015;95:275-284. PMID:26189885.

Narayanan SV, **Dave KR**, Saul I, **Perez-Pinzon MA**. Resveratrol Preconditioning Protects Against Cerebral Ischemic Injury via Nuclear Erythroid 2-Related Factor 2. *Stroke* 2015;46:1626-32.

Neal SE, Dabir DV, Tienson HL, Horn DM, Glaeser K, Ogozalek Loo RR, **Barrientos A**, Koehler CM. Mia40 serves as an electron sink in the Mia40-Erv1 import pathway. *J Biol Chem*. 2015;290:20804-14.

Neumann JT, Thompson JW, **Raval AP**, Cohan CH, Koronowski KB, **Perez-Pinzon MA**. Increased BDNF protein expression after ischemic or PKC epsilon preconditioning promotes electrophysiologic changes that lead to neuroprotection. *J Cereb Blood Flow Metab*. 2015;35:121-30.

Patel SR, Sotres-Alvarez D, Castañeda SF, Dudley KA, Gallo LC, Hernandez R, Medeiros EA, Penedo FJ, Mossavar-Rahmani Y, **Ramos AR**, Redline S, Reid KJ, Zee PC. Social and Health Correlates of Sleep Duration in a US Hispanic Population: Results from the Hispanic Community Health Study/Study of Latinos. *SLEEP* 2015;38:1515-22. Jun 11. pii: sp- 00591-14. PMID:26085298.

Patel SR, Weng J, Rueschman M, Dudley KA, Loredó JS, Mossavar-Rahmani Y, Ramirez M, **Ramos AR**, Reid K, Seiger AN, Sotres-Alvarez D, Zee PC, Rui Wang, R. Reproducibility of a Standardized Actigraphy Scoring Algorithm for Sleep in a US Hispanic/Latino Population. *SLEEP* 2015;38 pii: sp-00708-14. PMID: 258456.

Pinto M., **Moraes CT**. Mechanisms linking mtDNA damage and aging. *Free radical biology & medicine* 2015;85:250-258.

Ramos A, Tarraf W, Daviglius M, et al. Sleep duration is associated with worse neurocognitive function in Hispanic/Latinos: Results of the Hispanic Community Health Study/Study of Latinos. *Neurology* 2015;84 Supplement:100.

Ramos AR, Azizi A, Dib SI. Obstructive sleep apnea and stroke: links to health disparities. *Sleep Health: Journal of the National Sleep Foundation*. 2015 (in press).

Ramos AR, Tarraf W, **Rundek T**, Redline S, Wohlgemuth WK, Loredó JS, **Sacco RL**, Lee DJ, Arens R, Lazalde P, Choca JP, Mosely T, Gonzalez, HM. Obstructive Sleep Apnea and Neurocognitive Function among Hispanics/Latinos. *Neurology* 2015;84:391-398. PMID:25540308.

Ramos AR, Wallace DM, Pandi-Perumal SR, Williams NJ, Castor C, Sevick MA, McFarlane SI, Girardin Jean-Louis G. Associations between sleep disturbances and diabetes mellitus among blacks with metabolic syndrome: results from the Metabolic Syndrome Outcome Study (MetSO) *Ann Med*. 2015;9:1-5.

Ravenscroft TA, Pottier C, Murray ME, Baker M, Christopher E, Levitch D, Brown P, Barker W, Greig-Custo M, English M, **Sun X**, Ertekin-Taner N, Neill R, Graff-Radford N, Dickson D, Rademakers R. The Presenilin 1 p.Gly206Ala mutation is a frequent cause of Early-Onset Alzheimer's Disease in Hispanics in Florida. In preparation, *AJND*, 2015.

Riasco R, Heymann JC, Hakimelahi R, Hasan K, Sargsyan A, Barr YR, Tom J, **Alperin N**, Kramer L. Novel finding of optic nerve central T2 hypointensity utilizing 3 Tesla MR imaging. *Neuroradiol J*. 2015;28:133-6.

Ringstad G, Emblem KE, Geier O, **Alperin N**, Eide PK. *AJNR Am J Neuroradiol. Aqueductal Stroke Volume- Replay* 2015;36:1633-4. doi: 10.3174/ajnr.A4488. Epub 2015 Aug 6.

Ringstad G, Eeg Emblem K, Geier O, **Alperin N**, Eide P, *Aqueductal Stroke Volume: Comparisons with Intracranial Pressure Scores in Idiopathic Normal Pressure Hydrocephalus. AJNR Am J Neuroradiol*. 2015;36:1623-30. doi: 10.3174/ajnr.A4340.

Rossetti M, Piryatinsky I, Ahmed F, Klinge P, Relkin N, Salloway S, Ravdin L, Brenner E, Malloy P, **Levin B**, Broggi M, Gavett R, Maniscalco J, Katzen H. Two novel psychomotor tasks in Idiopathic Normal Pressure Hydrocephalus. *Journal of International Neuropsychological Society* (in press).

Ruetenik AL, **Barrientos A**. Dietary restriction, mitochondrial function and aging: from yeast to humans. *BBA: Bioenergetics* 2015;1847:1434–1447.

Sacco RL. Evolution from Stroke Risk Factors to Brain Health Determinants. *Cerebrovasc Dis*. 2015; 40:102-13.

Sacco RL, Sandercock P, Endres M, Feigin V, Pandian J, Shinohara Y, Spence JD. Review and prioritization of stroke research recommendations to address the mission of the World Stroke Organization: a call to action from the WSO Research Committee. *Int J Stroke*. 2015;10:4-9. Suppl A100.

Shah N, Allison M, Teng V, Wassertheil-Smoller S, Sotres-Alvarez D, **Ramos AR**, Zee P, Criqui M, Yaggi H, Gallo L, Redline S, Kaplan R. Sleep Apnea is Independently Associated with Peripheral Arterial Disease in the Hispanic Community Health Study/Study of Latinos. *Arterioscler Thromb Vasc Biol*. 2015;35:710-5. PMID:25657310.

Shah NH, **Dong C**, Elkind MS, **Sacco RL**, Mendez AJ, Hudson BI, Silverberg S, Wolf M, **Rundek T**,

Wright CB. Fibroblast Growth Factor 23 Is Associated With Carotid Plaque Presence and Area: The Northern Manhattan Study. *Arterioscler Thromb Vasc Biol.* 2015;35:2048-53. doi: 10.1161/ATVBAHA.115.305945. Epub 2015 Jun 25.

Soto I, **Barrientos A.** Cytochrome c oxidase biogenesis is regulated by the redox state of a heme-binding translational activator. *Antiox Redox Signal* (2015) (in press).

Sun X, Dong C, Levin B, Crocco E, Loewenstein D, Zetterberg H, Blenow K, **Wright CB,** and the Alzheimer's Disease Neuroimaging Initiative. APOE ϵ 4 carriers may undergo synaptic damage conferring risk of Alzheimer's disease. *Alzheimer's & Dementia* in revision 2015.

Tigano M, Ruotolo R, Dallabona C, Fontanesi F, **Barrientos A,** Donnini C, Ottonello S. Elongator- dependent modification of cytoplasmic tRNA^{Lys}UUU is required for mitochondrial function under stress conditions. *Nuc Ac Res.* July 2015. [Epub ahead of time].

Tiozzo E, Youbi M, **Dave K, Perez-Pinzon M, Rundek T, Sacco RL,** Loewenstein D, Lewis JE, **Wright CB.** Aerobic, Resistance, and Cognitive Exercise Training Poststroke. *Stroke* 2015;46:2012-6.

Tosto G, Fu H, Vardarajan BN, Lee JH, Cheng R, Reyes-Dumeyer D, Lantigua R, Medrano M, Jimenez-Velazquez IZ, Elkind MS, **Wright CB, Sacco RL,** Pericak-Vance M, Farrer L, Rogava E, St George-Hyslop P, Reitz C, Mayeux R. F- box/LRR-repeat protein 7 is genetically associated with Alzheimer's disease. *Ann Clin Transl Neurol.* 2015;2:810-20.

Tu YT, **Barrientos A.** The human mitochondrial DEAD-Box protein DDX28 resides in RNA granules and functions in mitoribosome assembly. *Cell Reports* 2015;10:854-64.

Valente TW, Palinkas LA, **Czaja S,** Chu KH, Brown CH. Social Network Analysis for Program Implementation. *PLoS ONE,* 2015;10, e0131712. doi:10.1371/journal.pone.0131712.

Verhaaren BF, DeBette S, Bis JC, Smith JA, Ikram MK, Adams HH, Beecham AH, Rajan KB, Lopez LM, Barral S, van Buchem MA, van der Grond J, Smith AV, Hegenscheid K, Aggarwal NT, de Andrade M, Atkinson EJ, Beekman M, Beiser AS, **Blanton SH,** Boerwinkle E, Brickman AM, Bryan RN, Chauhan G, Chen CP, Chouraki V, de Craen AJ, Crivello F, Deary IJ, Deelen J, De Jager PL, Dufouil C, Elkind MS, Evans DA, Freudenberger P, Gottesman RF, Gudnason V, Habes M, Heckbert SR, Heiss G, Hilal S, Hofer E, Hofman A, Ibrahim-Verbaas CA, Knopman DS, Lewis CE, Liao J, Liewald DC, Luciano M, van der Lugt A, Martinez OO, Mayeux R, Mazoyer B, Nalls MA, Nauck M, Niessen WJ, Oostra BA, Psaty BM, Rice KM, Rotter JI, von Sarnowski B, Schmidt H, Schreiner PJ, Schuur M, Sidney SS, Sigurdsson S, Slagboom PE, Stott DJ, van Swieten JC, Teumer A, Töglhofer AM, Traylor M, Trompet S, Turner ST, Tzourio C, Uhl HW, Uitterlinden AG, Vernooij MW, Wang JJ, Wong TY, Wardlaw JM, Windham BG, Wittfeld K, Wolf C, **Wright CB,** Yang Q, Zhao W, Zijdenbos A, Jukema JW, **Sacco RL,** Kardina SL, Amouyel P, Mosley TH, Longstreth WT Jr, DeCarli CC, van Duijn CM, Schmidt R, Launer LJ, Grabe HJ, Seshadri SS, Ikram MA, Fornage M. Multi-Ethnic Genome-Wide Association Study of Cerebral White Matter Hyperintensities on MRI. *Circ Cardiovasc Genet.* 2015;8:398-409. doi: 10.1161/CIRCGENETICS.114.000858. PMID: PMC4427240 [Available in 2016-04-01].

Wang L, Beecham A, Dueker N, **Blanton SH, Rundek T, Sacco RL.** Sequencing of candidate genes in Dominican families implicates both rare exonic and common non-exonic variants for carotid intima-media thickness at bifurcation. *Hum Genet.* 2015;134:1127-38. doi: 10.1007/s00439-015-1592-z. PMID: PMC4570583 [Available on 2016- 10-01].

Widerstrom-Noga E, Govind VB, Adcock J, **Levin BE,** Maudsley A. Subacute Pain after TBI is associated with lower insular N-acetyl-aspartate concentrations. *Journal of Neurotrauma* (in press).

Willey JZ, Moon YP, Sherzai A, Cheung YK, **Sacco RL**, Elkind MS. Leisure-time physical activity and mortality in a multiethnic prospective cohort study: the Northern Manhattan Study. *Ann Epidemiol.* 2015;25:475-479.e2.

Wright CB, Flores A. Vascular contributions to cognitive impairment. *Neurol Clin Pract.* 2015;5:201-208.

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;63:1540-5.

Xu Z, **Jiang H***, Tao A, Wu SQ, Yan WT, Yuan J, Liu C, DeBuc DC, Wang J. Measurement variability of the bulbar conjunctival microvasculature in healthy subjects using functional slit-lamp biomicroscopy (FSLB). *Microvascular Research* 2015;101:15-19.

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;40:136-43. doi: 10.1159/000434761. Epub 2015 Jul 25.

Zeki Al Hazzouri A, Haan MN, Robinson W, Gordon-Larsen P, Clayton E, Aiello A. Associations of intergenerational education with waist circumference, metabolic syndrome, and type-2 diabetes in US Latinos. *Obesity* 2015;23:1097-1104. PMC4414717.

Zeki Al Hazzouri A, Vittinghoff E, Sidney S, Reis JP, Jacobs DR Jr, Yaffe K. Intima-Media Thickness and Cognitive Function in Stroke-Free Middle-Aged Adults: Findings From the Coronary Artery Risk Development in Young Adults Study. *Stroke* 2015;46:2190-2196. PMC4519386.

3. Publications (other)

Crocco EA, Sabbag S, Curiel R. Bipolar Disorder in the Elderly, In: *Bipolar Book: History, Neurobiology and Treatment*, Nemeroff C, Ruiz P, Yildiz A ed., Oxford University Press: NY, 2015 ISBN: 978-0-199- 30053-2

Czaja SJ. Can Technology Empower Older Adults to Manage Their Health? In: *Generations*. Stein R, Hood A, Torgerson K ed., 2015;Chap 46, 46-51.

Czaja SJ, Sharit J, Charness N, Schmidt AC. The Implications of Changes in Job Demands for the Continued and Future Employment of Older Workers, In: *Age in the Workplace*, SIOP Frontier Series, Kanfer K, Finkelstein L, Truxillo D, Fraccaroli F ed., Psychology Press, Taylor & Francis Group: London. 2015;Chapter 7, 159-179.

Morrow D, **Czaja SJ**. The Implications of Aging for Human Systems Integration., In: *APA Handbook of Human Systems Integration*, Boehm-Davis DA, Durso FT, Lee JD ed., 2015;Chapter 33, 535-552. ISBN: 978-1-4338-1828-8.

4. Presentations at Scientific Meetings

Barrientos A. Mitochondrial Assembly and Dynamics in Health, Disease and Aging at the Assembly of Mitochondrial Ribosomes FASEB Summer Research Conference. Palm Beach, FL, May 17-22, 2015.

Chiquet B, Maili L, Plant R, Dyke J, Boyer R, Yuan Q, Swindell E, Letra A, **Blanton S**, Hecht J. Identification of NSCL/P candidate genes following knockdown of crispld2. Poster session at the 65th Annual Meeting of the American Society of Human Genetics, October 6-10, 2015 - Poster Presentation: Baltimore, MD.

Crocco E. Advances in the Diagnosis and Management of Preclinical AD and Geriatric Depression, Prevention and Treatment of Alzheimer's Disease (AD): at Research and Programs the University of Miami Miller School of Medicine at Mantovani Foundation Expo. Milan, Italy, October 2015.

Crocco E. Challenges in the Diagnosis and Management of Geriatric Depression and Anxiety, the Intersection of Age, Culture, and Mental Health at the Clinical Implications for the Treatment of Depression and Anxiety at the Elderly Symposium, ADAA National Conference. Miami, FL, April 2015.

Crocco E. Current Trends and New Directions in the Psychiatric Assessment of MCI and PreMCI States, Novel Cognitive and Functional Markers for the Earliest Detection of Prodromal Alzheimer's Disease at the Gerontological Society of America Annual Meeting. Orlando, FL, November 2015.

Crocco E. Management of Psychiatric Conditions in Cognitively Normal and at Risk Populations, Optimizing Cognitive and Emotional Functioning in At-Risk Older Populations at the Gerontological Society of America Annual Meeting. Orlando, FL, November 2015.

Curiel R, Loewenstein D, **Crocco E**, Grieg-Castro M, Rodriguez R, **Czaja S**, Rosado M, Barker W, Duara R. A Novel Measure of Cognitive Change in Preclinical Alzheimer's Disease and its Physiological Correlates in Normal and MCI Elderly. Poster session at the AAIC Annual Conference, 2015 - Poster Presentation: Washington DC. (Refereed)

d'Adesky N, de Rivero Vaccari JP, Bhattachary P, Bramlett H, **Raval AP**. Estrogen receptor beta regulates inflammasome activation in the hippocampus of female rats. Poster Session at the Brain: Neuroinflammation meeting, June 27-13 2015 - Poster Presentation: Vancouver, Canada. (Refereed)

Czaja SJ. Reducing Risks for Cognitive Impairment and Development of Interventions at the Annual Gerontological Society of America Meeting. Orlando, FL, November 18-22, 2015.

Czaja SJ. Designing with Older Adults. Panel Member. Discussion: What Do Gerontologists Know that Others Don't? Annual Gerontological Society of America Meeting. Orlando, FL, November 18-22, 2015.

Czaja SJ. Environments for Aging Conference. Invited Presentation. Baltimore, April 21, 2015.

Czaja SJ. Findings from CREATE: The Perceived Value of a Telehealth System by Frail Hypertensive Older Adults at the Annual Gerontological Society of America Meeting. Orlando, FL, November 18-22, 2015.

Czaja SJ. Long-Term Care Planning and Supports at the APA Annual Convention. Toronto, Canada, August 5-8, 2015.

Czaja SJ. Panel Member. Discussion: Compassion and Caregivers Psychological and Physical Health. Annual Gerontological Society of America Meeting. Orlando, FL, November 18-22, 2015.

Czaja SJ. Presidential Address. The Changing Face of Aging: The Role of Division 20 at the APA Annual Convention. Toronto, Canada, August 2015.

Czaja SJ. Technology Interventions for Caregivers. Panel Member. Discussion: User-Centered Approaches to the Design and Implementation of Low-Cost Technology-Based Interventions for

Older Adults Aging in Place. Annual Gerontological Society of America Meeting. Orlando, FL, November 18-22, 2015.

Czaja SJ. The Development and Validation of a Computer-Based Skills Training (CAST) Package at the 15th International Congress on Schizophrenia Research Conference. Colorado Springs, CO, March 28-31, 2015.

Czaja SJ. The Intersection of Age, Culture, and Mental Health: Clinical Implications for the Treatment of Depression and Anxiety in the Elderly at the Anxiety and Depression Conference (ADAA). Miami, FL, April 9-12, 2015.

Czaja SJ. The Role of Internet in Enhancing Social Connectivity Among Older Adults at the International Association of Gerontology and Geriatrics (IAGG) Conference. Dublin, Ireland, April 23, 2015.

Czaja SJ. Use of Technology for Family Caregivers: Opportunities and Challenges at the Annual Gerontological Society of America Meeting. Orlando, FL, November 18-22, 2015.

Dhamoon MS, **Dong C, Sacco RL.** Ideal Cardiovascular Health Predicts Functional Status: The Northern Manhattan Study The Northern Manhattan Study (NOMAS). Poster session at the International Stroke Conference, Feb 12, 2015 - Poster Presentation: Nashville, TN.

Dhamoon MS, McLaughlin-Mora C, Willey JZ, Cheung YK, Moon YP, **Sacco RL,** Elkind MS. Quality Of Life Independently Predicts Long-Term Vascular Events And Mortality: The Northern Manhattan Study. Poster session at the International Society for Quality of Life Research, Oct 22, 2015 - Poster Presentation: Vancouver, Canada.

Dong C, Rundek T, Marquez C, **Wright CB,** Elkind MSV, **Sacco RL.** Evidence to Maintain the SBP treatment threshold at 140 mmHg for Stroke Prevention in Persons Aged 60 Years or Older Without Diabetes Mellitus or Chronic Kidney Disease, the Northern Manhattan Study (NOMAS). Poster session at the International Stroke Conference, Feb 11, 2015 - Poster Presentation: Nashville, TN.

Dueker ND, Beecham A, Wang L, **Blanton S, Dong C,** Guo S, Cabral D, **Rundek T, Sacco RL.** Rare Variants in Previously Identified Linkage Region on Chromosome 7p Associated with Carotid Bifurcation Intima-Media Thickness in Dominican Families. Poster session at the 65th Annual Meeting of the American Society of Human Genetics, October 6-10, 2015 - Poster Presentation: Baltimore, MD.

Escuti N, **Monteith T.** Headache in a Patient with an Extracranial Lipoma: Report of a New Case. American Headache Society meeting, June 2015 - Poster Presentation: Washington, DC.

Espinel Z, **Crocco EA,** Rios J, Escobar I, Helmi J Loewenstein, D. Risk Appraisal of Alzheimer's Caregivers: The Depression Connection. Poster session at the APA Annual Conference, 2015 - Poster Presentation: Toronto, Canada. (Refereed)

Forte M, Ortega MR, Banerjee N, Anderson S, Bermudez C, Riesgo V, Katzen H, Rodriguez G, Delgado SR, Rammohan K, **Levin BE.** Moderate caffeine intake and verbal memory in multiple sclerosis at the 43rd Annual Meeting of the International Neuropsychological Society Meeting. Denver, CO, February 2015.

Gomes-Osman J, Hinchman C, Chu A, Pascual-Leone A. The influence of a 4-week regular aerobic exercise regimen on neuroplasticity assessed via transcranial magnetic stimulation - a preliminary and ongoing study. Poster session at the Rotman Research Institute Conference,

March 9-11, 2015 - Poster Presentation: Toronto, Canada.

Gutierrez J, Cheung K, Bagci A, Cespedes S, DeRosa J, **Rundek T, Alperin T, Sacco RL, Wright CB**, Elkind MSV. Brain Arterial Diameters and Risk of Vascular Events. Poster session at the International Stroke Conference, Feb 11, 2015 - Poster Presentation: Nashville, TN.

Stradecki HM, Cohan CH, Youbi M, Perez D, **Dave KR**, Neumann JT, **Perez-Pinzon M**. Physical exercise facilitates recovery of spatial memory and synaptic function after cardiac arrest at the 27th International Symposium on Cerebral Blood Flow, Metabolism and Function Conference. Vancouver, Canada, June 27-30, 2015. (Abstract refereed)

Katan M, Moon YP, DeRosa J, von Eckardstein A, Spanaus K, **Sacco RL**, Elkind MSV. Procalcitonin and midregional pro-atrial natriuretic peptide as markers of silent brain infarcts: the Northern Manhattan Study. Poster session at the European Stroke Conference, May 2015 - Poster Presentation: Vienna, Austria.

Katz J, **Dong C**, Stern Y, **Wright C, Blanton S, Sacco RL**. Genetic Association Study of Cognitive Performance. Poster session at the American Academy of Neurology (AAN) Annual Meeting, April 18-25, 2015 - Poster Presentation: Washington, DC.

Lee RHC, Couto e Silva A, Wilkins CS, Valido SE, Klein DD, Wu CY, Della Morte DD, **Lin HW**. Neuroprotective effects of sympathetic attenuation in the ischemic brain at the Annual Meeting of the Society for Neuroscience. Chicago, IL, 2015.

Lee RHC, Wilkins CS, Couto e Silva A, Valido SE, Klein DD, Goyanes JJ, Chen JA, **Lin HW**. Characterization of palmitic acid methyl ester: a novel vasodilator at the XXVIIth International Symposium on Cerebral Blood Flow, Metabolism and Function. Vancouver, Canada, 2015.

Lowenstein D, Curiel R, Grieg-Castro M, **Crocco E**, Rodriguez R, Barker W, Rosado M, Duara R. The relationship Between a Novel Test of Semantic Interference (LASSI-L) and Global and Regional Accumulation of Amyloid in the Brains of Community-Dwelling Elders at the Alzheimer's Association International Conference (AAIC). Washington, DC, July 2015.

Lin HW. Palmitic and stearic acid methyl esters as potential vasodilators and neurotransmitters at the Journees Chevreul Lipids and Brain III, French Society for the Study of Lipids and SCI. Paris, France, 2015.

Monteith T. Introduction: NIH Forum. Moderator and Chair. 57th American Headache Society Annual Scientific Meeting. Washington, DC, June 2015.

Monteith T. Chronic Pain: An Invisible Disease? Not Anymore at the American Association for the Advancement of Science Meeting. San Jose, CA, February 2015.

Moraes CT. MitoTALENS: A general approach to reduce mutant mtDNA loads and restore oxidative phosphorylation function in mitochondrial diseases at the Assembly of Mitochondrial Ribosomes FASEB Summer Research Conference. Palm Beach, FL, May 2015.

Moraes CT. Therapeutic Approaches to Mitochondrial Defects in Muscle at the Gordon Conference on Myogenesis. Barga, Italy, June 2015.

Moraes CT. Selective Targeting of MtDNA Sequences and Applications to Therapy at the 59th Annual Biophysical Society Meeting. Baltimore, MD, February 2015.

Moraes CT. Targeting Disease-Causing Defects of the Mitochondrial Genome with Engineered

Mitochondrial Nucleases at the Targeting Mitochondrial Dysfunction & Toxicity Conference (Healthtech.com). Boston, MA, March 2015.

Moraes CT. The use of mitochondrial-targeted nucleases to alter mtDNA heteroplasmy at the Symposium 2015: mitochondria at the crossroad. Strassburg, France, September 2015.

Perez E, **Dong C**, DeCarli C, Yoshita M, **Wright C**, Santiago M, Elkind M, **Sacco RL.** Subclinical Cerebral Vessel Lesions and Risk of Stroke: the Northern Manhattan Study. Platform Session. American Association of Neurology. Washington, DC, April 21, 2015.

Ramos A. Sleep Duration and Neurocognitive Function in the Hispanic Community Health Study/Study of Latinos at the American at the Academy of Neurology Annual Meeting. Washington, DC, April 22, 2015.

Ramos A. Sleep Duration and Neurocognitive Function in the Hispanic Community Health Study/Study of Latinos at the American. Poster Session at the Academy of Neurology Annual Meeting, April 22, 2015 - Poster Presentation: Washington, DC.

Ramos A. Stroke and Obstructive Sleep Apnea: The Hispanic Community Health Study at the Mid-Year Meeting for the Center for Stroke Disparities Solutions (CSDS) New York University School of Medicine. Nashville, TN, February 12, 2015.

Raval P. Patel H, Brand F, Bramlett H, De Rivero Vaccari JP. Estrogen Receptor Beta Regulates Inflammasome Activation in the Hippocampus of Female Rats. Poster Session at Brain: Neuroinflammation, June 27-13 2015 - Poster Presentation: Vancouver, Canada. (Refereed)

Rossetti MA, Campos Y, Mendez AJ, **Wright CB**, **Levin BE.** The relationship among adiponectin isoforms, memory performance, and gender. Poster session at the 43rd Annual Meeting of the International Neuropsychological Society Meeting, February 2015 - Poster Presentation: Denver, CO.

Sacco RL. Evolution from Stroke Risk Factors to Brain Health Determinants, The 11th Johann Jakob Wepfer Lecture at the European Stroke Conference. Vienna, Austria, May 13, 2015.

Sacco RL. Don't Happen Twice: Maximizing Stroke Prevention, at the Pre-Conference-International Stroke Conference. Nashville, TN, February 10, 2015.

Sacco RL. Stroke of Unknown Causation, Medscape CME Video Program at the International Stroke Conference. Nashville, TN, February 11, 2015.

Sacco RL. Together to End Stroke-Global Stroke Strategies for the 25 by 2025 WHO Targets at the International Stroke Conference. Nashville, TN, February 12, 2015.

Sullivan LS, Bowne SJ, **Blanton SH**, Koboldt DC, Wilson RK, Chen R, Wang F, Wheaton DK, Birch DG, Daiger SP. Disease-causing mutations in a cohort of autosomal dominant RP (adRP) families without detectable mutations in known adRP genes. Poster session at the 2015 Association for Research in Vision and Ophthalmology (ARVO) Annual Meeting, May 3-7, 2015 - Poster Presentation: Denver, CO.

Willey JZ, **Gardener H**, Cespedes S, DeCarli C, Yoshita M, Stern Y, **Sacco RL**, Elkind MS, **Wright CB.** Leisure Time Physical Activity and Cognitive Decline in the Northern Manhattan Study. Poster session at the AHA Epi/Lifestyle Scientific Session, March 6, 2015 - Poster Presentation: Baltimore, MD.

Wiley JZ, Moon YP, Sherzai A, Gervasi-Franklin P, Cheung K, **Sacco RL**. Leisure-Time Physical Activity and Mortality in the Northern Manhattan Study. AHA Epi/Lifestyle Scientific Session, March 5, 2015 - Poster Presentation: Baltimore, MD.

Yavagal D, Bhattacharya P, Zhao W, Khan A, Hare J, **Perez-Pinzon M, Raval AP**. Intra-Arterial Stem Cell Treatment Reduces Injury in a Reproductively Senescent Rat Model of Stroke. Poster Session at Brain: Stem cells and Cell Therapy, June 27-13 2015 - Poster Presentation: Vancouver Canada. (Refereed)

Zeki Al Hazzouri A, Elfassy T. Self-Reported Fast Walking Speed is Associated with Decreased Adverse Stroke Events In Older Adults at the Gerontological Society of America Meeting. Orlando, FL, November 18-22, 2015.

Zeki AL Hazzouri A. Impact of sustained economic hardship on cognitive functioning at the 48th Annual Society for Epidemiologic Research Meeting. Denver, CO, June 16-19, 2015.

Zeki Al Hazzouri A, Rose Mayeda E, Lee A, Elfassy T, Odden MC, Thekkethala D, **Wright CB**, Glymour M, Haan MN. Association Between Self-Reported Walking Speed and Stroke Risk Among Older Latino Adults. Poster session at the Society of Epidemiologic Research, June 16-19, 2015 - Poster Presentation: Denver, CO.

Zeki Al Hazzouri A, Rose Mayeda E, Lee A, Elfassy T, Odden MC, Thekkethala D, **Wright CB**, Glymour M, Haan MN. Association Between Self-Reported Walking Speed and Stroke Risk Among Older Latino Adults. Poster session at the International Stroke Conference, February 11-13, 2015 - Poster Presentation: Nashville, TN.

5. Presentations at Public (Non-Scientific) Meetings or Events

Barrientos A. Approaches to study mitochondrial ribosome biogenesis. Invited speaker at the University of Miami, Miller School of Medicine RNA-Club. Miami, FL. November 2015.

Barrientos A. Biogenesis of the mitochondrial ribosome. Invited speaker at the University of Miami, Miller School of Medicine Biology Seminar Series. Miami, FL. November 2015.

Barrientos A. Protein complexes, Genetics and advance literature reading. Invited lecturer at the University of Miami, Miller School of Medicine Graduated Program in Biomedical Sciences (PIBS). Miami, FL. 2015.

Barrientos A. Mitochondria and Neurodegenerative disease: lessons form yeast and cell culture models. Invited speaker at the Department of Neurology, University of Miami, Miller School of Medicine Grand Rounds Series. Miami, FL. January 2015.

Barrientos A. Mitochondrial biogenesis and skin disease. Invited speaker at the Department of Dermatology University of Miami, Miller School of Medicine Grand Rounds Series. Miami, FL. February 2015.

Barrientos A. Model organisms for mitochondrial research. Invited lecturer at the University of Miami, Miller School of Medicine course – “Mitochondrial Function and Dysfunction in Neurological Diseases.” Miami, FL. 2015.

Barrientos A. Physiological regulation of mitochondrial cytochrome c oxidase function. Invited speaker at the University of Miami, Miller School of Medicine Biochemistry and Molecular Biology Seminar Series. Miami, FL. December 2015.

Barrientos A. The mitochondrial translation machinery. Invited speaker at the Pennsylvania State

University, Biochemistry and Molecular Biology Seminar Series. University Park, PA. November 2015.
Blanton SH. Genomics and Translational Research. Invited speaker at the Dartmouth College Genomic Medicine Grand Rounds Series. Hanover, NH. September 2015.

Blanton SH. Approaches to Identifying Genes for Complex Diseases. Invited speaker at the Department of Otolaryngology, University of Miami, Miller School of Medicine 23rd Annual Chandler Society Research Forum. Miami, FL. June 2015.

Blanton SH. The Role of Family History in the Age of Genomics. Invited speaker at the Division of General Internal Medicine Monthly Educational Conference at the University of Miami, Miller School of Medicine. Miami, FL. February 2015.

Cabral D, Richardson M, **Gomes-Osman J.** Physical exercise as a potential tool to promote brain health in older adults with and without cognitive deficits: a review of the literature for dose-specific recommendations. Poster session at the University of Miami, Miller School of Medicine Neuroscience Day, November 20th, 2015 – Poster Presentation: Miami, FL.

Crocco E. Diagnosis and Management of Dementia. Invited speaker at the Baptist Health Hospital Mental & Behavioral Health Conference. Miami, FL. September 2015.

Crocco E. Management of Dementia Care for Patients and Caregivers. Speaker at the Miami VAMC/GRECC Miami Area Geriatric Educational Center (MAGEC). Miami, FL. June 2015.

Czaja SJ. Our Aging Population: Mental Health in the Advancing Years. Invited presenter at the National Alliance on Mental Health (NAMI) and University of Miami Stop the Stigma: A Mental Health Summit. Miami, FL. May 2nd, 2015.

Czaja SJ. Technology and Older Adults: Designing for Accessibility and Usability. Distinguished Speaker. Department of Industrial and Systems Engineering, University of Buffalo, State University of New York. February 13, 2015.

Czaja SJ. The Potential role of Technology in Enhancing the Health and Well-Being of Older Adults: Opportunities and Challenges. Invited speaker at the GRECC VA Medical Center Grand Rounds Series. Miami, FL. February 20th, 2015.

d'Adesky N, de Rivero Vaccari JP, Bhattachary P, Bramlett H, **Raval AP.** Estrogen receptor beta regulates inflammasome activation in the hippocampus of female rats. Poster session at the University of Miami Research Day, September 18th, 2015 - Poster Presentation: Miami, Florida.

d'Adesky N, de Rivero Vaccari JP, Bhattachary P, Bramlett H, **Raval AP.** Estrogen receptor beta regulates inflammasome activation in the hippocampus of female rats. Poster session at the University of Miami, Miller School of Medicine Neuroscience Day, November 20th, 2015 - Poster Presentation: Miami, Florida.

Dong C, Nabizadeh N, **Caunca M,** Cheung YK, **Rundek T,** Elkind MSV, DeCarli C, **Sacco RL,** Stern Y, **Wright CB.** Cognitive correlates of white matter lesion load and brain atrophy: The Northern Manhattan Study. Poster session at the Annual MD/PhD Student Research Symposium, April 2015 - Poster Presentation: Miami, FL.

Gomes-Osman J. Exercise, Brain Plasticity and Cognitive Performance. Invited speaker at the Department of Neurology, Harvard Medical School Cognitive Neurology Rounds Series. Boston, MA. March 2015.

Gomes-Osman J. Measuring plasticity using non-invasive brain stimulation--a potential tool for the

study of aging. Invited speaker at the University of Miami Evelyn F. McKnight Brain Institute Inter-Institutional Meeting. Miami, FL. May 2015.

Gomes-Osman J. Neurostimulation. Lecturer at the Department of Physical Therapy, University of Miami, Miller School of Medicine PhD course "Assistive Technology." Miami, FL. February 2015.

Gomes-Osman J. Physical exercise as a potential tool to promote brain health: challenges and opportunities. University of Miami Evelyn F. McKnight Brain Institute Monthly Research Seminar. Miami, FL. October 14th, 2015.

Gomes-Osman J. Non-Invasive Brain Stimulation. Invited lecturer at the Berenson-Allen Center for Non-Invasive Stimulation at Beth Israel Deaconess Medical Center at Harvard Medical School Intensive Course in Transcranial Magnetic Stimulation. Boston, MA. 2015.

Lin HW. Palmitic and stearic acid methyl esters as potential vasodilators and neurotransmitters. Invited speaker at the Journées Chevreul Lipids and Brain III, French Society for the Study of Lipids and SCI. Paris, France. 2015.

Lin HW. Sympathetic modulation in cerebral ischemia. Invited speaker at the Department of Systems Medicine, University of Rome TorVergata. Rome, Italy. 2015.

Monteith T. Chart Review Session. The 8th Annual Chair Summit: Master Class for Neuroscience Professional Development. Miami, FL. September 2015.

Monteith T. Current Advances in Migraine. Department of Neurology, University of Miami, Miller School of Medicine Grand Rounds Series. Miami, FL. May 2015.

Monteith T. Current Advances in Migraine. Neurology Update and Stroke Intensive. Miami, FL. January 2015.

Monteith T. Diagnosis and Treatment of Headache Disorders. Speaker at the University of Miami, Miller School of Medicine Internal Medicine Residency Program. Miami, FL. December 2015.

Monteith T. Press Conference titled "Chronic Pain: An Invisible Disease? Not Anymore," American Association for the Advancement of Science, San Jose, CA. February 2015.

Moraes CT. Potential alternative to preventing transmission of mtDNA diseases: heteroplasmy shift therapy. Invited speaker at the Institute of Medicine Public Workshop of the Committee on Ethical and Social Policy Considerations of Novel Techniques for Prevention of Maternal Transmission of Mitochondrial DNA Diseases. Washington, DC. April 2015.

Moraes CT. Recent Advances in the Genetics of Mitochondrial Disorders: From Diagnosis to Therapy. Neurology Update and Stroke Intensive. Miami, FL. January 2015.

Ramos A. Is sleep disruption a risk factor for dementia? University of Miami, Miller School of Medicine Neuroupdate. Miami, FL. January 16th, 2015.

Ramos A. Peer Mentor Development Program, NHLBI-New York University, NY. 2015

Ramos A. Tribulations of a Young Investigator. Speaker at the Young Investigator Research Forum, sponsored by the American Academy of Neurology and National Institutes of Health. Rockville, MD. April 8th, 2015.

Sacco RL. Taught the F.A.S.T. to the Balancing Act audience in a memorable way. 02 Media, Inc. for

the Balancing Act and Lifetime Television, March 17th, 2015.

Sacco RL. Addressing Stroke Disparities, From Prevention to Acute Treatment. Invited speaker at the New York University Langone Medical Center. New York, NY. April 7th, 2015.

Sacco RL. Addressing Stroke Disparities: From Prevention to Acute Treatment. Invited speaker at the 31st Irwin Levy Visiting Lectureship, Washington University School of Medicine. St. Louis, MO. April 3rd, 2015.

Sacco RL. Addressing Stroke Disparities. Invited speaker at the University of Nebraska, Omaha Medical Center Grand Rounds and Residency Graduation. Omaha, NB. June 4th, 2015.

Sacco RL. Addressing Stroke Disparities. Speaker at the NYPH Weill Cornell Medical College Grand Rounds. New York, NY. June 17th, 2015.

Sacco RL. Florida Puerto Rico Collaboration to Reduce Stroke Disparities (FL-PR CReSD). Speaker at the Department of Neurology, University of Miami, Miller School of Medicine Grand Rounds. Miami, FL. December 4th, 2015.

Sacco RL. Heart & Stroke – relationship between heart and stroke incidents as well as why it is more prevalent in women. Interview for the Miami Herald. Miami, FL. June 2nd, 2015.

Sacco RL. Prevention of Stroke. Speaker for the Mayo Clinic Cardiology Update. Miami Beach, FL. January 8th, 2015.

Sacco RL. Stroke in Florida – an update. Speaker at the Neurology Update. Miami, FL. January 24th, 2015.

Sacco RL. Primary and Secondary Stroke Prevention, Florida Stroke Symposium. Deerfield Beach, FL. May 2nd, 2015.

Schatz M, d'Adesky N, Bhattacharya P, **Raval AP**, Dietrich D, Bramlett H. Whole body vibration reduces ischemic brain damage in middle-aged female rats. Poster session at the University of Miami, Miller School of Medicine Neuroscience Day, November 20th, 2015 – Poster Presentation: Miami, Florida.

Zeki AL Hazzouri A. Life Course Determinants of Aging: Social and Cardiovascular Aspects. Presentation at the Miami Geriatric & Palliative Medicine Grand Rounds. Miami, FL. September 18th, 2015.

Zeki AL Hazzouri A. Organizer of the Workshop: Introduction to Causal Inference Methods: Using Counterfactuals and Directed Acyclic Graphs by Maria M. Glymour, November 19, 2015 in the Division of Epidemiology, UM Public Health Sciences. Part of the Society of Epidemiologic Research Talks (SER Talks).

6. Awards (other)

Dr. Alperin received an award from NASA to assess CSF (cerebrospinal fluid) flow dynamics in astronauts before and after spaceflights to assess susceptibility to visual impairments in microgravity.

Dr. Barrientos' trainee Dr. Myriam Bourens received a Post-Doctoral Fellowship from the AHA. Two graduate students working with him, Dasmanthie De Silva and Ya-Ting Tu received a Pre-Doctoral Fellowship from the AHA.

Dr. Barrientos was awarded an R01 grant from the NIH/NIGMS to study cytochrome c Oxidase assembly in health and disease and a supplement 2 R01 grant to study macromolecular interactions in cells. He was also awarded two other R01 grants from the NIH/NIGMS to study the biosynthetic pathway of mitochondrial respirasomes and biogenesis of the mitochondrial translation machinery.

Dr. Blanton was named a Field Reviewer, CDC study section, Special Emphasis Panel (SEP) to conduct the scientific peer review of applications responding to Funding Opportunity Announcement (FOA) RFA-DP-16-001: Pregnancy Risk Assessment Monitoring System (PRAMS).

Dr. Blanton was promoted to Full Professor in the Dr. John T. Macdonald Foundation Department of Human Genetics and was appointed to the search committee for the Dean of the Graduate School at the University of Miami.

Michelle Caunca was appointed Student Representative for the McKnight Brain Institute, University of Miami Miller School of Medicine. She was also named a Paul Ambrose Scholar and awarded a micro-grant by the Paul Ambrose Scholars Program funded by the Association for Prevention Teaching and Research through the Office of Health Promotion and Disease Prevention.

Dr. Crocco has been appointed Associate Clinical Professor in the Department of Psychiatry and Behavioral Sciences at the University of Miami Miller School of Medicine.

Dr. Czaja received the M. Powell Lawton Distinguished Contribution Award for Applied Gerontology.

Dr. Czaja received NIH R01 funding as the Co-Investigator for a project researching novel detection of early cognitive and functional impairment in the elderly. She is also the Principal Investigator of a P01 which received funds from the NIA/NIH, CREATE IV (Center for Research and Education for Aging and Technology Enhancement) an established multidisciplinary, cohesive center that focuses on aging and technology.

Dr. Dave was awarded a grant to study accelerated brain aging in diabetics: impact of recurrent hypoglycemia from the Advanced Magnetic Resonance Imaging and Spectroscopy (AMRIS) Facility at the University of Florida.

Dr. Jiang received an award from the North American Neuro-Ophthalmology Society as Principal Investigator of a research study on retinal microvascular alteration as a possible biomarker in Alzheimer's disease.

Dr. Monteith was named one of the South Florida Top Black Educators by Legacy Magazine and was named Scientific Reviewer for the Neurological Disorders Panel, PRMRP/CDMRP Reston, Virginia. She also joined the podcast panel for the Neurology Journal, joined the editorial board for Neurology Now, and became a peer reviewer for Cephalalgia.

Dr. Moraes received funding to support his research on the role of Mitochondrial Oxidative Phosphorylation Dysfunction in Alzheimers from the Ed and Ethel Moore Alzheimer's Disease Research Program (FL Biomedical Research Foundation). He also received NIH funding as Co-Investigator for the research project Imaging Mitochondrial Signaling in B-cells Ectopically Implanted in the Eye.

Dr. Ramos was awarded a travel award, to present at the U13 Conference Series: Sleep, Circadian Rhythms, and Aging: New Avenues for Improving Brain Health, Physical Health and Functioning. Supported by the National Institutes of Aging and the American Geriatric Society.

Dr. Ramos was selected as one of the trainees for the Peer Mentor Development Program, by the NHLBI-New York University, NY to mentor upcoming young investigators in the field of sleep medicine. Also, he is part of the Diversity Leadership Development Program that develops leadership skills and submerses neurologists from diverse backgrounds, that was awarded funding from the American Academy of Neurology (AAN).

Dr. Perez-Pinzon was awarded a supplemental project as a part of American Stroke Association Bugher Foundation centers of excellence in stroke collaborative research for regeneration, resilience and secondary prevention.

Dr. Perez-Pinzon's PhD student, KB Koronowski was awarded an NIH/NINDS F31 Ruth L. Kirschstein National Research Service Award Predoctoral Fellowship to work on neuroprotective mechanisms of resveratrol pre-conditioning as the Principal Investigator. His MD/PhD, Post-Doctoral Fellow M. Youbi, was awarded an AHA/ASA/Bugher Foundation Collaborative Fellowship Initiative. His MD/PhD student, H.M. Stradecki was awarded a Pre-Doctoral Fellowship grant from the American Heart Association.

Dr. Sacco has been awarded a 5 year continuation R01 grant by the NIH/NINDS for years 23-28 of the project titled, “Stroke Incidence and Risk Factors in a Tri-Ethnic Region”. The aims of the project are to determine the relationships between traditional and novel vascular risk factors for stroke, dementia, cognitive impairment, and disability within the prospective cohort of 3,298 community subjects from Northern Manhattan.

Dr. Sacco served as Committee Member for the Institute of Medicine (IOM), The National Academies Committee on Treatment of Cardiac Arrest: Current Status & Future Directions and the Committee on Decreasing the Risk of Developing Alzheimer's-Type Dementia, Mild Cognitive Impairment and Age-Related Cognitive Impairment.

Dr. Sacco has entered his first year of two, as American Academy of Neurology, President-elect.

Dr. Sacco was awarded the University of Miami Provost's Award for Scholarly Activity, the Johann Jacob Wepfer Award of the ESO and the American Heart Association's Gold Heart Award in 2015.

Dr. Wright received funding from the NIA as Co-Investigator of the (SOL-INCA) study that will examine health risks associated with neurocognitive decline including diabetes and cardiovascular diseases as well as lifestyle factors such as smoking.

7. Faculty

Faculty is divided between those receiving direct support from the Institute (Members) and those with whom the Institute is collaborating within the University of Miami (Collaborators). Faculty biosketches are attached at the end of the document.

Name	Center Role	Area of Expertise
Noam Alperin, PhD	Radiology	Physics (MRI)
Sara Czaja, PhD	Member	Aging, Psychology & Genetics
Kunjan R. Dave, PhD	Member	Neurobiology, Basic Science

Hong Jiang, MD, PhD	Member	Neurology, Neuroscience
Bonnie E. Levin, PhD	Schoninger Professor	Neuropsychology
Ralph L. Sacco, MD, MS	Executive Director	Neurology, Epidemiology & Genetics
Xiaoyan Sun, MD, PhD	Educational Director	Neuroscience, Biochemistry
Clinton B. Wright, MD, MS	Scientific Director	Neurology, Epidemiology & Cognition

Name	Center Role	Area of Expertise
Antonio Barrientos, PhD	Collaborator	Neuroscience, Genetics
Susan Blanton, PhD	Collaborator	Genetics
Elizabeth Crocco, MD	Collaborator	Psychiatry
Chuanhui Dong, PhD	Collaborator	Epidemiology, Biostatistics
Hannah Gardener, ScD	Collaborator	Epidemiology
Joyce Gomes-Osman, PhD	Collaborator	Neuroscience
Hung-Wen Lin, PhD	Collaborator	Neuroscience, Pharmacology
Teshame Monteith, MD	Collaborator	Headache
Carlos Moraes, PhD	Collaborator	Neuroscience
Miguel Perez-Pinzon, PhD	Collaborator	Neuroscience
Alberto Ramos, MD	Collaborator	Sleep Medicine, Neurology
Ami P. Raval, PhD	Collaborator	Neuroscience, Epidemiology
Tatjana Rundek, MD, PhD	Collaborator	Epidemiology, Neurology
Juan Young, PhD	Collaborator	Genetics
Adina Zeki Al Hazzouri, PhD	Collaborator	Epidemiology

8. Trainees

Name	Center Role	Area of Expertise
Kyle Andrade-Bucknor	Student	Pre-Med
Michelle Caunca*	Graduate Medical/PhD Student	Neurology
Elise Clark	Student	Neuroscience
Charles Cohan, PhD	Post-Doctoral Fellow	Neurology
Maria Diaz, MD	Research Assistant	Neurology
Kevin Koronowski, BS	Student	Neuroscience
Jonathan Landman, MD	Research Assistant	Neurology
Ava Marsh	Student	Biology
Ashish Rehni, PhD	Post-Doctoral Fellow	Neurology
Hesley Solano	Student	Neuroscience
Courtney Sparger	Undergrad Student	Neuroscience

Vibha Shukla, PhD	Post-Doctoral Fellow	Neurology
Holly Stradecki, BS	Student	Neuroscience
Mehdi Youbi, MD	Post-Doctoral Fellow	Neurology
Eduard Tiozzo, PhD	Fellow	Exercise Physiology/Nutrition
Marti Flothmann, BS	Research Assistant	Exercise Physiology
Kristopher Wolford, MPH	Student	Public Health
Andrew Yu, MS	Student	Exercise Physiology

*McKnight Student Representative

9. Clinical / Translational Programs

New Programs

The Northern Manhattan Study reached an important milestone with NINDS funding of its fifth cycle. Funding enters its 24th year and will allow a directional shift from the current NOMAS project that places new emphasis on dementia and cognitive impairment. Led by **Dr. Sacco**, multiple UM-MBI investigators will be involved in the new phase of this large population-based study. The new program will also focus on inflammation, using highly innovative and novel multiplex assays to find biomarkers in a variety of pathways that can then be linked to age-related cognitive decline, dementia and stroke risk. **Drs. Levin** and **Sun** have joined the dementia adjudication team led by **Dr. Wright** as part of a consensus panel for the study.

As a new faculty member, **Dr. Sun** has begun a research program to examine markers of synaptic function in relation to age-related memory loss. She has an approved NOMAS study that will generate pilot data in this area and is developing a K award application with a mentorship plan that capitalizes on her PhD in molecular biology and will allow her to develop expertise in synaptic markers (in collaboration with the Karolinska Institute in Sweden) and neuroimaging.

Another new initiative involves examining metabolic markers underlying pain and cognition changes following TBI (traumatic brain injury). **Dr. Levin** is a Co-Investigator on a newly funded Department of Defense (DoD) study in collaboration with members of the Radiology department.

As mentioned in the 2014 Annual Report we applied for funding from the National Institute on Aging to complete another round of cognitive testing in a sample of the 16,000 Hispanic participants from the Study Of Latinos. This grant was funded in 2015. In collaboration with investigators at the other four sites and led by Michigan State, **Dr. Wright** and other UM Investigators received a five-year grant for the Miami Field Center for the Study of Latinos-Investigation of Neurocognitive Aging (SOL-INCA) study. This study will examine health risks associated with neurocognitive decline including diabetes mellitus and cardiovascular diseases as well as lifestyle factors such as smoking. A major goal of the research is to differentiate mild cognitive impairment from normal aging.

A number of basic and translational science grants were funded in 2015. A new R01 grant was awarded to **Dr. Perez-Pinzon** on the effects of ischemic preconditioning on cognitive outcomes following cerebral ischemia. He was also awarded a supplement to the ongoing AHA Bugher project that will evaluate the synergistic effects of environmental enrichment and/or physical exercise on white matter stroke in young and aged rats.

A number of trainees received grant awards this past year. Jacob Neumann was awarded a Post-Doctoral fellowship award from the American Heart Association before he left UM for his first faculty position. **Kevin Koronowski** was granted an NIH/NINDS F31 Ruth L. Kirschstein National Research Service Award to study motor and sensory behaviors in rodents after cerebrovascular

damage. **Holly Stradecki** is a graduate student who was awarded a pre-doctoral fellowship by the American Heart Association to study the effects of physical exercise on cognitive recovery after stroke in a rodent model. **Michelle Caunca** is an MD/PhD student who was awarded a pilot grant entitled, “Stroke Caregiver Support Application Focus Group Study” that will generate data for a larger grant application.

Update on Existing Clinical Studies

Analysis of brain imaging data from NOMAS continued. **Dr. Alperin** neared completion of the FreeSurfer analyses with over 900 brain MRI scans for the NOMAS brain parcellation completed to date.

We continued to enroll participants with subjective memory complaints into the UM-MBI Clinical and Biorepository Registry. In addition, **Dr. Levin** has begun a project to retrospectively review a subset of participants referred from the Memory Disorders Clinic to enter more extensive neuropsychological testing data. These data will be entered into the database and allow analyses of important cognitive outcomes. **Dr. Alperin** added Automated Segmentation of Hippocampal Subfields for volumetric quantification of Hippocampal sub-regions. We have collected data on 60 participants and plan analyses in the coming year. **Dr. Gomes-Osman** began collecting data on brain plasticity using transcranial magnetic stimulation in the Registry sample. In addition, **Dr. Jiang** continued collecting novel ophthalmic data using the Retinal Function Imager. Her research team recruited more than 50 normal healthy subjects and 20 patients with either AD or MCI (mild cognitive impairment) to study the ocular microvascular function and its role in the pathogenesis of AD. As noted elsewhere in this report, **Dr. Jiang** received a favorable score with encouraging comments on a proposal for R01 funding involving memory clinic participants and this will be resubmitted in early 2016.

The University of Miami Stroke Prevention Intervention Research Program, Florida-Puerto Rico Collaboration to Reduce Stroke Disparities (FL-PR CRESD) aims to identify race-ethnic and sex disparities in acute stroke care and inform hospital quality improvement through the FL-PR CRESD disparities stroke registry. This year, the project successfully increased Florida and Puerto Rico hospital participation/data contribution to the FL-PR CRESD Registry; initiated linkage of pre-hospital (EMS Florida data) and post-hospital data (CMS nationwide data); disseminated a stroke disparities dashboard to provide benchmarking data for all hospitals to track and improve performance; developed an educational interactive module on “Door To Needle” protocol (to address sex and race-ethnic disparities identified through the FL-PR CRESD Registry); and presented findings at professional conferences on disparity trends in Puerto Rico, as well as sex and race-ethnic disparities identified among ischemic stroke patients (predominantly adults over 60 years of age) from Florida hospitals.

The University of Miami American Heart Association/Bugher Center of Excellence program project entered its second year. Complementary studies in Clinical and Basic Science research comprise the translational science dedicated to enhancing cognitive recovery and quality of life after stroke. With the primary aim to evaluate combined aerobic and resistance exercise training and Cognitive Training Intervention in post-stroke survivors, the Clinical study team has continued to refine enrollment and operational procedures to maximize the numbers of study participants. As noted elsewhere, the Clinical study team has successfully obtained supplementary funds to test the viability of the activity-monitoring device (developed at UCLA) that measures physical activity quantitatively in these post-stroke participants. Post-Doctoral fellow **Dr. Eduard Tiozzo** received supplemental funding from the American Heart Association as part of a cross-institution collaboration with UCLA to examine polymorphisms in the BDNF gene as they relate to the effects of exercise on fitness and cognitive performance.

The Northern Manhattan Study (Stroke Incidence and Risk Factors in a Tri-Ethnic Region) completed funding cycle 4 (years 17-22) this year, successfully monitoring and documenting the NOMAS cohort to study determinants of stroke. Analysis of data from the prospective cohort of 3,298 community

subjects from Northern Manhattan has resulted in studies describing the effects of risk factors including subclinical carotid and brain disease on stroke, MI, vascular death and cognitive decline. This year, at least 22 manuscripts related to risk factors and clinical outcomes, subclinical carotid disease, brain measurements, and cognitive performance have been published.

Dr. Sun continued work as a Co-Investigator in the NIH R01 funded project Novel Detection of Early Cognitive and Functional Impairment in the Elderly. She will continue collecting CSF samples and monitoring lab measurement of amyloid 42, phosphorylated tau and total tau protein from these samples. Also, as Co-Investigator of Identification of novel AD genes and disease associated pathways through (FPADS), she has completed the project and is working on the manuscript.

The SUENO ancillary sleep study to HCHS/SOL (sleep habits as a risk factor; R01 HL098297) has recruited 2,200 participants to date, with the goal of defining the predictors of abnormal sleep using actigraphy (a wristwatch-like device that records movement and can be used to infer sleep from awake states). The study published three articles in 2015 and **Dr. Ramos** has been active in this study, also serving on the publication committee.

Headache is an important area that continues to develop in the UM-MBI. **Dr. Teshamae Monteith** has three subjects with chronic migraine who underwent MR spectroscopy to measure key neurometabolites. She will continue to collect MR spectroscopy data and plans to do cognitive testing on a subset of these patients to better understand cognitive impairments in chronic migraine. She is also working on a Phase 3 Randomized, Double-Blind, Placebo-Controlled Study of LY2951742 with a Long-Term Open-Label Extension in Patients with Chronic Cluster Headache that is awaiting IRB submission.

Update on Translational Studies

The Basic Science project of the Bugher Center led by **Dr. Perez-Pinzon** has made significant progress. The team finalized the protocol for middle cerebral artery occlusion that produces cerebral ischemia in aged rats, completed the design and production of an enriched environment cage, and began testing older rats and the effects of enriched environment and physical activity on cognitive performance post-infarction. The group analyzed the effects of forced treadmill exercise at various speeds on spatial memory tests after focal cerebral ischemia in rats. Focal cerebral ischemia impaired cognitive function, however moderate intensity physical exercise provided the most beneficial impact on cognitive recovery compared to other exercise intensities. The group also obtained a supplemental award from the American Heart Association/Bugher Foundation to study the biology of white matter stroke, one of the leading causes of dementia.

To initiate studies on the effect of physical exercise on white matter stroke in aged rats, Post-Doctoral trainee **Charles Cohan** has been hired and trained; and the research team is refining the subcortical white matter stroke model in rats (currently standardized in the mouse model). The group also carried out a study to determine if forced treadmill exercise improved performance of rats on spatial memory tests (e.g. Barnes Maze and contextual fear conditioning) and restored induction of long term potentiation (LTP) after moderate global cerebral ischemia. Preliminary data collected by graduate student trainee **Holly Stradecki** suggest that three days after global cerebral ischemia, there is reduced ability to induce LTP as compared to naïve animals. When global ischemia animals are exercised, LTP induction is similar to naïve controls. Global cerebral ischemia induces cognitive deficits as measured by reduced percentage of time in target quadrant during probe trials on the Barnes Maze. Exercise after global cerebral ischemia enhances duration of freezing on fear conditioning chamber. Our results demonstrate that global cerebral ischemia impairs cognitive functioning. Early induction of exercise restores synaptic functioning and may also improve performance on spatial memory tasks.

In prior work funded by NINDS the group, led by **Dr. Perez-Pinzon** observed that global cerebral ischemia induced activation of delta protein kinase C (PKC), and inhibition of delta PKC prior to

cerebral ischemia provided neuroprotection. The group therefore tested the hypothesis that activation of delta PKC alters memory formation (i.e., LTP) following cerebral ischemia. As part of a Post-Doctoral award from the American Heart Association and the parent R01, trainee **Jacob Neumann** used hippocampal slices from naïve rats to investigate the specific effects of delta PKC activation or inhibition on LTP. As part of his Post-Doctoral work, he observed that specific activation of delta PKC resulted in a significant reduction of LTP and a reduction in paired pulse facilitation (PPF). In contrast, inhibition of delta PKC did not alter LTP or PPF. These studies indicate that activation of delta PKC may contribute to the synaptic dysfunction following cerebral ischemia and suggest delta PKC as a potential therapeutic target for improving cognitive function. Future studies will investigate the signaling pathways by which delta PKC depresses LTP in order to ameliorate LTP suppression following ACA.

10. Technology Transfer

N/A

11. Budget Update

Status of matching funds, if applicable (see attached).

Projected budget for coming year (see attached).

Extramural funding

A Tailored Technology Intervention for Diverse Family Caregivers of AD Patients

Source: NINR/NIH 1R01NR014434-01

Principal Investigator: Sara Czaja

2015 Budget: \$363,798

Accelerated brain aging in diabetics: impact of recurrent hypoglycemia.

Source: Advanced Magnetic Resonance Imaging and Spectroscopy Facility, University of Florida, Gainesville. Proposal P12541.

Principal Investigator: Kunjan Dave

2015 Budget: \$5,000

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

Source: NIA/NIH

Principal Investigator: Sara Czaja

2015 Budget: \$1,105,769

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

Project I

Source: UM DBA 2015-13

Principal Investigator: Sara Czaja

2015 Budget: \$73,300

FGF-23 and the Risk of Stroke and Cognitive Decline

Source: NHLBI (R01 HL108623)

Principal Investigator: Clinton Wright

2015 Budget: \$404,492

Improving the Functional Outcomes in Older Adults with Schizophrenia

Source: NIH/NIA 1R21AG041740-01

Principal Investigator: Sara Czaja

2015 Budget: \$267,750

Increased Cerebral Ischemic Injury by Repeated Hypoglycemic Episodes in Diabetes.

Source: NIH, NINDS (R01 NS073779)

Principal Investigator: Kunjan Dave

2015 Budget: \$298,206

Ischemic Preconditioning: Mechanisms of Neuroprotection.

Source: NIH, NINDS (R01NS034773)

Principal Investigator: Miguel Perez-Pinzon

2015 Budget: \$365,774

NANOS Pilot 2015

Source: North American Neuro-Ophthalmology Society

Principal Investigator: Hong Jiang

2015 Budget: \$25,000

Neuroprotective mechanisms of resveratrol pre-conditioning.

Source: NIH/NINDS F31 Ruth L. Kirschstein National Research Service Award Predoctoral Fellowship # 1F31NS089356-01A1

Principal Investigator: Kevin B. Koronowski (PhD student in Perez-Pinzon lab)

2015 Budget: \$36,720

Novel Factors for Unexplained Phenotypes of Subclinical Carotid Artherosclerosis

Source: NIH, NINDS (R01 NS065114)

Principal Investigator: Tatjana Rundek

2015 Budget: \$324,713

Physical Exercise Mechanisms that Facilitate Cognitive Recovery after Global Cerebral Ischemia

Source: AHA, Greater Southeast Affiliate Summer 2014 Predoctoral Fellowship (15PRE22360000)

Principal Investigator: Holly Stradecki (PhD student in Perez-Pinzon lab)

2015 Budget: \$26,000

Stroke Incidence and Risk Factors in a Tri-ethnic Region

Source: NIH, NINDS (R01 NS029993)

Principal Investigator: Ralph Sacco

2015 Budget: \$1,738,353

Supplemental award: American Stroke Association-Bugher Foundation Centers for Excellence in Stroke Collaborative Research for Regeneration, Resilience and Secondary Prevention, Title: Activity-

Dependent Mechanisms of White Matter Repair after Stroke. Project Site PI: Dr. Perez-Pinzon

2015 Budget: \$99,507

The Systolic Blood Pressure Intervention Trial (SPRINT)

Source: Wake Forest University (subcontract)

Principal Investigator: Clinton Wright

2015 Budget: \$66,090

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

Source: American Heart Association Bugher Foundation

Principal Investigator: Ralph Sacco

2015 Budget: \$604,000

University of Miami, Ocular microvascular biomarkers in Alzheimer's disease

Source: UM RSA 2015-41, University of Miami
 Principal Investigator: Hong Jiang
 2015 Budget: \$16,646

12. Educational Programs Focusing on Age-Related Memory Loss

1. General education program

Dr. Sun oversees the UM-MBI monthly Research Seminar Series (see Table 1). An array of research material is presented in the series. Each research seminar fosters fruitful dialogue about improving existing research as well as identifying the disparities and needs for future work. She also coordinates the UM-MBI monthly Journal Club presentations (see Table 2). Speakers are invited from a group of interdisciplinary members, collaborators, students, fellows and residents. A wide range of scientific topics is presented, promoting discussion on strengths and weaknesses of the research and improving methodology for better research outcomes.

Dr. Zeki Al Hazzouri mentors a PhD student in Epidemiology and is chairing her dissertation committee. She also mentors and works with an MD/PhD student. She teaches EPH 623: Epidemiology and Public Health Aspects of Diabetes Mellitus at the UM- Department of Public Health Sciences.

Dr. Crocco has continued her work with the Miami Area Geriatric Education Center (MAGEC). She contributes to the planning, development and implementation of educational programs for diverse health care professionals who provide services to older adults in a variety of settings in South Florida. Select lectures provided include intensive psychiatric courses in agitation in dementia, geriatric depression and other aging issues. Outreach and education include Caregiver Training Seminars on Dementia in Miami-Dade County and the Caregiving Training Program on Dementia to ADI Respite Care and Day Care Centers in Monroe County. She developed and coordinated a 4-hour state-mandated training program (English and Spanish) for caregivers, ADI Respite and Day Care professionals and para-professionals for CEU accreditation. She also coordinates the four hours of state-mandated dementia training she developed for caregivers in Respite and Day Care Centers in Monroe County. The state of Florida mandated trainings are crucial to making sure individuals are adequately educated to work with this population.

Dr. Monteith organizes clinical Headache Group Meetings and research discussions every three months to better understand and treat complex headache disorders as well as to share research findings.

Table 1. 2015 UM McKnight Brain Institute Research Seminar Series		
Speaker	Area of Expertise	Title
Xiaoyan Sun, MD, PhD	Neurology, Neuroscience & Biochemistry	<i>In vivo Detection of synaptic damage and its clinical correlation in the patients at risk for Alzheimer's disease</i>
Hong Jiang, MD, PhD	Neurology, Neuroscience	<i>In vivo characterization of retinal microvascular function in Alzheimer's disease</i>

Joyce Gomes-Osman, PT, PhD	Neuroscience	<i>Non-Invasive Brain Stimulation - a potential tool for the understanding of the influence of physical exercise on cognitive performance</i>
Kyle Klingbeil, Medical Student	Community and Public Health	<i>Accelerated brain aging in diabetics: the impact of recurrent hypoglycemia</i>
Holly Cukier, PhD	Neuroscience and Human Genomics	<i>Utilizing Extended Multiplex Families to Investigate Neurogenetic Disorders</i>
Judi Hamelburg, PT, CDRS	Rehabilitation for the Aging Driver	<i>The Aging Driver</i>
Adina Zeki Al Hazzouri, PhD	Epidemiology	<i>Social and Cardiovascular determinants of Aging: A life Course Perspective</i>

Table 2. 2015 UM McKnight Brain Institute Journal Club

Speaker	Area of Expertise	Title
Holly Cukier, PhD	Neuroscience & Human Genomics	<i>Genetic contributions to variation in general cognitive function: a meta-analysis of genome-wide association studies in the CHARGE consortium</i>
Courtney Sparger, Student	Neuroscience	<i>Plasma phospholipids identify antecedent memory impairment in older adults</i>
Jonathan Landman, MD	Neurology	<i>Assessing cognitive effects of anticholinergic medications in patients with coronary artery disease</i>
Michelle Caunca, Medical Student	Neurology	<i>Vascular and amyloid pathologies are independent predictors of cognitive decline in normal elderly</i>
Carolina Mendoza-Puccini, IMG, CCRC	Neurology	<i>Relationships between default-mode network connectivity, medial temporal lobe structure, and age-related memory deficits</i>
Sharlet Anderson, PhD	Neuropsychology	<i>Educational Inequalities in aging-related declines in fluid cognition and the onset of cognitive pathology</i>

Xiaoyan Sun, MD, PhD	Neurology, Neuroscience & Biochemistry	<i>Normal Cognitive Aging: Memory for Normal Aging</i>
-------------------------	--	--

2. Education of medical students, residents and doctoral students

Dr. Barrientos coordinates the Journal Club for students in the MD/PhD program.

Dr. Crocco leads Doctoring II: Dementia Small Groups Miller/UM SOM for small groups of 20-25 medical students in diagnosis and evaluation of cognitive disorders and age-related memory loss. She also leads Doctoring II: Neuroscience and Behavioral Science, mood and anxiety disorders and addiction, for small groups Miller/UM for small groups of 20-25 medical students in evaluation and management of common psychiatric disorders in aging. For the Geriatric Psychiatry Lecture Series Miller/UM SOM 3rd year psychiatry clerkship, she carries out comprehensive geriatric psychiatry lectures to all third year medical students. Lecture topics include: aging and normal aging, late-life depression and anxiety, ECT, bereavement, neurodegenerative disorders, Alzheimer's, vascular and lewy body disease. Dr. Crocco also develops and implements comprehensive geriatric specialty lectures in all 4 years of general psychiatric residency training on age-related memory loss and related topics.

Dr. Czaja oversees the Certificate in Gerontology Program at the University of Miami's Center On Aging. The Certificate Program provides education and training in the science of aging with the aim of increasing the number of qualified providers to work with and study the growing aging population. She also coordinates and teaches the "Introduction to Research Seminar Series" given to the second and third year Psychology residents as part of the Graduate Medical Education program. By educating students on the science of aging including the psychiatric aspects, she is dedicated to preparing the next generation of medical professionals.

Dr. Gomes-Osman taught a 3-credit graduate level class to physical therapy students - Neuroscience II 541. In this class, students learn about clinical neurophysiology and functional performance in the healthy nervous system and in neurologic conditions.

Dr. Levin gives weekly neuropsychology lectures to upper level PhD students to fulfill didactic teaching requirements for practicum placement. She holds weekly supervision meetings with PhD students to review all clinical referrals and develop treatment planning and effective interventions. She is also the Senior Supervisor for the University of Miami Practicum Placement Site, Department of Psychology. The Division of Neuropsychology has a close teaching relationship with the graduate program in Psychology and serves as a major training site. Each year 2-5 doctoral students spend two semesters (15 hr/wk) to fulfill practicum placement requirements for doctoral training.

Dr. Sun manages the neurology educational component of the (UM-MBI). She is implementing an age-related memory loss career track for medical students. Multiple programs for various levels of academic training have been developed to accomplish the goal of providing training for many groups.

Dr. Wright lectures the MD and MD/MPH candidates on age-related cognitive disorders as part of their Neuroscience Module.

Dr. Zeki Al Hazzouri and Michelle Caunca are drafting a proposal for a Neuroepidemiology Intersession, designed as a crash course introduction into neuroepidemiology, with the goal of encouraging more students to consider studying neurology and cognitive aging.

3. Research fellow and research assistant training

Dr. Crocco plays an integral role in the Jackson Memorial Hospital Geriatric Psychiatry Training Program, including conducting a weekly case conference. She coordinates and supervises weekly presentations for geriatric psychiatry fellows of patient case history, including biological, psychological and sociological data and formulates an integrated treatment plan with special emphasis on aging. She also holds a weekly journal club overseeing the coordination and supervision of all geriatric psychiatry fellows with the objective of critical evaluation of peer-reviewed, original research articles and applies this knowledge to the care of their geriatric patients and aging issues.

Dr. Czaja coordinated the Geriatric Fellowship Didactics Series - These didactics include lectures given by university faculty, case conferences and a journal club that will enhance the quality of education provided to the geriatric Fellows. She also gives various lectures on topics regarding caregiving, technology, aging and cognition.

Drs. Dave and **Perez-Pinzon** mentor and train 4 Post-Doctoral Fellows, 1 MD/PhD student and 1 PhD student in their labs. **Dr. Wright** mentors a K-awardee as well as a doctoral student in Epidemiology.

Dr. Ramos became a peer-mentor in the NHLBI-funded Program to Increase Diversity in Behavioral Medicine and Sleep Disorders Research (PRIDE) during the summer of 2015. This is an intense year round program, hosted by New York University, that focuses on training young investigators interested in sleep health disparities.

Dr. Levin gives weekly neuropsychology lectures to Post-Doctoral Fellows to fulfill Post-Doctoral hours for licensure (Fellows). She also holds weekly supervision meetings with Fellows to review all clinical referrals and to develop treatment planning and effective interventions.

13. Collaborative Programs with other McKnight Institutes, Institutions and Research Programs

While we have not been as involved in the Epigenetics Core by design, we have collaborated with the Core through data exchange. In particular, Juan Young provided data obtained at UM pertaining to the presence of RNA transcripts in the cerebrospinal fluid (CSF) of elderly donors. In collaboration with Tom Foster, these data were compared with genes altered with age in mouse prefrontal cortex with the ultimate goal of identifying potential CSF biomarkers.

The McKnight MRI and Cognitive Cores have been a major focus of work in 2015. The development of a standardized brain MRI protocol and neurocognitive assessment battery will allow the collection of data in those above the age of 85 without cognitive impairment. In 2016 we plan to enroll people into the cross UM-MBI Brain Aging Registry that will provide data for novel grant applications in this unique age stratum to better understand the correlates of successful cognitive aging. A Special Topic in *Frontiers in Aging Neuroscience* has been approved and will be focused on state-of-the-art brain imaging in studies of cognitive aging. Drs. Alexander, Cohen, Visscher, Woods and Wright are Topic editors of this publication.

We resubmitted a grant to NIA that was initially in response to the NIA/McKnight RFA and was redesigned as a smaller, but still very substantial submission. In collaboration with UF (Dr. Woods, PI) and the University of Arizona, this clinical trial will test if transcranial direct current stimulation (tDCS) of frontal cortices enhances cognitive performance and functional outcomes among older adults experiencing age-related cognitive decline.

14. Collaborative Programs with Non-McKnight Institutes, Institutions and Research Programs

The UM-MBI has extensive collaborations with many other institutions through grant awards with other universities and through major consortia. These are detailed above, but larger projects include the Northern Manhattan Study (Columbia University, Mount Sinai [New York]), the Bugher Center of Excellence (UCLA, U. Colorado), the Systolic Pressure Intervention Trial (Wake Forest), and the Hispanic Communities Health Study (Michigan State).

15. Briefly describe plans for future research and/or clinical initiatives.

A number of initiatives will be implemented in 2016. Including data from detailed neuropsychological testing will enhance the UM-MBI memory clinic Registry. A major focus will be the Brain Aging Registry that will begin to collect data on the oldest old as part of the MRI and Cognitive Cores. We also plan to propose several ancillary projects to large epidemiologic cohort studies to NIH, including the Multi-ethnic Study of Atherosclerosis and the Hispanic Communities Health Study. Dr. Czaja and Dr. Ramos are applying for a program project (P30) proposal titled, "Cardio-Metabolic and Behavioral Pathways for Healthier Aging", where Dr. Ramos plans to evaluate with a pilot project sleep and cardiometabolic disease in an older sample of Hispanics in Miami. Two mentees also plan K award applications to NIA and NINDS in 2016.

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

See attached report.

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


Clinton B. Wright, M.D.

Scientific Director, Evelyn F.
McKnight Brain Institute

1/14/2016
Date

Financial and Budget Sheets

McKnight
Budget For FY16 June 1, 2015 - May 31, 2016

			<u>Budget</u>	<u>Actual as of Dec. 31, 2015</u>	<u>Projected at Year End</u>	<u>Variance to Budget</u>
Revenue			549,707.93	322,718.98	570,522.08	20,814.15
McKnight Project Clinical and Clinical Research Program						
Personnel						
Faculty	Role In Project	Effort	225,951.11	104,505.75	172,193.09	53,758.02
Clinton Wright, MD	Scientific Director	16%				
Ralph Sacco, MD	Executive Director	5%				
Xiaoyan Sun, MD	Educational Director	20%				
Noam Alperin	Radiology	5%				
Bonnie Levin, PhD (Schoninger)	Neuropsychology	30%				
Dave Kunjan, PhD	Basic Science	5%				
Jiang Hong, MD, PhD	Neurologist	5%				
Sara Czaja, PhD	Psychiatry	5%				
Subtotal Staff Salary and CFB						
Staff	Role in Project+A1		253,286.82	170,887.77	289,458.81	(36,171.99)
Carolina Gutierrez	Administrative Support	10%				
Stacy Merritt	McKnight Project Manager	50%				
Ahmet Bagci	Radiology	20%				
Charles Cohan	Med Grad Student-Basic Science	25%				
Maria Mendoza-Puccini	Clinical Research Coordinator	90%				
Nooshin Nabizadeh	Teaching Assistant	50%				
Isabel Saul	Research Support Specialist-Basic Science	30%				
Hui Chao Lee	Research Asst/Technician-Basic Science	50%				
Sharlett Anderson/Katalina McInerney	Neuropsychology	20%				
Laura Segala	Post-Doctoral Associate	50%				
Talia Robinson	Research Asst	50%				
Total Personnel			479,237.93	275,393.52	461,651.90	17,586.03
Non Personnel Expenses						
Communications			3,470.00	103.00	1,603.00	1,867.00
Internal UM Services Provided	Animal Care Service		21,000.00	20,757.33	20,757.33	242.67
Supplies			7,000.00	56.99	7,000.00	-
Travel			1,200.00	211.13	1,200.00	-
Equipment & Furniture			500.00	66.32	500.00	-
Conference & Registration			1,000.00	-	1,000.00	-
Other			36,300.00	42,928.01	76,809.85	-(40,509.85)
Total Non-Personnel Expenses			70,470.00	64,122.78	108,870.18	(38,400.18)
Grand Total Expenses			549,707.93	339,516.30	570,522.08	(20,814.15)
Net Operating Income			0.00	(16,797.32)	0.00	(0.00)

McKnight
 Budget For FY17 June 1, 2016 - May 31,2017

				Budget
<u>Revenue</u>				642,700.56
<u>Personnel</u>				
<u>Faculty</u>	<u>Role In Project</u>	<u>CFB Rate</u>	<u>Effort</u>	272,119.80
Clinton Wright, MD	Scientific Director	21.00%	20%	
Ralph Sacco, MD	Executive Director	21.00%	5%	
Xiaoyan Sun, MD	Educational Director	21.00%	25%	
Xiaoyan Sun, MD	Research for Age-related Cognitive Disorder	21.00%	25%	
Bonnie Levin, PhD	Neuropsychology	27.00%	20%	
Noam Alperin, PhD	Radiology	27.00%	5%	
Dave Kunjan, PhD	Basic Science	27.00%	5%	
Jiang Hong, MD, PhD	Neurologist	21.00%	3%	
Sara Czaja, PhD	Psychiatry	27.00%	2%	
<u>Subtotal Staff Salary and CFB</u>				
<u>Staff</u>	<u>Role in Project+A1</u>			307,289.83
Stacy Merritt	McKnight Project Manager	43.00%	55%	
Ahmet Bagci	Radiology	43.00%	20%	
Maria Mendoza-Puccini	Clinical Research Coordinator	43.00%	50%	
Maria Diaz	Clinical Research Coordinator	43.00%	100%	
Isabel Saul	Research Support Specialist-Basic Science	43.00%	28%	
Yessica Campos	Neuropsychology	43.00%	0%	
Hui Chao Lee	Research Asst/Technician-Basic Science	43.00%	0%	
Katalina McInerney	Neuropsychology	43.00%	40%	
Laura Segala	Post-Doctoral Associate	43.00%	100%	
TBA	Research Asst for Neuro-Psychology	43.00%	50%	
Total Personnel				579,409.63
<u>Non-Personnel Expenses</u>				
Communications				3,500.00
Internal UM Services Provided	<u>Animal Care Service</u>			10,000.00
Supplies				6,690.93
Travel				5,000.00
Equipment & Furniture				500.00
Conference & Registration				1,000.00
Other				36,600.00
<u>Total Non-Personnel Expenses</u>				63,290.93
<u>Grand Total Expenses</u>				642,700.56
<u>Net Operating Income</u>				0.00

Evelyn F. McKnight Brain Institute's Endowments
at the Miller School of Medicine
Market Value Analysis
11/30/2015

2002 Gift & Match

McKnight Contribution	\$5,000,000
UM Match	5,050,913
Transfers from Other University Funds	1,362,153
Investment Return	3,870,301
Distributions for Spending	(4,210,971)
11/30/15 Endowment Balance	<u>\$11,072,397</u>
Unmatched Balance	<u>\$0</u>

2014 Gift & Match

McKnight Contribution	\$1,500,000
UM Match	2,000,000
Transfers from Other University Funds	0
Investment Return	(16,590)
Distributions for Spending	(48,001)
11/30/15 Endowment Balance	<u>\$3,435,409</u>
McKnight Foundation Pledge Balance	<u>\$500,000</u>

University of Miami
Evelyn F. McKnight Brain Institute's Endowments
Summary Analysis at Market Value
June 1, 2015 - November 30, 2015

2002 Gift & Match

	Evelyn F. McKnight 262080	F. Peterson/ McKnight 262293	Schoninger Professorship in Neurology 262453	Schoninger Neuropsychology Clinic 262454	Other sources	Total
Beginning Balance at Market, 6/1/15	\$7,245,253	\$1,120,910	\$1,017,780	\$2,544,450	\$0	\$11,928,394
Investment Return	(353,067)	(54,623)	(49,597)	(123,992)		(581,279)
Distributions for Spending	(166,862)	(25,815)	(23,440)	(58,600)		(274,718)
Transfers from other University funds						0
Matching gifts						0
Ending Balance at Market, 11/30/15	<u>\$6,725,324</u>	<u>\$1,040,472</u>	<u>\$944,743</u>	<u>\$2,361,858</u>	<u>\$0</u>	<u>\$11,072,397</u>

2014 Gift & Match

	Schoninger Professor in Memory Disorders 262471	Evelyn F. McKnight Endowed Chair 262490	Total
Beginning Balance at Market, 6/1/15	\$2,084,226	\$1,033,569	\$3,117,795
Investment Return	(101,566)	(32,819)	(134,385)
Distributions for Spending	(48,001)	0	(48,001)
Transfers from other University funds			0
Matching gifts			0
McKnight Foundation gifts		500,000	500,000
Ending Balance at Market, 11/30/15	<u>\$1,934,659</u>	<u>\$1,500,749</u>	<u>\$3,435,409</u>

Member
and
Collaborator
Biosketches

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: **Alperin, Noam**

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

POSITION TITLE: Professor of Radiology and 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 Tel Aviv, Israel	B.Sc.	10/1980	Physics
Hebrew University, Jerusalem		08/1983	Medicine
University of Chicago, Chicago, IL	Ph.D	8/1992	Medical Physics
University of Chicago, Chicago, IL	Postdoctoral	10/1994	MRI

A. Personal Statement

Even before attending graduate school I was attracted to medical imaging. I started my career in imaging working as a physicist in the R&D department of a medical imaging company developing digital subtraction angiography systems. During graduate school I shifted my focus to MRI, fascinated by the ability to image blood vessels and flow without the need to inject contrast agent. One of my early publications utilized blood vessels as landmarks for registering X-ray with MR angiography data (1). During my postdoctoral training I was introduced to Chiari Malformations, a poorly understood and debilitating neurosurgical problem associated with altered cerebrospinal fluid (CSF) dynamics. I used velocity-encoding MR to image and measure CSF pulsation in the cranio-spinal system and was puzzled by the large inter-individual variability, even among healthy subjects. We were among the first to investigate the relationship between CSF and blood flow pulsations and the first to demonstrate that the cranio-spinal CSF pulsation is driven by the change in the intracranial blood volume during the cardiac cycle (2). The characterization of the driving force for the CSF pulsation has clarified what information can be derived from the CSF pulsation and to the development of a novel methodology to noninvasive measure intracranial compliance and pressure by MRI (MRICP) (3). I was fortunate to receive R21 grant to demonstrate the feasibility of the MRICP method followed by RO1 grant to apply the method in the clinical setting of Chiari Malformation (the same disorder that got me involved in CSF dynamics). This effort resulted with advancement and new insight into this disorder (4). Consistent focus on the CSF physiology and dedicated research effort helped establish our group among the leaders in this field.

In the current application, we identify another CSF related clinical challenge that can benefit from the MRICP technique, the need for reliable noninvasive test to assess CSF shunt function. Incorporating the MRICP as part of a shut function test will likely yield a reliable test, which in turn, will have a significant impact on management of many pediatric and adult patients with CSF shunts. Our track record and my previous experience leading a multi-disciplinary teams will benefit the project and the likelihood for successful completion.

1. Alperin N, Levin DN, and Pelizzari CA. (1994). Retrospective registration of x-ray angiograms with MR images by using vessels as intrinsic landmarks. *Journal of Magnetic Resonance Imaging*, 4:139-144
2. Alperin N, Vikingstad EM, Gomez-Anson B, Levin DN. (1996). Hemodynamically-independent analysis of CSF and brain motion observed with dynamic phase-contrast MRI. *Magn. Reson. in Med.*, 35:741-754
3. Alperin N, Lee SH, Loth F, Raksin P, Lichtor T. (2000). MR-Intracranial Pressure (ICP): A method for noninvasive measurement of intracranial pressure and elastance. Baboon and Human Study. *Radiology*, 217 (3); 877–885.
4. Alperin N, Loftus JR, Oluu CJ, Bagci AM, Lee SH, Ertl-Wagner B, Green B, Sekula R. (2014). MRI measures of Posterior Cranial Fossa Morphology and CSF Physiology in Chiari Malformation Type I. *Neuroradiology* 75:515–522 (Editor's Choice)
Neuroradiology 75:515–522 (Editor's Choice)

B. Positions and Honors

POSITIONS AND EMPLOYMENT

1985-1987	Physicist, Elscint Medical Imaging, Inc.
1987-1988	Product Manager, Mennen Medical, Inc.
1989-1994	Research Associate, MRI Center, University of Chicago
1994-1995	MRI Application Scientist, SMIS Inc.
1995-2001	Assistant Professor, Departments of Radiology and Bioengineering, Uni. of Illinois, Chicago
2001-2009	Associate Professor, Departments of Radiology and Bioengineering, Uni. of Illinois, Chicago
2009-	Professor, Department of Radiology and Biomedical Engineering, University of Miami

Other Experience and Professional Memberships

1990-2008	Member, American Association of Medical Physicists
1994-	Member, American Society of Magnetic Resonance in Medicine
2004-	Ad hoc member, reviewer for several NIH study sections
2011-	Member of the American Society of Neuroradiology

C. Contribution to Science

1. My early publications related to the investigations of the CSF flow dynamics aimed to characterize the origin of the cranio-spinal CSF pulsation (a-d). Effort to explain the origin of CSF pulsation started in the early 1940s where invasive measurements showed that CSF pressure pulsation is synchronous with the blood pressure pulsation. In each decade since till the late 1970s a new view of the origin of CSF pulsation was proposed, from only arterial origin through only venous origin and sometimes a complex combination of the two. In the 1990s, MRI provided new perspective into CSF pulsation, enabling quantitation of the volumes of blood and CSF entering and leaving the cranium during the cardiac cycle. Our publications adopted a system approach to describe the CSF volumetric flow rate dynamics and proposed transfer function to describe the link between CSF and blood flow, where the CSF is the output driven by the momentary difference between arterial inflow and venous outflow (the input). The CSF flow is also modulated by the mechanical properties of the intracranial compartment (i.e., compliances and resistances). This provided the first subject-specific noninvasive estimation of the lumped mechanical properties of the cranio-spinal system. This approach however, does not yield individual parameters such as the intracranial compliance, but instead, it provides measures, such as the natural frequency of the system, which is a combination of several parameters. Therefore, an alternative approach was needed to obtain a measurement of intracranial compliance from which intracranial pressure is derived.
 - a. Alperin N, Vikingstad EM, Gomez-Anson B, Levin DN. (1996). Hemodynamically-independent analysis of CSF and brain motion observed with dynamic phase-contrast MRI. *Magn. Reson. in Med.*, 35:741-754.
 - b. Chu D, Levin DN, and Alperin N. (1998). Assessment of the biomechanical state of intracranial tissue by dynamic MRI of Cerebrospinal fluid pulsations: a phantom study. *Magn. Reson. Imag.* 16:(9)1043-48.
 - c. Alperin N, Kulkarni K, Loth F, Mafee M, Lichtor T. (2001). Analysis of MRI-Based Blood and CSF Flow Measurements in Patients with Chiari I Malformations: A System Approach. *Neurosurgical Focus*, 11(1):1-10.
 - d. Tain and RW, Alperin N. (2009). Noninvasive Intracranial Compliance from MRI-Based Measurements of Transcranial Blood and CSF Flows: Indirect vs. Direct Approach; *IEEE Transaction in Biomedical Engineering*, 56(3):544-54.
2. Following efforts were focused on developing a direct measure of intracranial compliance based on its physical definition, the change in volume for a given change in pressure (i.e., dV/dP). Our effort was motivated by the possibility to derive ICP noninvasively by MRI. Because of the mono-exponential relationship between intracranial pressure and intracranial volume, intracranial compliance is inversely related to intracranial pressure (ICP). Our initial publication demonstrated the feasibility of the MRICP.

The volume change was derived from volumetric flow rate of blood and CSF to and from the cranium, and the pressure change was derived from the change in the pressure gradient. The following publications describe important improvements that made the MRICP method more robust. The first was the modeling of the CSF flow in the cervical canal in order to formulate the relationship between the pulse pressure

and the pulse pressure gradient replacing the previous empirical relationship (b). The second important contribution was the development of a novel method for automated segmentation of lumens conducting non-steady flow for reliable quantitation of volumetric CSF and blood flow rates by MRI (c). Our lumen segmentation method incorporates temporal information in multiple images compared to available methods that are primarily based on spatial information in a single image. This method has been adopted by other investigators who utilize velocity-encoded MRI for flow quantitation (e.g., Huang et al 2004). The MRICP method is now beginning to be used independently by other groups (e.g., Muehlmann et al 2013) and by other investigators in collaboration with our group who assists with guidance and with the data analyses. For example, the MRICP methodology was very recently employed to investigate the elusive pathophysiology of *Acute Mountain Sickness*. Results published in the *Annals of Neurology* revealed that the severity of headaches symptoms is correlated with the change in ICP between the normal and the hypoxic conditions (d).

- a. Alperin N, Lee SH, Loth F, Raksin P, Lichtor T. (2000). MR-Intracranial Pressure (ICP): A method for noninvasive measurement of intracranial pressure and elastance. Baboon and Human Study. *Radiology*, 217 (3); 877–885.
 - b. Loth FM, Yardimici MA, and Alperin N. (2001). Hydrodynamic modeling of Cerebrospinal Fluid Motion within the spinal cavity. *Jour. of Biomechanical Engineering*, 123:71-79,
 - c. Alperin N, Lee SH. (2003). PUBS: Pulsatility based segmentation of lumens conducting nonsteady flow, *Magnetic Resonance in Medicine*, 49:934–44.
 - d. Lawley J, Alperin N, Bagci A, Lee S, Mullins O, Oliver S, Macdonald J. (2014). Acute mountain sickness: Elevated brain volume and intracranial hypertension. *Annals of Neurology*. 75(6):890-8.
3. Our recently completed RO1 project focused on the potential role of the MRICP in the setting of Chiari Malformation Type I (CMI). Adult CMI affects primarily women with onset of symptoms occurring during childbearing age. Symptoms include severe headaches and motor and sensory deficits. If left untreated, patients experience poor quality of life and deficits worsen. A surgical procedure, termed decompression, where a portion of the skull base is removed, was found to provide symptomatic relief. However, due to a lack of reliable diagnostic criteria (currently diagnosis is based on an arbitrary radiologic finding of tonsillar herniation greater than 5mm), 3 to 4 out of 10 patients undergoing surgery do not improve. Therefore, there is a clear need for a fresh look at this disorder. During the award period, we collected data from CMI patients and healthy subjects. It was evident that cranial morphology, especially of the posterior cranial fossa (PCF), plays a role and should be considered together with the CSF hydrodynamics. We therefore developed an automated method for PCF parcelation (a), computed over 20 morphologic and hydrodynamic measures, and assessed differences between CMI and the control cohorts. In addition, these measures were correlated with symptomatology. The results of this work have led to a new characterization of CMI using combined morphologic-physiologic quantitative measures. We identified 10 measures that were significantly different in the CMI and were strong differentiators of CMI (b). Outcome analyses reveal that some of these new CMI markers were outside the CMI range in patients that had poor outcome following surgery. We therefore hypothesize that the combined morphologic-physiologic criterion for CMI would significantly improve diagnostic accuracy and surgical outcome. Interestingly, MRICP was among the predictive parameters and is moderately elevated in CMI. Increased ICP was proposed as a possible mechanism for CMI by the discoverer of CMI, H. Chiari, in 1891. Our latest paper on CMI addresses the different types of headaches reported in CMI (c). This work is important because neurosurgeons rely on specific symptoms for surgery consideration. We found that headaches worsen with Valsalva maneuver, which is considered a hallmark symptom of CMI, is associated with lower compliance and higher MRICP due to a smaller intracranial volume and not, as previously suggested, smaller PCF. This information has implications on utilization of symptoms in the diagnosis of CMI.
- a. Bagci AM, Lee SH, Nagornaya N, Green BA, Alperin N. (2013). Automated posterior cranial fossa volumetry by MRI: applications to Chiari malformation type I. *AJNR* 34(9):1758-63.

- b. Alperin N, Loftus JR, Olu CJ, Bagci AM, Lee SH, Ertl-Wagner B, Green B, Sekula R. (2014). *MRI measures of Posterior Cranial Fossa Morphology and CSF Physiology in Chiari Malformation Type I*. *Neurosurgery* 75:515–522. (Editor's Choice)
 - c. Alperin N, Loftus JR, Olu CJ, Bagci AM, Lee SH, Ertl-Wagner B, Sekula R, Lichtor T, Green AB. (2015). *Imaging-Based Features of Headaches in Chiari Malformation Type I*. *Neurosurgery*. Mar 23.

4. In 2010, after relocating my lab to the University of Miami I initiated collaboration with the Bascom Palmer Eye Institute focusing on another complex CSF related disorder, idiopathic intracranial hypertension (IIH). IIH is characterized by elevated ICP of unknown cause and is manifested mainly by severe headaches and often with visual impairments caused by increased CSF pressure that compresses the optic nerve and the eye globe. IIH can occur both in males and females of a wide age range, though it is most frequent in overweight women of childbearing age. Our research focused on the obesity related IIH that often presents with edema of the optic nerve (papilledema). We since published 5 important publications that were well received. Two were selected by Biomed Updater as 1st and 3rd in a list of top 20 articles in this domain published since 2013 and another article featured by AJNR news digest. Our first contribution employed our lamped parameter modeling of the cranio-spinal system to document reduced spinal canal compliance in IIH, which likely explains the associated with obesity through increased abdominal pressure (a). The following paper provided evidence for impaired CSF homeostasis and the involvement of the extra cranial venous drainage in the etiology of IIH (b). We documented increased intracranial CSF volume in the extra- ventricular spaces in IIH, consistent with the reduced ability of the spinal canal to accommodate the increased CSF volume. We made an important contribution by developing an automated method for quantitation of the eye globe deformation in IIH that provide quantitative measures of the optic nerve protrusion and posterior sclera flattening (c). Using these novel quantitative measures we found that the degree of papilledema severity is proportional to the nerve protrusion length, an observation that favors a “mechanical” over a “vascular cause of papilledema. We then correlated MRI and Optical coherence tomography (OCT) imaging of the globe and were able to translated the method to measured nerve protrusion with OCT, which is a more widely used imaging modality for the eye globes
 - a. Tain RW, Bagci AM, Lam BL, Sklar EM, Ertl-Wagner B, Alperin N. (2011). Determination of cranio- spinal canal compliance distribution by MRI: Methodology and early application in idiopathic intracranial hypertension. *Jour. Magn. Reson. Imag.* 34:1397-404.
 - b. Alperin N, Ranganathan S, Bagci AM, Adams DJ, Ertl-Wagner B, Saraf-Lavi E, Sklar E, Lam BL. (2013). MRI Evidence of Impaired CSF Homeostasis in Obesity-Associated Idiopathic Intracranial Hypertension. *AJNR*. 34(1):29-34.
 - c. Alperin N, Bagci AM, Lam BL, Sklar E. (2013). Automated quantitation of the posterior scleral flattening and optic nerve protrusion by MRI in idiopathic intracranial hypertension. *AJNR Am J Neuroradiol*. 34(12):2354-9.
 - d. Chang YC, Alperin N*, Bagci AM, Lee SH, Rosa PR, Giovanni G, Lam BL (2015). Relationship between Optic Nerve Protrusion Measured by OCT and MRI and Papilledema Severity. *Invest Ophthalmol Vis Sci*. 2015 Mar 17 (*co-first author)

5. In this section we report two recent important contributions. The first relates to another disorder of impaired CSF homeostasis that occurs in the elderly, idiopathic normal-pressure hydrocephalus (iNPH). iNPH is a reversible syndrome of gait impairment, dementia, and incontinence. Currently, the only effective treatment is surgical implantation of a shunt. The need for a pharmacologic adjunctive treatments due to high failure rates and mortality associated with shunt has been already noted at several NIH workshops. I initiated a collaboration with Weill Cornell Medical College in New York to assess the effect of acetazolamide (a drug that is effective in IIH). Results of this pilot study were recently reported in *Neurology* and included first radiologic evidence for the potential efficacy of pharmacologic treatment in iNPH- reversal of periventricular white matter hyperintensities in patients who had improved gait following treatment (a).

BIOGRAPHICAL SKETCH

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

NAME: **BARRIENTOS, Antoni**

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

POSITION TITLE: **Professor**

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

The study of mitochondria is critical to the understanding of key cellular metabolic functions. It is also key to understand aging and the pathogenesis of several diseases with wide social impact, including the Veterans population, such as neurodegenerative disorders. Alterations in mitochondrial energy production are also the cause of fatal childhood diseases, mostly encephalomyopathies.

My main research interest focuses on the understanding of mitochondrial **biogenesis and oxidative phosphorylation function in health, disease and aging**. 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* as a model organism to speed discovery that can then be translated to mammalian models and eventually help patients. *S. cerevisiae* is a very favorable organism for the study of mitochondrial biogenesis and physiology in health and disease since its metabolism (fermentative *versus* respiratory) can be easily controlled by changes in media composition. Over the last five years we have been working on the regulation of aging by mitochondrial energy production and reactive oxygen species (ROS) signaling using the yeast chronological lifespan model of aging. We have also gained insight into the cause/effect relationships among mitochondrial dysfunction, ROS generation and cellular proteotoxicities using the mitotic yeast models of proteinopathies. We have actively searched for suppressors of proteotoxicities and found that enhancement of mitochondrial biogenesis suppresses polyglutamine- and α -synuclein-induced cytotoxicities. Now we have developed innovative inducible yeast models that will allow us to study cellular proteotoxicities in the context of cellular aging. Additionally, we have established patient-based neuronal cell culture models of neurodegenerative proteotoxicities to validate the results obtained in the yeast model. Over the last few years, we have established collaborations with Dr. Lisa Ellerby (Buck Institute for Research on Aging, CA), expert in the generation of induced pluripotent stem cells from patient's skin fibroblasts, and with Dr. Grace Zhai (Department of Molecular and Cellular Pharmacology, University of Miami Miller School of Medicine) to understand the mechanism by which neurodegenerative proteotoxicities can be alleviated by modulation of mitochondrial bioenergetics and enhancement of resistance to stress.

During my 12 years as an academic faculty I have trained 9 postdoctoral trainees; I have mentored 9 graduate students (5 currently), have been in the dissertation committee of 20 graduate students and was a mentor of 6 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 feed back 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. Over the last 13 years we have 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. Studies during my postdoctoral training at Columbia University had shown that most COX mutants had low levels of Cox1 synthesis. Subsequently, 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 bc₁ 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 that mitochondrial supercomplexes or respirasomes are assembled by incorporation of individual complex subunits rather than by assembly of preexisting fully assembled complexes [5]. 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 holocomplexes, 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 [5]. 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 [6].

5 Moreno-Lastres, D., *et al.* (2012) Mitochondrial Complex I Plays an Essential Role in Human Respirasome Assembly. ***Cell Metab.*** 15, 324-335

6 Barrientos, A. and Ugalde, C. (2013) I Function, Therefore I Am: Overcoming Skepticism about Mitochondrial Supercomplexes. ***Cell Metab.*** 18, 147-149

(iii) 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) [7] and more recently we have characterized the first DEAD box helicase that plays a role in LSU assembly, called Mrh4 in yeast [8] and DDX28 in mammals [9]. For example, we have reported that Mrh4 binds to the 21S rRNA to facilitate the incorporation of three late-assembly LSU subunits [8]. 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 [8].

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 [9]. 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” [9].

7 Barrientos, A., *et al.* (2003) *MTG1* codes for a conserved protein required for mitochondrial translation. **Mol. Biol. Cell** 14, 2292-2302.

8 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

9 Tu, Y.T. and Barrientos, A. (2015) The Human Mitochondrial DEAD-Box Protein DDX28 Resides in RNA Granules and Functions in Mitochondrial Assembly. **Cell Rep.** 12, 00058-00053

10 De Silva D, Tu YT, Amunts A, Fontanesi F, Barrientos A. (2015) Mitochondrial ribosome assembly in health and disease. **Cell Cycle.** Jun 1:0. [Epub ahead of print]

(iv) 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 [10]. 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 [11]. 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 [12].

11 Pan, Y., *et al.* (2011) Regulation of yeast chronological life span by TORC1 via adaptive mitochondrial ROS signaling. **Cell Metab.** 13, 668-678.

12 Ocampo, A., *et al.* (2012) Mitochondrial respiratory thresholds regulate yeast chronological life span and its extension by caloric restriction. **Cell Metab.** 16, 55-67

13 Barrientos, A. (2012) Complementary roles of mitochondrial respiration and ROS signaling on cellular aging and longevity. **Aging (Albany NY)** 4, 578-579

14 Ruetenik AL and Barrientos A. Dietary restriction, mitochondrial function and aging: from yeast to humans. **BBA: Bioenergetics.** 2015 (Epub ahead of print)

(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 [13]. 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 [14], 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 [15]. 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 [15].

13 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

14 Ocampo, A., *et al.* (2010) Suppression of polyglutamine-induced cytotoxicity in *Saccharomyces cerevisiae* by enhancement of mitochondrial biogenesis. **FASEB J.** 24, 1431-1441

15 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

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.**

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.**

Completed Research Support over the last three years

2010-2013. Research Challenge grant from the Florida Department of Health / James & Esther King Biomedical Research Program. "*Slowing degenerative processes by bolstering cellular bioenergetics*" **PI: Antoni Barrientos,** PI: C. T. Moraes (multiple PI grant).

2006-2011. RO1 grant from NIH (NIH # R01GM071775). Research project: "*Cytochrome c oxidase assembly in health and disease*". **PI: Antoni Barrientos.**

2009-2011. Competitive ARRA supplement NIGMS 3 R01 GM071775-04S1. Research project: "*Cytochrome c oxidase assembly in health and disease*". **PI: Antoni Barrientos.**

2011-2013. Research Grant from the Muscular Dystrophy Association. Research project: "*Characterization of novel conserved cytochrome c oxidase chaperones*". **PI: Antoni Barrientos.**

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:	Blanton, Susan Halloran		
eRA COMMONS USER NAME (credential, e.g., agency login):	Shblanton		
POSITION TITLE:	Professor of Human Genetics		
EDUCATION/TRAINING (<i>Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.</i>)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Virginia Commonwealth University, Richmond VA	B.S.	1980	Biology
Virginia Commonwealth University, Richmond VA	Ph.D.	1985	Human Genetics
University of Pittsburgh, Pennsylvania	(Post-Doc)	1986	Biostatistics
Fox Chase Cancer Center, Philadelphia PA	(Post-Doc)	1988	Population Oncology

A. Personal Statement

1. I am a Genetic Epidemiologist with an interest in cognitive decline and its relationship to cardiovascular disease. I have been involved in mapping genes for complex disorders and traits for nearly three decades. These disorders include birth defects such as cleft lip/palate and clubfoot and common quantitative traits such as carotid plaque and intima media thickness. These carotid phenotypes are important for their role in cardiovascular disease and stroke. They may also impact cognition. Working with the NOMAS dataset, we are identifying primary loci associated with cognition and cognitive decline.
 - a. 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*, Dec 15;323(1-2):93-8, 2012. PMID: PMC3483411.
 - b. Wang L, Beecham A, Zhuo D, Dong C, **Blanton SH**, Rundek T, Sacco RL. Fine Mapping Study Reveals Novel Candidate Genes for Carotid Intima-Media Thickness in Dominican Families. *Circ Cardiovasc Genet*, Apr 1;5(2):234-41, 2012. PMID: PMC3341091.
 - c. Lu W, Bacino CA, Richards BS, Alvarez C, VanderMeer JE, Vella M, Ahituv N, Sikka N, Dietz FR, **Blanton SH**, Hecht JT. Studies of TBX4 and chromosome 17q23.1q23.2: an uncommon cause of nonsyndromic clubfoot. *Am J Med Genet A*, Jul;158A(7):1620-7, 2012. PMID: PMC3381434.
 - d. Weymouth KS, **Blanton SH**, Bamshad MJ, Beck AE, Alvarez C, Richards S, Gurnett CA, Dobbs MB, Barnes D, Mitchell LE, Hecht JT. Variants in genes that encode muscle contractile proteins influence risk for isolated clubfoot. *Am J Med Genet A*, Sep;155(9):2170-9, 2011. PMID: PMC3158831.

B. Positions and Honors

Positions and Employment

1980-1983	Graduate Asst, Dept of Human Genetics, VCU, Richmond
1983-1985	Graduate Asst, Div of Human Genetics, Univ of Maryland at Baltimore
1985-1986	Research Assoc, Dept of Biostatistics, U of Pittsburgh, Pittsburgh, PA
1987-1988	Postdoc, Population Oncology, Fox Chase Cancer Ctr, Philadelphia PA
1988-1989	Instructor, Dept of Pediatrics, U of Conn Health Center, Farmington
1989-1991	Asst Professor-Research, Medical Genetics Center, U of TX, Houston
1991-1996	Asst Professor of Research, Dept of Pediatrics, UVA, Charlottesville
1996-2006	Assoc Professor of Research, Dept of Pediatrics, UVA, Charlottesville
1997-2007	Assoc Professor, Collateral Faculty, Dept of Human Genetics, VCU, Richmond, VA
2006	Assoc Research Professor, Center for Human Genetics, Duke, Durham, NC
2007-2015	Assoc Professor, Dr. John T. Macdonald Foundation Department of Human Genetics, University of Miami Leonard M. Miller School of Medicine, Miami, Florida
2012-2015	Executive Director, John P. Hussman Institute for Human Genomics University of Miami Leonard M. Miller School of Medicine, Miami, Florida

2015-present	Associate Director, Collaborations and Compliance, John P. Hussman Institute for Human Genomics University of Miami Leonard M. Miller School of Medicine, Miami, Florida
2015-present	Professor, Dr. John T. Macdonald Foundation Department of Human Genetics, University of Miami Leonard M. Miller School of Medicine, Miami, Florida
2015-present	Professor, Department of Otolaryngology University of Miami Leonard M. Miller School of Medicine, Miami, Florida

Honors

1980	Phi Kappa Phi, Virginia Commonwealth University
1980	Biology Award to Outstanding Senior, Virginia Commonwealth University, Dept. of Biology
1980-1983	NIH Pre-Doctoral Fellowship, Medical College of Virginia
1982	Alpha Sigma Chi, Virginia Commonwealth University
1983-present	Sigma Zi
1994	IBM Shared University Resource Award

Other Experience and Professional Memberships

1990-1995	Member, Tuberous Sclerosis Advisory Board
1995-1998	Research Proposal Reviewer, MD Anderson Cancer Center
1995-2000	Research Proposal Reviewer, Wellcome Trust, England
1997	Ad Hoc, NIDDK NIH study section
2001-2003	Ad Hoc, NINDS NIH study section NSD-C
2002/2005	Research Proposal Reviewer, Alzheimer's Association
2003-2005	Member, NINDS NIH study section NSD-C
2005/2006	Member, Special emphasis panel, NINDS
2005-2007	Member, Ad Hoc, NINDS study section NST
2007-2011	Member, NINDS study section NST
2008-2013	Editorial Board, Journal of Biomedicine and Biotechnology
2008	Reviewer, March of Dimes
2011	NCBDDD, Fragile X/Rare Disorders special emphasis panel
2012	Research proposal Reviewer, Gallaudet Research Institute
2014	Field Reviewer, CDC study section, Center for Research and Training to Promote the Health of People with Developmental and Other Disabilities
2015	Member, NICHD, ZHD1 DRG-D (13), special emphasis panel (April 8, 2015)

C. Contribution to Science

1. I have played a major role in the mapping of Mendelian disorders since the early days of linkage analysis. For some of these disorders, this was the first gene identified, providing insight into the underlying mechanism. While my role has primarily revolved around the analysis of the data, I am also involved in other aspects, including study design, phenotype definition and sample collection.
 - a. **Halloran SL**, Boughman JA, Dryja TP, Mukai S, Long D, Roberts DF and Craft AW. Accuracy of detection of the retinoblastoma gene by esterase D linkage. *Arch Ophthal*, 103(9):1329-1331, 1984
 - b. **Blanton SH**, Heckenlively JR, Cottingham AW, Freidman J, Sadler LA, Wagner M, Freidman LH and Daiger SP. Linkage mapping of autosomal dominant retinitis pigmentosa (RP1) to the pericentric region of human chromosome 8. *Genomics*, 11:857-869, 1991.
 - c. Kumar A, Girimaji SC, Duvvari MR, **Blanton SH**. Mutations in *STIL*, encoding a pericentriolar and centrosomal protein, cause primary microcephaly. *Am J Hum Genet*, Feb;84(2):286-290, 2009. PMID: PMC2668020.
 - d. Sullivan LS, Koboldt DC, Bowne SJ, Lang S, **Blanton SH**, Cadena E, Avery CE, Lewis RA, Webb-Jones K, Wheaton DH, Birch DG, Coussa R, Ren H, Lopez I, Chakarova C, Koenekoop RK, Garcia CA, Fulton RS, Wilson RK, Weinstock GM, Daiger SP. A Dominant Mutation in Hexokinase 1 (HK1) Causes Retinitis Pigmentosa. *Invest Ophthalmol Vis Sci*. 2014 Sep 4;55(11):7147-58. PMID: PMC4224580.

2. In addition to identification of the loci for a variety of Mendelian disorders, I have also played a key role in the establishment of heterogeneity and phenotype-genotype correlations in these disorders. This information is critical for reliable counseling of affected individuals and their families, as well as providing insight into disease etiology.
 - a. Northrup H, Kwiatkowski DJ, Roach ES, Dobyns WB, Lewis RA, Herman GE, Rodriguez E, Daiger SP and **Blanton SH**. Evidence for genetic locus heterogeneity in tuberous sclerosis: one locus on chromosome 9 and at least one locus elsewhere. *Am J Hum Genet*, 51(4):709-720, 1992. PMID: PMC1682771.
 - b. Cook A, Raskind W, **Blanton SH**, Pauli RM, Gregg RG, Francomano CA, Puffenberger E, Conrad EU, Schmale G, Schallenberg G, Wijsman E, Hecht JT, Wells D, Wagner MJ. Genetic heterogeneity in families with hereditary multiple exostoses. *Am J Hum Gen*, 53:71-79, 1993. PMID: PMC1682231.
 - c. Daiger SP, Bowne SJ, Sullivan LS, **Blanton SH**, Weinstock GM, Koboldt DC, Fulton RS, Larsen D, Humphries P, Humphries MM, Pierce EA, Chen R, Li Y. Application of Next-Generation Sequencing to Identify Genes and Mutations Causing Autosomal Dominant Retinitis Pigmentosa (adRP). *Adv Exp Med Biol*, Mar 25;801:123-9, 2014. PMID: PMC4121110.
 - d. **Blanton SH**, Burt A, Garcia E, Mulliken JB, Stal S, Hecht JT. Ethnic Heterogeneity of IRF6 AP-2a Binding Site Promoter SNP Association With Nonsyndromic Cleft Lip and Palate. *Cleft Palate Craniofac J*, Nov;47(6):574-7, 2010. PMID: PMC3039881.

3. I have been studying different aspects of deafness for almost two decades. In addition to mapping novel genetic loci for Mendelian forms, I have contributed to the delineation of the heterogeneity, phenotype-genotype correlations, and population genetics, as well as social aspects of hearing loss.
 - a. **Blanton SH**, Nance WE, Norris VW, Welch KO, Burt A, Pandya A, Arnos KS. Fitness among individuals with early childhood deafness: studies in alumni families from Gallaudet University. *Ann Hum Genet*, Jan;74(1):27-33, 2010. PMID: PMC2804774.
 - b. Dodson KM, **Blanton SH**, Welch KO, Norris VW, Nuzzo RL, Wegelin JA, Marin RS, Nance WE, Pandya A, Arnos KS. Vestibular dysfunction in DFNB1 deafness. *Am J Med Genet A*, May;155(5):993-1000, 2011. PMID: PMC3080433.
 - c. Lasisi A, Bademci G, Foster J, **Blanton S**, Tekin M. Common Genes for Non-syndromic Deafness are uncommon in Sub Saharan Africa: A report from Nigeria. *Int J Pediatr Otorhinolaryngol*. 2014 Nov;78(11):1870-3. doi: 10.1016/j.ijporl.2014.08.014. PMID: PMC4208623 [Available on 2015-11-01].
 - d. Tekin D, Tutar E, Ozturkmen Akay H, **Blanton S**, Foster J 2nd, Tekin M. Comprehensive genetic testing can save lives in hereditary hearing loss. *Clin Genet*. 2014 Apr 2. doi: 10.1111/cge.12376. [Epub ahead of print], 2014. PMC Journal-In-Process.

Complete List of Published Work in MyBibliography:

<http://www.ncbi.nlm.nih.gov/sites/myncbi/susan.blanton.1/bibliography/43755049/public/?sort=date&direction=ascending>

D. Research Support

Most Relevant Research Support

7R01NS040807-09 (Sacco, Ralph)

10/01/09-06/30/17

NINDS

“Family Study of Stroke Risk and Carotid Atherosclerosis”

The purpose of this grant is to identify genetic determinants of quantitative cerebrovascular risk phenotypes.

Role: Co-investigator

1R01NS065114-05 (Tatjana Rundek, Susan Blanton)
extension)

07/01/10-06/30/16

(no-cost)

NIH-NINDS

“Novel factors for unexplained extreme phenotypes of subclinical atherosclerosis”

The purpose of this grant is to identify genes associated with extreme phenotypes of subclinical atherosclerosis.

Role: Principal Investigator

Ongoing Research Support

2 P50 DC000422-26 (Dubno, J) (Med Univ SC)

10/01/13–09/30/18

NIH/NIDCD

(Liu, X – subcontract Project 3)

“Experimental and Clinical Studies of Presbycusis –

Project 3: Identification of Susceptibility Genes for Age-Related Hearing Loss”

This proposal will investigate the genetic and molecular basis of human presbycusis.

Role: Co-Investigator on Project 3

1R01 DC012836-02 (Tekin, M)

03/01/13-02/28/18

NIH

“Genetic Studies of Inner Ear Anomalies”

The goals of the project are to identify new genes for deafness associated with inner ear anomalies and to establish a resource for research in inner ear anomalies including biological samples and clinical data from large numbers of affected families. Role: Co-Investigator

1R01DC012115-01A1-02 (Liu, X)

03/08/13 – 02/28/18

NIH

“Implementing Genomic Medicine in Clinical Care of Deaf Patients”

We will develop a comprehensive genetic testing platform and genomic deafness database for clinical care of deaf individuals to: 1) improve the clinical care of deaf and hard of hearing persons; and 2) determine the epidemiology of hereditary hearing loss in the United States. The successful completion of the proposed aims will significantly improve our ability to provide genetic counseling for affected patients/families and to expand our knowledge on the genomic basis of hereditary hearing.

Role: Co-Investigator

2R01EY007142-12A2 (Daiger) - UTHSC

09/15/08-

08/31/12

NIH-NEI

“DNA Linkage Studies of Degenerative Retinal Diseases”

The purpose of this grant is to identify the genes and mutations causing autosomal dominant retinitis pigmentosa.

Role: PI on subcontract

1 R01 DC009645-01A2-06 (Tekin, M)

06/01/10-05/31/16

(no-cost)

extension)

NIH

“A Collaborative Search for New Genes for Non-Syndromic Deafness”

The purpose of this grant is to identify new genes for deafness in inbred families from Turkey.

Role: Co-investigator

2R01DE011931-13 (Hecht, J; Blanton S) University of Texas

12/26/12-11/30/17

NIH-NIDCR

“Mapping nonsyndromic cleft lip and palate genetic loci”

Nonsyndromic cleft lip with or without cleft palate (NSCLP) is a common birth defect affecting 4000 newborns in the US and 135,000 worldwide each year. The etiology is poorly understood and currently, only 20% of the NSCLP genetic liability has been identified, limiting our ability to identify at-risk individuals or provide accurate

counseling for families. In these studies, we apply the newest technology to identify the genetic variation underlying NSCLP in families with multiple cases, will test the variants for expression and functionality in a fish model and develop ethnic-specific risks. The results of this study will ultimately be utilized to identify and test for potential at-risk genotypes.

Role: Principal Investigator

Completed Research Support (Last Three Years)

1U54NS0657-12-03 (Shy, ME)

09/01/09-08/31/14

NIH/RDCRC/WSU

"Inherited Neuropathies Consortium - Project 2: Inherited neuropathies; an integrated approach leading to therapy"

The proposed CMT consortium will deliver high quality clinical data and collect a large number of CMT families/patients; apply innovative study designs using the latest technology to tackle some of the most pressing genetic issues in CMT that will ultimately pave the way for new therapeutic approaches.

Role: Senior Statistical Geneticist and Epidemiologist

2 T15 HG000026-17 (Scott, WK)

03/01/10-11/30/14

NIH/NHGRI

"Genetic Analysis Methods for Medical Researchers"

In order to successfully move into the next phase of disease gene mapping, and thus attain one of the primary goals of the Human Genome Initiative, it is critical that physician scientists and laboratory scientists be educated with respect to pedigree ascertainment, sampling and basic gene localization experimental design along with the understanding of the plethora of analytic tools available.

Role: Co-course organizer.

(Dong, C)

07/01/11-06/30/13

James and Esther King Biomedical Research

"Gene-Smoking Interactions and Atherosclerosis"

Role: Collaborator

5R01NS047655-07 (Rundek) PI – University of Miami

01/01/04-03/31/13

"Genetic Determinants of Subclinical Carotid Disease"

The main goal of this research is to study the genetic polymorphisms associated with carotid IMT and distensibility in the three race/ethnic groups (whites, blacks and Hispanics) from the Northern Manhattan Study (NOMAS) cohort.

Role: Co-Investigator

1R56DE021862-01 (Hedges, D/Blanton, S)

09/27/11-08/31/12

NIH/NIDCR

"Multiprong Screening Strategy for Gene Discovery in Nonsyndromic Cleft Lip Palate"

Role: Co-Principal Investigator on Subcontract

5R01DE011931-13 (Hecht) PI – University of Texas

04/01/99-03/31/12

3R01DE011931-10S1 (Hecht) PI – University of Texas

09/22/09-08/31/11

NIH

"Mapping nonsyndromic cleft lip and palate genetic loci"

To map the genes for non-syndromic cleft lip/palate.

Role: PI on Subcontract

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: **Crocco, Elizabeth A.**

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

POSITION TITLE: Associate Clinical Professor of Psychiatry and Behavioral 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
Douglas College, Rutgers University, New Brunswick, NJ	B.A.	05/1989	Biology
Rutgers-Robert Wood Johnson Medical School, Piscataway, NJ	M.D.	05/1993	Medicine
Mount Sinai Medical Center, New York, NY	Residency	06/1997	General Psychiatry
Mount Sinai Medical Center, New York, NY	Admin.Chief Resident	06/1997	General Psychiatry
University of Miami/Jackson Memorial Hospital, Miami, FL	Fellowship/ Chief Fellow	06/1998	Geriatric Psychiatry

A. Personal Statement

I am currently the Director of the Memory Disorders Clinic (MDC) at the University Of Miami Miller School Of Medicine. I am Board-Certified in the sub-specialty of Geriatric Psychiatry. As the Director of the University of Miami Memory Disorder Clinic, I am an expert in conduct comprehensive memory disorder evaluations and other patient examinations and participate in multidisciplinary staffing conferences to determine patient diagnosis and treatment in neurodegenerative diseases as part of our Registry. I am a key educator on aging and aging issues for medical students, residents, and fellows at UM/Jackson Memorial Hospital as well as the South Florida Community. I am also involved in support, education and interventions to assist their caregivers. In the UM Center on Aging, I have collaborated on several successful caregiving intervention studies with Dr. Sara Czaja. I have had a significant role in both developing and testing novel neuropsychological and functional measures developed to detect Mild Cognitive Impairment (MCI) and preclinical MCI leading to Alzheimer's Dementia (AD).

1. **Crocco, EA**, Sabbag, S, Curiel, R. Bipolar Disorder in the Elderly, In: *The Bipolar Book: History, Neurobiology and Treatment*, A Yildiz, P Ruiz, CB Nemeroff, ed., Oxford University Press: NY, Chapter 40, 2015. ISBN: 978-0-199-30053-2
2. **Crocco, EA**, Eisdorfer, C. Research in Mental Health and Caregiving, In: *The Challenges of Mental Health and Caregiving*, RC Talley, GL Fricchion, BG Druss ed., Springer, NY, 205-221, 2014. ISBN: 978-1-4614-8791-3
3. Ownby, R.L., Hertzog, C., **Crocco, E.**, & Duara, R. (2006). Factors related to medication adherence in memory disorder clinic patients. *Aging and Mental Health*, 10(4), 378-385. PMID: PMC3543157.

4. **Crocco, EA**, Sabbag, S (in Press). Cholinesterase Inhibitors and Memantine, In: *Kaplan & Sadock's Comprehensive Textbook of Psychiatry, Tenth Edition*, BJ Sadock, VA Sadock, P Ruiz ed., Lippincott Williams & Wilkins: Philadelphia, PA

B. Positions and Honors

Positions and Employment

- 1998-2006 Clinical Director of Psychiatry, Wien Center for Memory Disorder, Mount Sinai Medical Center, Miami Beach, FL
- 1998-2015 Clinical Assistant Professor, Department of Psychiatry and Behavioral Sciences, University of Miami Miller School of Medicine, Miami, FL
- 2001- Director, Geriatric Psychiatry Training Program, Jackson Memorial Hospital, Department of Psychiatry and Behavioral Sciences, Miami, FL
- 2001-2006 Clinical Director of Consultation-Liaison Psychiatry, Mt. Sinai Medical Center, Miami Beach, FL
- 2000-2006 Medical Director, Mount Sinai Medical Center Geriatric Psychiatry Inpatient Unit, Miami, FL
- 2006- Medical Director, Geriatric Medical/Psychiatry Inpatient Unit, Jackson Memorial Hospital, Miami, FL
- 2010- Director, Memory Disorder Center, Department of Psychiatry and Behavioral Sciences, Miller School of Medicine at University of Miami, FL
- 2009- Division Chief, Geriatric Psychiatry, Department of Psychiatry and Behavioral Sciences, Miller School of Medicine at University of Miami, Miami, FL
- 2015- Associate Clinical Professor, Department of Psychiatry and Behavioral Sciences, University of Miami Miller School of Medicine, Miami, FL

Other Experience and Professional Memberships

- 1994-2009 Member, American Psychiatric Association
- 1998- Member, American Association of Geriatric Psychiatry
- 2003- Florida Psychiatric Society
- 2009-2014 Fellow, American Psychiatric Association
- 2013- Associate Member, Academy of Medical Educators, University of Miami Miller School of Medicine
- 2014- Distinguished Fellow, American Psychiatric Association
- 2014- Member, The American College of Psychiatrists
- 2014- Member, Gerontological Society of America
- 2014- Member, Anxiety and Depression Association of America

Honors

2007, 2008	Geriatric Psychiatry Training Program Teacher of the Year Award, JMH, Miami, FL
2010	University of Miami/Miller School of Medicine Faculty Citizenship Award, Miami, FL
2010	Nancy C.A. Roeske, M.D., Certificate of Recognition for Excellence in Medical Student Education, American Psychiatric Association
2011	Irma Bland Certificate of Excellence in Teaching Residents, American Psychiatric Association
2012	Geriatric Fellowship Excellence in Teaching Award, JMH, Miami, F

C. Contribution to Science

1. **Early detection of Alzheimer's disease and Mild Cognitive Impairment (MCI):** I have had a significant role in both developing and testing novel neuropsychological and functional measures developed to detect Mild Cognitive Impairment (MCI) and preclinical MCI leading to Alzheimer's Dementia (AD). The importance of early detection of AD is crucial to the current science in testing and developing disease-modifying treatment for this neurodegenerative disease. I have served as Co-PI on 1 NIA-funded grant previously (2003-2008) and am currently Co-PI on a current 5 year study predicting rates of cognitive decline in the elderly using these measures over 5 years in conjunction with other select diagnostic biomarkers and tests such as atrophy on structural Brain MRI, amyloid, tau and phosphorylated tau in CSF as well as ApoE4 genotype. I have worked closely with both Dr. David Loewenstein and Dr. Sara Czaja in this important field and have had several significant publications documenting this important work.
 - a. **Crocco, E.,** Curiel, R.E., Acevedo, A., Czaja, S.J., & Loewenstein, D.A. (2014). An evaluation of deficits in semantic cueing and proactive and retroactive interference as early features of Alzheimer's disease. *The American Journal of Geriatric Psychiatry*, 22(9), 889-897.
 - b. Curiel, R., **Crocco, E.,** Duara, R., Acevedo, A. & Loewenstein, D.A. (2013). A new scale for the evaluation of proactive and retroactive interference in Mild Cognitive Impairment and early Alzheimer's disease. *Journal of Aging Science*, <http://dx.doi.org/10.4172/jasc.1000102>.
 - c. Loewenstein, D.A., Acevedo, A., Small, B.J., Agron, J., **Crocco, E.,** & Duara, R. (2009). Stability of different subtypes of mild cognitive impairment among the elderly over a 2-to 3-year follow-up period. *Dementia and Geriatric Cognitive Disorders*, 27(5), 418-23. PMID: PMC2814021.
 - d. Loewenstein, D.A., Acevedo, A., Agron, J., Isaacson, R., Strauman, S., **Crocco, E.,** Barker, W., & Duara, R. (2006). Cognitive profiles in Alzheimer's disease and in mild cognitive impairment of different etiologies. *Dementia and Geriatric Cognitive Disorder*, 21(5-6), 309-315.
2. **Depression and Cognition:** The relationship between depression and cognitive impairment in the elderly is important but is not well delineated. The role of depression as risk factor, prodromal event, or symptom of dementia is not well understood. I have published several journal articles related to cognition and dementia in the elderly. This includes a widely cited meta-analysis and meta regression analysis relating early depression as a risk factor for Alzheimer's disease (AD). I have also published on the relationship of depression and other psychiatric symptoms in MCI and cognitive changes related to geriatric depression in general.

- a. Ownby, R.L., **Crocco, E.**, Acevedo, A., John, V., & Loewenstein, D. (2006). Depression and risk for Alzheimer's disease: systematic review, meta-analysis and meta-regression analysis. *The Archives of General Psychiatry*, 63(5), 530-538. PMID: PMC3530614.
- b. **Crocco, E.A.**, Castro, K., & Loewenstein, D. (2010). How late-life depression affects cognition: neural mechanisms. *Current Psychiatric Reports*, 12(1): 34-38.
- c. **Crocco, E.** & Loewenstein, D.A. (2005). Psychiatric aspects of mild cognitive impairment. *Current Psychiatric Reports*, 7(1), 32-36.
- d. Duara, R, Loewenstein, DA, Wright, C, **Crocco, E**, Varon, D. Mild Cognitive Impairment, In: *Neurology in Practice: Dementia*, J Quinn ed., Wiley-Blackwell Pub, UK, Chapter 6, 2014 ISBN: 978-0-470-67424-6

Complete List of Published Work in My Bibliography:

<http://www.ncbi.nlm.nih.gov/sites/myncbi/1Pg52WCUHj95C/bibliography/47914940/public/?sort=date&direction=ascending>

D. Research Support

Ongoing Research Support

XZ203 State of Florida Department of Elder Affairs Alzheimer's Disease Initiative/Memory Disorder Clinic Crocco(PI) 05/2010-Present
 The University of Miami Memory Disorders Clinic (MDC) is funded by an ongoing state of Florida Department of Elder Affairs contract. The role of the Principal Investigator in the clinic is to provide clinical and diagnostic services, research and training for individuals about Alzheimer's disease or related disorders, as well as to their caregivers.
 Role: Principal Investigator

1R01AG047649-01A1 Loewenstein (PI) 02/01/15-01/31/20
 National Institute on Aging
 Novel Detection of Cognitive and Functional Impairment in the Elderly
 The role of the Co-investigator is to examine the utility of a unique set of neuropsychological and daily functioning tests in individuals ranging from cognitively normal (NC) to those with preclinical mild cognitive impairment (preMCI) and those with amnesic mild cognitive impairment (aMCI), in combination with select diagnostic biomarkers and tests such as atrophy on structural MRI, amyloid, tau and phosphorylated tau biomarkers in CSF and in predicting rate of cognitive decline.
 Role: Co-Investigator

1 R01 AG047146-03 Devanand (PI) 2015-2018
 National Institute on Aging
 Treatment of Psychosis and Agitation in Alzheimer's Disease (Lithium Study)
 I am a Co PI with a subcontract involved in the recruitment of patients in this study examining the effects of lithium on psychosis and agitation in Alzheimer's disease.
 Role: Co-Investigator

Otsuka Pharmaceutical Development & Commercialization, Inc. (OPDC) Protocol 331-12-283
 Crocco (PI) 2014-
 A Phase 3, 12-week, Multicenter, Randomized, Double-blind, Placebo-controlled Trial to Evaluate the Efficacy, Safety, and Tolerability of 3 Fixed Doses of Brexpiprazole (OPC-34712) in the Treatment of Subjects with Agitation

Associated with Dementia of the Alzheimer's Type.

Otsuka Pharmaceutical Development & Commercialization, Inc. (OPDC) Protocol 331-13-211

Crocco (PI) 2014-

A 2-month, Observational, Rollover Trial to Evaluate the Safety of Subjects with Agitation Associated with Dementia of the Alzheimer's Type who were Previously Treated with Brexpiprazole (OPC-34712) or Placebo in a Phase 3, Double-blind Trial.

UB4HP19066

Olsen (PI)

07/01/10-06/30/15

Health Services Research Administration (HRSA) Miami Area Geriatric Education Center (MAGEC)

The Miami Area Geriatric Education Center (MAGEC) is a Consortium of organizations that work together to coordinate and provide interdisciplinary continuing education for professionals who serve the elderly in the southeast and central areas of Florida. The role of the faculty member is to contribute to the planning and development of educational programs to health care professionals who provide services to older adults in a variety of settings.

Role: Funded Educator/Faculty Member

BIOGRAPHICAL SKETCH

NAME Sara J. Czaja, Ph.D.		POSITION TITLE Professor	
eRA COMMONS USER NAME (credential, e.g., agency login) sczaja			
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
State University of NY College at Buffalo, NY	B.S.	1975	Psychology
State University of NY at Buffalo, NY	M.S.	1976	Industrial Engineering
State University of NY at Buffalo, NY	Ph.D.	1980	Human Factors/Industrial Engineering

A. Personal Statement

Overall, I am well recognized for my expertise in aging and behavioral intervention research. Specifically I have extensive experience in interventions aimed at diverse populations of family caregivers of patients with AD as well as older adults of varying levels of cognitive and functional status. I served at these PI for the Miami site of the Resources for Enhancing Alzheimer's Caregivers Health (REACH II) program; the PI of the REACH Community Program and the VideoCare projects. Each of these projects were concerned with developing and delivering interventions to family caregivers of older adults. I am currently the PI of an NIH funded study (Caring for the Caregiver Network), which is evaluating an technology-based psychosocial interventions for diverse family caregivers of AD patients. I am also serving on an Institute of Medicine (IOM) Committee that is focusing on family caregivers of older adults and recently I served on an IOM Committee concerned with cognitive aging. I am also the PI of a project which is evaluating a functional skills training program, using computer-based simulations of everyday tasks developed at the UM Center on Aging, with Schizophrenia patients and non-impaired older adults. In addition, I have vast expertise with technology-based interventions and with the implementation of these interventions with diverse older adult populations including the oldest old. A particular focus of our work at the Center on Aging at the University of Miami Miller School of Medicine of which I am the Scientific Director, has been on aging and cognition and on strategies to enhance the functional performance of older people. Our approach to interventions is based on a person-centered design approach, which is commensurate with my background in Industrial Engineering. I am also the Director of the NIH, multi-site Center for Research on Aging and Technology Enhancement (CREATE). CREATE has been funded for the past 16 years and focuses on the interaction of older adults with technology systems in living, work and healthcare settings. We recently completed a cross-site trial, The PRISM Trial, which evaluated the efficacy of a software application in enhancing the well-being and social connectivity of older adults (aged 65+) who live alone in the community and were at risk for social isolation. I have received extensive funding from the NIH in these areas and am also well published (examples provided below in the description of my scientific contributions).

B. Positions and Honors

- 1980-1982 Senior Research Associate, Buffalo Organization for Social and Technological Innovation, Inc
- 1984-1988 Assistant Professor, Department of Industrial Engineering, SUNY at Buffalo
- 1988-1991 Associate Professor, Tenured, Department of Industrial Engineering, SUNY at Buffalo
- 1989-1990 Research Associate, Professor, Department of Industrial Engineering, University of Miami

1988-1993 Research Director, Stein Gerontological Institute, Miami, FL
1991-1994 Associate Professor, Department of Industrial Engineering, University of Miami
1993-1999 Director, Center on Human Factors & Aging Research, University of Miami School of Medicine
1994-present Professor, Dept. of Psychiatry and Behavioral Sciences, University of Miami School of Medicine
1994-present Professor, Department of Industrial Engineering, University of Miami, Coral Gables, FL
1999-present Director, Center on Aging and Technology Research, University of Miami School of Medicine
2002-present Co-Director, Center on Aging, University of Miami, Miami, FL
2010-present Scientific Director, Center on Aging, University of Miami Miller School of Medicine

Other Experience and Professional Memberships

Member, IOM Committee on Family Caregiving for Older Adults, Oct 2014-April 2016

Member, Advisory Board for Rehabilitation Engineering Research Center TechSAge, Georgia Tech 2014 –

Member, IOM Committee on Public Health Dimensions of Cognitive Aging, 2014 –present

Ad Hoc Reviewer, NIH Risk Prevention & Health Behavior Study Section, 2014-present

Ad Hoc Reviewer, NIH Health Disparities Study Section, 2014-present

Member, External Advisory Committee for the Center for Accessibility and Safety for an Aging Population. FSU, FAMU, UNF, December 2013

Reviewer, NIA Division of Behavioral and Social Research Quadrennial Review, September 2013

Reviewer, Veteran's Administration Panel for the Under Secretary's Award for Outstanding Achievement in Health Services Research, September 2014-present

Chair, Fellows Selection Committee, Human Factors and Ergonomics Society (HFES) October 2013 -present

President, Division 20 (Division of Adult Development and Aging), American Psychological Association, 2013-2016

Member, Fellows Selection Committee, Human Factors and Ergonomics Society, 2013-present

Member, Board on Human-Systems Integration, National Research Council/National Academy of Sciences, November 2010 – present.

Honors

M. Powell Lawton Distinguished Contribution Award for Applied Gerontology, August 2015

Panel Member, Nobel Prize Week Dialogue, Stockholm Sweden, December 2014

Jack A. Kraft Award for Innovation, Human Factors and Ergonomics Society, 2013

Social Impact Award for the Association of Computing Machinery (ACM), Special Interest Group for Human Computer Interaction (SIGCHI), 2013

The Scottish Informatics & Computer Science Alliance Distinguished Visiting Professor, School of Computing, University of Dundee, March, 2010.

IBM, University Cooperative Research Award, 2007-2009.

IBM Faculty Award, 2006

Provost's Scholarly Activity Award, 1998.

Researcher of the Year, College of Engineering, University of Miami, 1995.

C. Contribution to Science

1. A key area of my research has been on issues surrounding family caregiving. I have a very active research portfolio and publication record in the area of family caregiving for the past several decades. My work has focused on diverse family caregiver populations for a broad range of patient populations including patients with dementia, spinal cord injury, cancer, chronic fatigue syndrome and LGBT elders. This work has been funded by the National Institutes of Health, the Administration on Aging, the Retirement Research and Langeloth Foundations, Johnson & Johnson, AT&T, Cisco and the Community Alliance Against Aids.

In terms of specifics, I served as the PI for the Miami site for the Resources to Enhance Caregiver Health (REACH) project and as the Co-PI on a study examining caregiving issues for family caregivers of Spinal Cord Injured Patients. I am currently the PI of a study that is evaluating efficacy of a technology-based culturally tailored psychosocial intervention for minority family caregivers and Co-PI on a project that is examining partners of patients with chronic fatigue syndrome. The NIH has provided support for all of these projects. I completed a project that examined issues confronted by working caregivers and a demonstration project, funded by the Administration on Aging, that involved collaboration with a community agency to translate the evidenced-based REACH II intervention in community settings. A unique feature of my work in the area of caregiving has been on the examination of the use of technology to deliver programs and services to family caregivers in diverse contexts. Examples of relevant publications include:

Czaja, S.J., Sabbag, S., Lee, C.C., Schulz, R., Lang, S., Vlahovic, T., Jaret, A.J., Thurston, C. (2015). "Concerns about aging and caregiving among middle-aged and older Lesbian and Gay Adults". *Aging & Mental Health*, doi:10.1080/13607863.2015.1072795.

Czaja, S.J., Loewenstein, D., Schulz, R., Nair, S.N., Perdomo, D. (2013) A Videophone Psychosocial Intervention for Dementia Caregivers. *Nov*; 21(11):1071-81. doi: 10.1016/j.jagp.2013.02.019. E pub 2013 Jul 3. *Am J of Geriatric Psychiatry*.

Czaja, S.J., Gitlin, L.N., Schulz, R., Zhang, S., Burgio, D., Stevens, A.B., Nichols, L.O., Gallagher-Thompson, D. (2009) Development of the Risk Appraisal Measure (RAM): A Brief Screen to Identify Risk Areas and Guide Interventions for Dementia Caregivers. *J AM Geriatr Soc* 57:1064-1072.

Czaja, S.J. (contributing author) (2006). Enhancing the Quality of Life of Hispanic/Latino, Black/African American, and White/Caucasian Dementia Caregivers: The REACH II Randomized Controlled Trial REACH II Investigators. *Annals of Internal Medicine*, 145, 727-738.

Belle, S. H., Zhang, S., Czaja, S.J., Burns, R., & Schulz, R. (2004). Cognitive enhancement medication utilization among persons with Alzheimer's disease who have a family caregiver: Findings from the Resources for Enhancing Alzheimer's Caregiver Health (REACH) project. *American Journal of Geriatric Psychiatry*, 12, 250-257.

Eisdorfer, C. E., Czaja, S. J., Loewenstein, D. L., Rubert, M. P., Arguelles, S., Mitrani, V., & Szapocznik, J. (2003). The effect of a family therapy and technology-based intervention on caregiver depression. *The Gerontologist*, 43 (4) 521-531.

2. A second key area is related to cognition and functional assessment in diverse older populations. A central focus of this work is on understanding the implications of normative age-related changes in cognition for everyday functioning and the performance of everyday tasks. An additional focus is on understanding how conditions such as mild cognitive impairment or persistent mental illnesses such as schizophrenia impact on cognition and everyday functioning. In addition we are examining the efficacy of cognitive remediation strategies in improving functional performance. I currently am the PI (Dr. Philip Harvey and Dr. David Loewenstein are Co-PIs) of a grant from the National Institute on Aging that is focusing on these issues with older adults with Schizophrenia (Czaja, S.J., Harvey, P., Loewenstein, D., PI's 1R21AG041740-01, NIH/NIA,

Title: "Improving the Functional Outcomes in Older Adults with Schizophrenia".) Some relevant publications in this area include:

Crocco, E., Curiel, R.E., Acevedo, A., **Czaja, S.J.**, Loewenstein, D.A. (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*, Vol. 22, Issue 9, pg. 889-897, September.

Harvey, P.D., Stone, L., Loewenstein, D., **Czaja, S.J.**, Heaton, R.K., Twamley, E.W., Patterson, T.L. (2013) The convergence between self-reports and observer ratings of financial skills and direct assessments of financial capabilities in patients with schizophrenia: More detail is not always better. *Schizophrenia Research* 147 (2013) 86-90.

Harvey, Phillip D., Loewenstein, D., **Czaja, S.J.** (2013) Hospitalization and Psychosis: Influences on the Course of Cognition and Everyday Functioning in People with Schizophrenia. *Neurobiology of Disease* 53 (2013) 18-25.

Czaja S. J. & Loewenstein, D. (2013) Cognition and Functional Status in Adult and Older Patients with Schizophrenia. In P.D. Harvey (Ed.). *Cognitive Impairment in Schizophrenia*. London: Cambridge University Press (pp. 110-125).

3. A third key area of my contribution relevant to this application is in behavioral intervention research. Most notably, in the use of technology to deliver interventions to diverse populations of older adults and family caregivers. I have also received extensive NIH funding and funding from foundations such as the Retirement Research Foundation and the Langeloth Foundation for this work and am widely published in this area. For example, I am currently the Principal Investigator of a study funded by the National Institute of Nursing Research (NINR) that is examining the efficacy of an evidenced-based caregiver intervention delivered via technology for minority caregivers of patients with dementia (1R01NR014434-01, Czaja, S.J., PI NINR/NIH A Tailored Technology Intervention for Diverse Family Caregivers of AD Patients".) As noted, in my personal statement, I also recently served as PI for an NIH funded (as part of CREATE) multi-site randomized clinical trial that examined the efficacy of a software application in enhancing the well-being and social connectivity of older adults (aged 65+) who live alone in the community and were at risk for social isolation (The PRISM TRIAL). Examples of relevant publications in this area include:

Czaja, S. J., Zarcadoolas, C., Vaughn, W., Lee, C. C., Rockoff, M., & Levy, J. (2015). The Usability of Electronic Personal Health Record System for an underserved Adult Population. *Human Factors*. Vol. 57, No. 3, pp. 491-506, DOI: 10.1177/0018720814549238 May.

Czaja, S. J., Boot, W. R., Charness, N., Rogers, W. A., Sharit, J., Fisk, A. D., Lee, C. C., & Nair, S. N. (2014). The Personalized Reminder Information and Social Management System (PRISM) Trials: Rationale, Methods, and Baseline Characteristics. *Contemporary Clinical Trials* 40 (2015) 35-46. November.

Taha, J., **Czaja, S.J.**, Sharit, J., Morrow, D.G. (2013) Factors Affecting Usage of a Personal Health Record (PHR) to Manage Health. *Psychology and Aging*, Vol. 28, No.4, 1124-1139.

D. Research Support

Ongoing research

Czaja, S. J., PI

7/1/15-3/30/20

NIA/NIH

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

This application is a request for continued support for the Center for Research and Education on Aging and Technology Enhancement (CREATE), an established multidisciplinary, cohesive Center that focuses on aging and technology. CREATE's goal is to ensure that older adults are able to use and realize the benefits of technology. Our objectives are to: develop a database on user preferences, needs, and problems with emerging and existing systems; assess the efficacy of design solutions; gather information on the value of technology; promote new research; support new investigators; and disseminate outcomes to a broad community.

1R01AG047649-01A1

2/1/2015-1/31/2020

Loewenstein, David, PI

Czaja, S.J., Co-Investigator

NIH

"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. We will examine performance on these novel measures with changes in brain MRI volumes over time as well as associations with amyloid, tau, and phosphorylated tau biomarker levels in the CSF.

Loewenstein, David, PI

1/1/15 - 6/30/15

Czaja, S.J., Co-Investigator

Grant #: 5AZ02

NIH

"A Consortium to Study Novel Markers of Early Alzheimer's Disease"

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. We will examine performance on these novel measures with changes in brain MRI volumes over time as well as associations with amyloid, tau, and phosphorylated tau biomarker levels in the CSF.

UM DBA 2015-13 (Czaja, S.J.)

9/1/14-8/31/15

Dean NIH Bridge Funding

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

This application is a request for continued support for the Center for Research and Education on Aging and Technology Enhancement (CREATE), an established multidisciplinary, cohesive Center that focuses on aging and technology. CREATE's goal is to ensure that older adults are able to use and realize the benefits of technology. Our objectives are to: develop a database on user preferences, needs, and problems with emerging and existing systems; assess the efficacy of design solutions; gather information on the value of technology; promote new research; support new investigators; and disseminate outcomes to a broad community.

1R01NR014434-01 (Czaja, S.J.)

4/1/13-3/31/18

NINR/NIH

Title: A Tailored Technology Intervention for Diverse Family Caregivers of AD Patients”.

The aims of this project are to evaluate the acceptability and efficacy of a culturally tailored technology-based psychosocial intervention for reducing the stress and burden and enhancing quality of life of diverse family caregivers of AD patients. The intervention is designed to address known areas of caregiver risk and to foster the ability of caregivers to leverage the type of supports they need for themselves and the AD patient. The target population is Black/African American, Hispanic, and White non-Hispanic family caregivers of AD patients.

1R21AG041740-01

04/01/12 – 03/31/15

Principal Investigators Sara J. Czaja, Phillip Harvey, David Loewenstein

NIH/NIA

Title: “Improving the Functional Outcomes in Older Adults with Schizophrenia”

This developmental project examines the feasibility and efficacy of using a technology-based approach that combines a customized cognitive enhancement intervention, cognitive assessment, and measurement of FC. The study will involve a randomized clinical trial. Eighty older patients with schizophrenia will be randomized in equal numbers to a customized cognitive remediation intervention or to a video games control condition used in previous studies.

Czaja, Sara J., PI

12/1/2013 – 11/30/2014

Wallace H. Coulter Foundation

Title: The Development and Validation of Computer Based Cognitive Assessment and Functional Skills Training Package

The overall goal of our project is to develop a commercially available technology-based functional skills training and assessment package.

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 Laboratories (CVDRL), University of Miami Miller School of Medicine under mentorship of Dr. Miguel A. Perez-Pinzon. Since joining CVDRL I have participated in several projects studying different aspects of cerebral ischemia which resulted in over 30 peer-reviewed publications. 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. In this collaborative project, with Dr. Perez-Pinzon and colleagues, we propose to determine importance of metabolic signaling pathways involved in protection of neurons and glia following cerebral ischemia. The following qualifications makes me well-suited as a collaborator on this grant: (1) Experience of my laboratory on models of cerebral ischemia. (2) Track record on studies of mitochondria, PKC ϵ and ischemia protection. And (3) Presently we have ongoing collaboration between Dr. Perez-Pinzon (PI on this application). Based on my past training and experience in the field of cerebral ischemia and neuroprotection, I believe that I am uniquely qualified to participate in this project and I also trust that I will be able complete my part in this project with utmost competence.

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.

C. Contribution to Science

1. Mitochondria play an important role in neurodegeneration in acute (e.g. cerebral ischemia) and chronic (e.g. Amyotrophic lateral sclerosis) neurodegenerative conditions. Besides, mitochondria also play an important role in neuroprotection. While working in Dr. Perez-Pinzon's laboratory, I participated in studies aimed to determine contribution of mitochondrial dysfunction in brain damage following cerebral ischemia and in a mouse model of amyotrophic lateral sclerosis. We characterized and identified potential mechanisms of mitochondrial dysfunction in above mentioned conditions. I also participated in studies aimed to determine mechanisms by which mitochondria contributes to ischemia tolerance in the brain.
 - a. 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*. 2011;6(7):e22057.
 - b. 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.
 - c. 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.
 - d. 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.
 - e. Dave K.R., Saul I., Busto R., Ginsberg M. D., Sick T. J., Perez-Pinzon M. A. Mitochondrial function following global cerebral ischemia in rat hippocampus. *Journal of Cerebral Blood Flow and Metabolism*, 21:1401-1410, 2001.
2. 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)

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. In collaboration with Dr. Perez-Pinzon, I participated in projects aimed to determine the mechanism of neuronal death following cardiac arrest-induced cerebral ischemia.
- 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.
 - 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.
 - 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.
 - 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.
 - Dave K.R., Raval A. P., Prado R., Katz L. M., Sick T. J., Ginsberg M. D., Busto R., Perez-Pinzon M. A. Mild cardiopulmonary arrest promotes synaptic dysfunction in rat hippocampus. *Brain Res.* 1024:89-96, 2004.

Complete List of Published Work in PubMed:

http://www.ncbi.nlm.nih.gov/sites/entrez?orig_db=PubMed&db=pubmed&cmd=Search&term=%22Dave%20KR%22

D. Research Support

1R01NS073779

Dr. Dave, P.I.

3/1/2012 – 12/31/2016

NIH/NINDS

Increased cerebral ischemic injury by repeated hypoglycemic episodes in diabetes.

The major goal of this project is to determine the mechanism by which repeated hypoglycemic episodes increases cerebral ischemic injury in diabetics.

Role: Principal Investigator

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 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

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: **Chuanhui Dong**

eRA COMMONS USER NAME (credential, e.g., agency login): CHDONG07

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
Tongji Medical University, Wuhan, China	M.D.	07/1984	Preventive Medicine
Hubei Medical University, Wuhan, China	M.A.	06/1989	Epidemiology
Shanghai Medical University, Shanghai, China	Ph.D.	07/1998	Molecular Epidemiology
Karolinska Institute, Stockholm, Sweden	Post-Doc	12/2000	Genetic Epidemiology
University of Pennsylvania, Philadelphia	Post-Doc	10/2003	Statistical Genetics

A. Personal Statement

I am a biostatistician and research associate professor in the Department of Neurology at the University of Miami. Over 10 years, my research interest has been focused on investigation of independent and interactive effects of social-demographic, environmental, behavioral, metabolic and genetic factors on the risk of complex diseases such as cognition impairment, depression, subclinical and clinical cardiovascular diseases, and efficacy of drug treatment in animal models and clinical trials. With the successful collaboration with many researchers, I have published over 100 peer-reviewed research articles. The research work in Evelyn F. McKnight Brain Institute aligns well with my extensive research experience in population-based, clinical and animal studies and my intensive training in biostatistics and epidemiology. I will direct and perform the data analyses as needed.

1. **Dong C**, Beecham A, Slifer S, Wang L, Blanton SH, Wright CB, Rundek T, and Sacco RL (2010). Genomewide linkage and peakwide association analyses of carotid plaque in Caribbean Hispanics. *Stroke* 41, 2750-2756.
2. **Dong C**, Rundek T, Wright CB, Anwar Z, Elkind MS, and Sacco RL (2012). Ideal cardiovascular health predicts lower risks of myocardial infarction, stroke, and vascular death across whites, blacks, and hispanics: the northern Manhattan study. *Circulation* 125, 2975-2984.
3. Wright CB, **Dong C**, Stark M, Silverberg S, Rundek T, Elkind MS, Sacco RL, Mendez A, and Wolf M (2014). Plasma FGF23 and the risk of stroke: the Northern Manhattan Study (NOMAS). *Neurology* 82, 1700-1706.
4. **Dong C**, Zadeh N, Caunca MR, Cheung Y, Rundek T, Elkind MSV, DeCarli C, Sacco RL, Stern Y, Wright CB (2015). Cognitive correlates of white matter lesion load and brain atrophy: The Northern Manhattan Study. *Neurology* 85(5):441-9.

B. Positions and Honors

Positions and Employment

1998-2000 Research Fellow, Epidemiology, Dept. of Biosciences, Karolinska Institute, Stockholm, Sweden
2001-2003 Postdoctoral Researcher, Statistical Genetics, Dept. of Psychiatry, University of Pennsylvania, PA
2003-2006 Research Associate, Statistical Genetics, Dept. of Psychiatry, University of Pennsylvania, PA
2006-2007 Research Biostatistician, Clinical Research, American College of Radiology, PA
2007-2009 Research Assistant Professor, Dept. of Psychiatry & Behavioral Sci., University of Miami, FL
2009-2014 Research Assistant Professor, Dept. of Neurology, University of Miami, FL
2014- Research Associate Professor, Dept. of Neurology, University of Miami, FL

Professional Memberships

2012- Member, American Heart Association
2002- Member, American Association of Human Genetics
2008- Member, International Genetic Epidemiology Society
2008- Member, American Statistical Association
2002-2006 Member, International Epidemiological Association

C. Contribution to Science

1. In the collaboration with clinicians, one of my major research activities was to evaluate the cognitive correlates in population-base cohort. As a statistician, I served as the analyst in several projects.
 - a. Glazer, H., **Dong, C.**, Yoshita, M., Rundek, T., Elkind, M.S.V., Sacco, R.L., DeCarli, C., Stern, Y., Wright, C.B. (2015) Subclinical cerebrovascular disease inversely associates with learning ability: The NOMAS Study. *Neurology* 84(23):2362-2367
 - b. Wright, C.B., Gardener, H., **Dong, C.**, Yoshita, M., DeCarli, C., Sacco, R.L., Stern, Y., Elkind, M.S.V. (2015). Infectious Burden and Cognitive Decline in the Northern Manhattan Study. *Journal of the American Geriatrics Society* 63(8):1540-5
 - c. Levin, B.E., Llabre, M.M., **Dong, C.**, Elkind, M.S., Stern, Y., Rundek, T., Sacco, R.L., and Wright, C.B. (2014). Modeling metabolic syndrome and its association with cognition: the northern Manhattan study. *Journal of the International Neuropsychological Society* 20, 951-960.
 - d. Ramos, A.R., **Dong, C.**, Elkind, M.S., Boden-Albala, B., Sacco, R.L., Rundek, T., and Wright, C.B. (2013). Association between sleep duration and the mini-mental score: the Northern Manhattan study. *Journal of Clinical Sleep Medicine* 9, 669-673.

2. As a collaborator, I served as the statistician to evaluate the response of various medications in clinical studies and examined the factors influencing response of treatments.
 - a. Wong ML, **Dong C**, Flores DL, Ehrhart-Bornstein M, Bornstein S, Arcos-Burgos M, and Licinio J (2014). Clinical Outcomes and Genome-Wide Association for a Brain Methylation Site in an Antidepressant Pharmacogenetics Study in Mexican Americans. *The American Journal of Psychiatry* 171, 1297-1309. PMID: 25220861
 - b. Waldrop-Valverde, D, **Dong C**, and Ownby RL (2013). Medication-taking self-efficacy and medication adherence among HIV-infected cocaine users. *The Journal of the Association of Nurses in AIDS Care* 24, 198-206.

- c. Yavagal DR, Lin B, Raval AP, Garza PS, **Dong C**, Zhao W, Rangel EB, McNiece I, Rundek T, Sacco RL, et al. (2014). Efficacy and dose-dependent safety of intra-arterial delivery of mesenchymal stem cells in a rodent stroke model. *PloS One* 9, e93735.
 - d. **Dong C**, Wong ML, Licinio J (2009). Sequence variations of ABCB1, SLC6A2, SLC6A3, SLC6A4, CREB1, CRHR1 and NTRK2: association with major depression and antidepressant response in Mexican-Americans. *Mol Psychiatry*, 14(12):1105-1118. PMID: 19844206
3. In population-based and clinical studies, I took a lead in many data analyses to identify the factors influencing the subclinical and clinical outcomes.
- a. Nirav S, **Dong C**, Elkind MS, Sacco RL, Mendez A, Barry H, Silverberg S, Wolf M, Rundek T, and Wright CB, (2015). Fibroblast Growth Factor 23 is associated with Carotid Plaque Presence and Area: the Northern Manhattan Study. *Arteriosclerosis, Thrombosis, and Vascular Biology* 35(9):2048-53
 - b. **Dong C**, Della-Morte D, Beecham A, Wang L, Cabral D, Blanton SH, Sacco RL, Rundek T (2015) Genetic variants in LEKR1 and GALNT10 modulate sex-difference in carotid intima-media thickness: A genome-wide interaction study. *Atherosclerosis* 240:462-7
 - c. Dhamoon MS, **Dong C**, Elkind MS, Sacco RL (2015). Ideal cardiovascular health predicts functional status independently of vascular events: The northern manhattan study. *Journal of the American Heart Association* 4(2), e001322
 - d. Xu WH, **Dong C**, Rundek T, Elkind MS, and Sacco RL (2014). Serum albumin levels are associated with cardioembolic and cryptogenic ischemic strokes: Northern Manhattan Study. *Stroke* 45, 973-978.

Complete List of Published Work in MyBibliography:

<http://www.ncbi.nlm.nih.gov/sites/myncbi/1piUox9klssQ2/bibliography/42015963/public/?sort=date&direction=ascending>.

D. Research Support

Ongoing Research Support

- | | |
|---|-------------|
| R01MD009164, Olveen Carrasquillo (PI)
Hispanic Secondary Stroke Prevention Initiative (HISSPI)
To examine the effectiveness of a combined multilevel intervention consisting of Community Health Workers and mobile based phone technologies in lowering of systolic blood pressure which is the most important risk factor for recurrent stroke.
Role: Statistician | 07/14-03/19 |
| 14BFSC17690000 Ralph Sacco (PI)
American Heart Association/ASA-Bugher Foundation
To evaluate the effects of a Combined Aerobic and Resistance Exercise Training (CARET) program, a Cognitive Training Intervention (CTI), and the combination of the CARET and CTI interventions on cognitive performance in stroke patients.
Role: Co-investigator/Statistician | 04/14-03/18 |
| 1U54NS081763, Ralph Sacco (PI) | 01/13-12/17 |

Hispanic stroke prevention intervention research program
To create the Florida Puerto Rico Stroke Registry to identify and reduce stroke disparities in acute stroke and secondary prevention.
Role: Co-investigator/Statistician

R01 HL108623-01A1 Clinton Wright (PI) 03/12-02/16
FGF-23 and the Risk of Stroke and Cognitive Decline
To examine the relationship between FGF-23 and the risk of stroke and cognitive decline.
Role: Co-investigator/Statistician

R37 NS 029993 Ralph Sacco (PI) 02/03-03/15
Stroke Incidence and Risk Factors in a Tri-Ethnic Region
To determine the effects of risk factors for stroke, MI, and vascular death in a prospective cohort study of 3 race-ethnic groups from Northern Manhattan.
Role: Statistician

NATL MULTIPLE SCLEROSIS SOCIETY, Melissa Ortega (PI) 12/12-11/15
(Fast-Forward) A Randomized Double-Blind Placebo-Controlled Study of Caprylic Triglyceride for Cognitive Impairment in Subjects with Multiple Sclerosis
To determine the efficacy of Caprylic Triglyceride for Cognitive Impairment in Subjects with Multiple Sclerosis
Role: Biostatistician

R01NS065114 Tatjana Rundek (PI) 07/10-06/15
Novel factors for unexplained phenotypes of subclinical carotid atherosclerosis
To identify genetic variants influencing unexplained phenotypes of subclinical carotid atherosclerosis.
Role: Co-investigator/Statistician

Completed Research Support (within the last three years):

2KN01, Florida JEK Program, Chuanhui Dong (PI) 07/11-06/14
Gene-smoking interactions and atherosclerosis
To identify genetic moderators in the association between smoking and atherosclerosis.
Role: PI/Statistician

2KN09, Florida JEK Program, Dileep Yavagal (PI) 07/11-06/14
Intra-arterial mesenchymal stem cell delivery in a canine model of acute ischemic stroke
To evaluate safety sub-acute endovascular intra-carotid administration of MSCs in a canine stroke model.
Role: Co-investigator/Statistician

1U01NS069208 Kittner Steven(PI) 07/10-06/14
NINDS Ischemic Stroke Genetics Consortium
To assemble ischemic stroke phenotypic data and DNA samples from 11 stroke studies.
Role: Statistician

1K02NS059729-01A1 Clinton Wright (PI) 09/08-08/13
Vascular Risk and Cognition in a Multi-ethnic Cohort
To examine vascular risk factors for cognitive dysfunction in a stroke-free multi-ethnic sample.
Role: Statistician

The Miami CTSI, CTSI-2013-P02, Dileep Yavagal (PI) 01/13-12/13
Time Window of Intracarotid Mesenchymal Stem Cell Therapy in a Large Animal Model of Stroke
To determine the time window of intracarotid mesenchymal stem cell therapy in animal model of stroke.

Role: Co-investigator/Biostatistician

2R01NS040807

Ralph Sacco (PI)

09/09-08/13

Family study of stroke risk and carotid atherosclerosis

To investigate genes influencing carotid atherosclerosis through linkage and association studies.

Role: Statistician

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: **Assistant 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, Assistant 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. She has been conducting research on risk factors for clinical and subclinical vascular outcomes in the Northern Manhattan Study for over eight years. She is particularly interested in dietary behavior and other modifiable vascular risk factors in relation to vascular events, carotid disease, and age-related changes in brain structure and cognitive decline. 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:

2009-present 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 recent finding of a role for infectious burden in executive function as well as memory decline over time.

1. 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.
2. Del Brutto OH, Mera RM, Del Brutto VJ, Maestre GE, **Gardener H**, Zambrano M, Wright C. Influence of depression, anxiety and stress on cognitive performance in community-dwelling elders living in rural Ecuador. Results of the Atahualpa Project. *Geriatr Gerontol Int*. 2015;15(4):508-514.
3. Del Brutto OH, **Gardener H**, Del Brutto VJ, Maestre GE, Zambrano M, Montenegro JE, Wright CB. Edentulism Associates with Worse Cognitive Performance in Community-Dwelling Elders in Rural Ecuador: Results of the Atahualpa Project. *J Community Health*. 2014;39(6):1097-1100.
4. **Gardener H**, Wright CB, Rundek T, Sacco RL. Brain health and shared risk factors for dementia and stroke. *Nat Rev Neurol*. 2015;11(11):651-657.

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.

1. 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.
2. 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.
3. Modir R, **Gardener H**, Wright C. Blood pressure and white matter hyperintensity volume – a review of the relationship and implications for stroke prediction and prevention. *European Neurological Review*, 2012;7(3):174–7.
4. **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.

5. Marcus J, **Gardener H***, Rundek T, Elkind MSV, Sacco RL, DeCarli C, Wright CB. Baseline and longitudinal increases in diastolic blood pressure are associated with greater white matter hyperintensity volume: The Northern Manhattan Study. *Stroke*. 2011;42(9):2639-2641.

C.3. Epidemiology of stroke. Over the past 8 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. Specifically, I have published on the role coffee and tea, soft drinks, sodium, and egg consumption as well as adherence to a Mediterranean-style diet in relation to risk of stroke, cardiovascular disease, and vascular death. 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. Romano JG, Smith EE, Liang L, **Gardener H**, Camp S, Shuey L, Cook A, Campo-Bustillo I, Khatri P, Bhatt DL, Fonarow GC, Sacco RL, Schwamm LH. Outcomes in mild acute ischemic stroke treated with intravenous thrombolysis: a retrospective analysis of the Get With the Guidelines-Stroke registry. *JAMA Neurol*. 2015;72(4):423-431.
3. Global Burden of Metabolic Risk Factors for Chronic Diseases Collaboration (BMI Mediated Effects), Lu Y, Hajifathalian K, Ezzati M, Woodward M, Rimm EB, Danaei G. Metabolic mediators of the effects of body-mass index, overweight, and obesity on coronary heart disease and stroke: a pooled analysis of 97 prospective cohorts with 1.8 million participants. *Lancet*. 2014;383(9921):970-983.
4. **Gardener H**, Rundek T, Wright CB, Elkind MSV, Sacco RL. Coffee and tea consumption are inversely associated with mortality. *J Nutr*. 2013;143(8):1299-1308.
5. **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.
6. **Gardener H**, Rundek T, Wright CB, Elkind MSV, Sacco RL. Dietary sodium and risk of stroke in the Northern Manhattan Study. *Stroke*. 2012;43(5):1200-1205.
7. **Gardener H**, Rundek T, Markert M, Wright CB, Elkind MSV, Sacco RL. Diet soft drink consumption is associated with an increased risk of vascular events in the Northern Manhattan Study. *Journal of General Internal Medicine*. 2012;27(9):1120-1126.
8. The Global Burden of Disease Stroke Expert Group: Bennett DA, Anderson LM, Nair N, Truelsen T, Barker-Collo S, Connor M, **Gardener H**, Krishnamurthi R, Lawes CMM, Moran A, O'Donnell M, Parag V, Sacco RL, Ezzati M, Mensah G, Feigin VL. Methodology of the global and regional burden of stroke study. *Neuroepidemiology*. 2011;38(1):30-40.
9. **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.
10. 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.
11. 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. 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. In particular, I have studied the roles of diet (egg consumption and adherence to a Mediterranean-style diet) and 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. Haussen DC, Rose DZ, Drazin D, Newsome SD, **Gardener H**, Edgell RC, Boulos A, Bernardini G, Rundek T, Yavagal DR. Ipsilateral infarct in newly diagnosed cervical internal carotid artery atherosclerotic occlusion. *Interv Neurol*. 2015;3(3-4):142-148.
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. Rundek T, **Gardener H**, Della-Morte D, Dong C, Cabral D, Tiozzo E, Roberts E, Crisby M, Cheung K, Demmer R, Elkind MS, Sacco RL, Desvarieux M. The relationship between carotid intima-media thickness and carotid plaque in the Northern Manhattan Study. *Atherosclerosis*. 2015;241(2):364-370.
4. Hudson BI, **Gardener H**, Liu-Mares W, Dong C, Cheung K, Elkind MS, Wright CB, Sacco RL, Rundek T. Serum soluble RAGE levels and carotid atherosclerosis: the Northern Manhattan Study. *Atherosclerosis*. 2015;240(1):17-20.
5. Tiozzo E, **Gardener H**, Hudson BI, Dong C, Della-Morte D, Crisby M, Goldberg RB, Elkind MS, Cheung YK, Wright CB, Sacco RL, Rundek T. High-density lipoprotein subfractions and carotid plaque: the Northern Manhattan Study. *Atherosclerosis*. 2014;237(1):163-168.
6. Goldberg S, **Gardener H***, Tiozzo E, Cheung YK, Elkind MSV, Sacco RL, Rundek T. Egg Consumption and Carotid Atherosclerosis in the Northern Manhattan Study. *Atherosclerosis*. 2014;235(2):273-280.
7. **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.
8. 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.
9. 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. *Journal of the Neurological Sciences*. 2012;323(1-2):93-98.
10. Kuo F, **Gardener H**, Dong C, Cabral D, Della-Morte D, Blanton SH, Santiago M, Elkind MSV, Sacco RL, Rundek T. Traditional cardiovascular risk factors explain only small proportion of the variation in carotid plaque. *Stroke*. 2012;43(7):1755-1760.
11. **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.
12. Markert MS, Della-Morte D, Cabral D, Roberts EL, **Gardener H**, Dong C, Wright CB, Elkind MS, Sacco RL, Rundek T. Ethnic differences in carotid artery diameter and stiffness: the Northern Manhattan Study. *Atherosclerosis*. 2011;219(2):827-832.
13. **Gardener H**, Beecham A, Cabral D, Yanuck D, Slifer S, Wang L, Blanton SH, Sacco RL, Juo SH, Rundek T. Carotid plaque and candidate genes related to inflammation and endothelial function in Hispanics from Northern Manhattan. *Stroke*. 2011;42(4):889-896.
14. Wang L, Yanuck D, Beecham A, **Gardener H**, Slifer S, Blanton SH, Sacco RL, Rundek T. A candidate gene study revealed sex-specific association between the ORL1 gene and carotid plaque. *Stroke*. 2011;42(3):588-592.
15. Ramos A, Wohlgemuth WK, **Gardener H**, Lorenzo D, Dib S, Wallace D, Nolan B, Boden-Albala B, Elkin MSV, Sacco RL, Rundek T. Snoring and insomnia are not associated with subclinical atherosclerosis in the Northern Manhattan Study (NOMAS). *International Journal of Stroke*. 2010;5(4):264-268.
16. Morte D, **Gardener H**, Denaro F, Boden-Albala B, Elkind MSV, Paik, MC, Sacco RL, Rundek T. Metabolic syndrome increases arterial stiffness: The Northern Manhattan Study. *International Journal of Stroke*. 2010;5(3):138-144.
17. **Gardener H**, Morte D, Elkind MSV, Sacco RL, Rundek T. Lipids and carotid plaque in the Northern Manhattan Study (NOMAS). *BMC Cardiovascular Disorders*. 2009;9:55.
18. Sacco RL, Blanton SH, Slifer S, Beecham A, Glover K, **Gardener H**, Wang L, Sabala E, Juo SH, Rundek T. Heritability and linkage analysis for carotid intima-media thickness: The family study of stroke risk and carotid

atherosclerosis. *Stroke*. 2009;40(7):2307-2312.

*Shared first authorship

Link to my full list of publications:

<http://www.ncbi.nlm.nih.gov/pubmed/?term=Gardener+h>

D. Research Support

Novel Factors for Unexplained Phenotypes of Subclinical Carotid Atherosclerosis

NIH/NINDS R01 NS 065114

PI: T. Rundek

07.01.10-06.3.15

This is a selective genotype study of individuals with high burden of atherosclerosis and no risk factors and those with high burden of risk factors but no evidence of atherosclerosis.

Stroke Incidence and Risk Factors in a Tri-Ethnic Region

NIH/NINDS R37 NS 029993-11

PI: R.L. Sacco

02.01.03-01.31.15

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.

Stroke Prevention/Intervention Research Program in Hispanics

NIH/NINDS U54 NINDS SPIRP U54NS081763

PI: R.L. Sacco

01.01.13-12.31.17

The goal is to develop high-impact stroke disparities interventions that have the ability to reduce stroke disparities in distinct Hispanic groups in Miami and Puerto Rico using effective and culturally appropriate methods.

Mild and Rapidly Improving Stroke Symptoms Study

Genentech

PI: J. Romano

11.01.12-10.31.16

The goal is to conduct an analysis of the national Get With The Guidelines-Stroke quality improvement database to determine the characteristics and short-term outcomes of patients with mild and rapidly improving stroke symptoms in relation to thrombolytic therapy.

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):

POSITION TITLE: Assistant Professor, Departments of Physical Therapy and Neurology
Research Fellow, Berenson-Allen Center for Non-Invasive Brain Stimulation

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	B.S.	06/07	Physical Therapy
University of Miami Miller School of Medicine	Ph.D.	09/13	Motor Control
Harvard Medical School	Post-Doc	09-13 (to present)	Non-Invasive Brain Stimulation

A. Personal Statement

I am a rehabilitation scientist with extensive expertise in clinical research, non-invasive brain stimulation approaches and outcome measures of functional performance. In my career, I have explored pertinent questions regarding the potential for non-invasive brain stimulation (including transcranial magnetic stimulation [TMS] and transcranial direct current stimulation [tDCS]) to aid in the characterization of remaining function, and augment rehabilitation approaches aimed at restoring functional hand use after impairment due to spinal cord injury. As a result of these previous experiences, I have successfully carried out all aspects of research projects (subject recruitment, data analysis, data synthesis and manuscript preparation) effectively, as can be seen in my publication record. I have continued my training in clinical research and non-invasive brain stimulation during my postdoctoral fellowship with Dr. Alvaro Pascual-Leone at the Berenson-Allen Center for Non-Invasive Stimulation at Beth Israel Deaconess Medical Center at Harvard Medical School. My current work is focused on applying my knowledge of neuroplasticity and functional performance to better understand the influence of exercise and its potential to improve function and promote neuroplasticity throughout the lifespan. By collaborating with Dr. Clinton Wright and the Evelyn F. McKnight Brain Institute, I believe I will be able to continue developing this line of work, and transition to a successful independent researcher.

B. Positions and Honors

Positions and Employment

- 2013- Assistant Professor, Departments of Physical Therapy and Neurology, University of Miami Miller School of Medicine, USA.
- 2013- Research Fellow, Beth Israel Medical Center, Harvard Medical School, USA.

- 2010-2013 Research Support Specialist, The Miami Project to Cure Paralysis, University of Miami, Florida, USA
2007-2010 Research Associate, the Miami Project to Cure Paralysis, University of Miami, Florida, USA

Honors

- 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 First Scholarship for young Scientists among the Physical Therapy Students in the State of Bahia, Brazil by the Foundation to Support Research in the State of Bahia (Fundacao de Amparo a Pesquisa do Estado da Bahia- FAPESB)

Other Experience and Professional Memberships

- 2015 Peer Review Committee: Journal of Neuroscience, *ad hoc reviewer*
2015 Peer Review Committee: Annals of Neurology, *ad hoc reviewer*
2015 Peer Review Committee: Frontiers in Psychology, *ad hoc reviewer*
2015 Peer Review Committee: The Lancet Neurology, *ad hoc reviewer*
2014 Peer Review Committee: European Journal of Neuroscience, *ad hoc reviewer*
2010- Member, American Physical Therapy Association
2010- Member, Society for Neuroscience
2009- Peer Review Committee: Journal of Neurologic Physical Therapy, *ad hoc reviewer*

C. Contribution to Science

My early work was focused on identifying approaches to augment the effects of fine motor training, in healthy individuals and in after spinal cord injury. I found that tDCS augmented bimanual typing performance in healthy adults. In addition, I found that fine motor training augmented by transcranial magnetic stimulation was associated with greater improvement in hand function than fine motor training alone. Furthermore, I found differences in the potential for NIBS techniques to augment fine motor performance, with centrally applied techniques (tDCS) demonstrating greater potential than peripherally applied techniques (transcutaneous electrical nerve stimulation [TENS] and vibratory stimulus [VIB]), when directly compared. By demonstrating the successful augmentation of fine motor training with NIBS and clinically available devices such as TENS and VIB, this body of work provides alternatives for physical therapists and patients to advance the quality of their rehabilitation programs. I served as primary author on all these publications.

Gomes-Osman, J., Field-Fote EC. Improvements in Hand Function in Adults With Chronic Tetraplegia Following a Multiday 10-Hz Repetitive Transcranial Magnetic Stimulation Intervention Combined With Repetitive Task Practice. **J Neurol Phys Ther.** 2015.

Gomes-Osman, J., Field-Fote EC. Cortical vs. afferent stimulation as an adjunct to functional task practice training: A randomized, comparative pilot study in people with cervical spinal cord injury. **Clin Rehabil.** 2015.

Gomes-Osman, J., Field-Fote EC. Bihemispheric anodal corticomotor stimulation using transcranial direct current stimulation improves bimanual typing task performance. **J Mot Behav.** 2013.

Rios-Gomes, J., De Ornelas, M., Ponski, E, Field-Fote EC. Bilateral excitatory transcranial direct current stimulation (tDCS) improves bimanual motor performance in non-disabled individuals-A pilot study. **Neuroscience 2010.** Poster November 2010.

Complete List of Published Work in My Bibliography, and also below:

<http://www.ncbi.nlm.nih.gov/pubmed/?term=Gomes-Osman>

<http://www.ncbi.nlm.nih.gov/pubmed/?term=Joyce+Gomes>

S

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. **J Neurotrauma**. 2015.

Gomes-Osman J., Field-Fote EC. Improvements in Hand Function in Adults With Chronic Tetraplegia Following a Multiday 10-Hz Repetitive Transcranial Magnetic Stimulation Intervention Combined With Repetitive Task Practice. **J Neurol Phys Ther**. 2015.

Gomes-Osman J., Field-Fote EC. Cortical vs. afferent stimulation as an adjunct to functional task practice training: A randomized, comparative pilot study in people with cervical spinal cord injury. **Clin Rehabil**. 2015.

Gomes-Osman J., Field-Fote EC. Bihemispheric anodal corticomotor stimulation using transcranial direct current stimulation improves bimanual typing task performance. **J Mot Behav**. 2013.

Rios-Gomes J., De Ornelas, M., Ponski, E, Field-Fote EC. Bilateral excitatory transcranial direct current stimulation (tDCS) improves bimanual motor performance in non-disabled individuals-A pilot study. **Neuroscience 2010**. Poster November 2010.

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. **J Peripher Nerv Syst**. 2009.

Baptista AF, **Gomes J.R.**, Oliveira JT, Santos SM, Vannier-Santos MA, Martinez AMB. High and low frequency transcutaneous electrical nerve stimulation delay sciatic nerve regeneration in the mouse. **J Peripher Nerv Syst**, 2007.

Baptista AF, **Gomes J.R.**, 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. **J Neurosci Methods**. 2007.

D. Research Support

Completed

2007-2012 **National Institutes of Health (NIH) R01 HD053854**. Improving Arm and Hand Function in Individuals with SCI. This project consists 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) R01HD053854-03S1**. Improving Arm and Hand Function in Individuals with SCI. This project consists of a comparison of different approaches to improve upper extremity function and repetitive transcranial magnetic stimulation. Investigator: Edelle Field-Fote, PT, PhD. Role: Project Coordinator | 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**

eRA COMMONS USER NAME (agency login):

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)	Completion Date MM/YYYY	FIELD OF STUDY
Zhejiang Medical University, Hangzhou, Zhejiang	MD	07/1988	Medicine
Zhejiang Medical University, Hangzhou, Zhejiang	MS	07/1993	Neurology
University of Hong Kong, Hong Kong	PHD	07/2001	Neuroscience
Zhejiang Medical University, Hangzhou, Zhejiang	Other training	07/1990	Internship (Internal Medicine)
University of Rochester, Rochester, New York	Postdoctoral Fellow	07/2005	Neuroscience
Rochester General Hospital, Rochester, New York	Other training	07/2006	Internship (Internal Medicine)
Jackson Memorial Hospital/University of Miami, Miami, FL	Resident	07/2010	Neurology
Bascom Palmer Eye Institute, University of Miami, Miami, FL	Fellow	07/2011	Neuro-Ophthalmology

A. Personal Statement

Vascular dysfunction is a possible contributor to the pathogenesis of Alzheimer's disease. We proposed to study the relationship between ocular microvascular dysfunction and cognitive decline in patients with mild cognitive impairment and Alzheimer's disease (AD) by using advanced ophthalmic imaging techniques. The goal is to identify the role of vascular derangement in the pathogenesis of AD. The preliminary data obtained with the grant support from North American Neuroophthalmology Society and University of Miami revealed ocular microvascular dysfunction and retinal microstructural alterations exist in patients with AD. 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 AD clinical trials. 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 5 years. My work has been reflected in my recent publications as the corresponding author in the field of retina and conjunctiva functional imaging. I have initiated Functional Slit-lamp Biomicroscopy (FSLB) imaging for the conjunctival microvasculature, which yielded the invention of single shot microvascular network quantification. I also explored the Retinal Function Imager (RFI) while studying various diseases like diabetic retinopathy, cerebral small vessel diseases, multiple sclerosis and other ocular diseases. The build-up of the versatile FSLB and further development of the RFI imaging processing approach indicate that the team is well capable of conducting the proposed study. In summary, my expertise and experience make me well equipped and qualified for working in this proposed project.

1. 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](#).
2. 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. 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. 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](#).

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, North American Neuro-Ophthalmology Society
- 2012 - Member, Member of American Heart 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

To image microvasculature on the conjunctiva in studying cerebral small vessel diseases, a system called functional slit-lamp biomicroscope (FSLB) was developed and a patent of single shot for generating conjunctival microvascular network map was filled. This novel system enables easily imaging the conjunctival microvascular network and small vessel blood flow velocity.

1. 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](#).
2. 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](#).
3. Stuebiger N, Smiddy W, Wang J, Jiang H, DeBuc DC. Assesment of Conjunctival Microangiopathy in a Patient with Diabetes Mellitus Using the Retinal Function Imager. *J Clin Exp Ophthalmol.* 2015 Feb;6(1)PubMed PMID: [26301125](#); PubMed Central PMCID: [PMC4541803](#).

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*. 2015 Aug 20;PubMed PMID: [26299696](#).
5. I have initiated the development of 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.
6. 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](#).
7. 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*, 2015 Aug 20 [Epub ahead of print] PubMed PMID [26299696](#).
8. To study retinal degeneration in neurological diseases such as multiple sclerosis, I have contribute to the development of slit-lamp based ultra-high resolution OCT for imaging the retina. Our segmentation software can segment 9 retinal sub-layers. Recent development of segmentation software enables automatic segmentation of 6 maps of retinal sub-layers.
9. 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](#).
10. 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](#).

Complete List of Published Work in My Bibliography:

<http://www.ncbi.nlm.nih.gov/myncbi/1buofoatUF5Q8/bibliography/48052483/public/?sort=date&direction=ascending>

D. Research Support

Ongoing Research Support

NANOS Pilot 2015, North American Neuro-Ophthalmology Society

Hong Jiang (PI)

04/15/15-04/15/16

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 SAC 2015-27R1, University of Miami

Jianhua Wang (PI)

01/01/15-12/31/15

Conjunctival Microvasculature and its association with tear protein biomarkers in dry eye syndrome

The purpose is to characterize conjunctival microvasculature in dry eye

Role: Co-Investigator

UM RSA 2015-41, University of Miami

Hong 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

Novartis FTY720/Fingolimod, Novartis

Khema Shama (PI)

12/01/12-11/30/15

Efficacy and safety of fingolimod in CIDP patients

This study is a double-blind, randomized, multicenter, placebo-controlled, parallel-group study to study the efficacy and safety of fingolimod in CIDP patients.

Role: Co-Investigator

JJVC, Johnson & Johnson Vision Product Clinical Research

Jiang, Hong (PI)

12/01/14-12/31/16

Conjunctival microvascular characterization of contact lens wear

The purpose is to characterize conjunctiva microvasculature in contact lens wearer.

Role: PI

Completed Research Support

NMSS Pilot 2014, National Multiple Sclerosis Society

Jiang, Hong (PI)

07/01/14-04/30/15

Retinal vascular dysfunction in multiple sclerosis

The purpose of this project is to characterize the retinal microvascular dysfunction and optical properties in MS patients using the Retinal Function Imager (RFI) and Polarization Sensitive Optical Coherence Tomography (PS-OCT).

Role: PI

R01EY020607S, NIH supplemental award

Delia 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

Start-up research project, Bascom Palmer Eye Institute
Jiang, Hong (PI)
07/01/11-06/30/12

Functional Imaging of optical coherence tomography

The purpose of this project was to assess retinal hemodynamics and structure morphology differences between normal healthy subjects and multiple sclerosis using spectral analysis of images obtained with ultra-high resolution optical coherence tomography.

Role: PI

US202, Toyama (pharmaceutical company)
Clinton Wright (PI)
11/21/13-05/31/18

A Phase 2 multi-center, randomized, double blind, placebo-controlled, parallel group study to evaluate the efficacy and safety of T-817MA in patients with mild to moderate Alzheimer's Disease (US202)

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 <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
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 and I am the founder and Director of the Division of Neuropsychology. I direct the Neuropsychology Assessment Teaching Program and 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 in 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 a study examining cognitive and behavioral changes, including symptoms of frailty, among the oldest old, funded by the Mcknight Brain Research Institute. 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 also a co-investigator on the Bugher AHA grant and a recently approved study (Dept of Defense) examining brain metabolites underlying pain associated with traumatic injury. I believe I have the qualifications, expertise and administrative and leadership abilities serve as the PI or Co-I on studies of examining cognitive function over the life span.

These peer reviewed publications highlight my experience and qualifications for this project:

1. **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.
2. 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. [Epub ahead of print]
PMID: 25333480
3. **Levin BE**, Katzen HL, Maudsley A, Post J, Myerson C, Govind V, Nahab F, Scanlon B, Mittel A. Whole-brain proton MR spectroscopic imaging in Parkinson's disease. *J Neuroimaging.* 2014 Jan-Feb;24(1):39-44

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
2011-	Professor of Neurology, 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. *Journal of Neurotrauma* (in press)

Complete List of Published Work at NCBI:

[http://www.ncbi.nlm.nih.gov/pubmed/?term=\(%22levin%2C%20bonnie%22%5BAI%20Fields%5D\)&cmd=DetailsSearch](http://www.ncbi.nlm.nih.gov/pubmed/?term=(%22levin%2C%20bonnie%22%5BAI%20Fields%5D)&cmd=DetailsSearch)

D. Research Support

Ongoing Research Support

7 R01 NS 029993 (PI, Sacco) NIH/NINDS **02/01/03-03/31/21** **1.20 calendar**

Stroke Incidence and Risk Factors in a TriEthnic Region **\$1,795,509**

(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

\$169,003

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.

AHA/ASA 14BFSC1759000 (PI: Sacco)

04/01/14 – 03/31/18

0.6 calendar

AHA (B. Levin, Co-Investigator)

\$234,667

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

DoD/CDMRP/USAMRMC (PI: Widerstrom-Noga)

11/2015-10/2018

.84 calendar

(B. Levin, Co-Investigator)

\$977,099 (direct)

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.

Prior Research Support

NINDS 1 UO1 NS052478-01A2 (Adelson)

7/30/07 – 6/30/2011

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.

NIH/NINDS 2U01NS38529-07A1 (Benavente/ Romano, site PI) 02/01/2008 – 6/30/2011

Secondary Prevention of Small, Subcortical Strokes (SPS3)

NIH/NINDS R01 NS055107 (Maudsley)

6/1/2006 –

12/31/2012

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.

NIH/NINDS R01 NS060874 (Govind)

1/1/2009 – 8/31/2012

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.

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: **Hung Wen Lin**

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

POSITION TITLE: Research Assistant 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)	Completion Date MM/YYYY	FIELD OF STUDY
University of Wisconsin-Madison, Madison, WI	B.S.	05/1999	Biochemistry
Southern Illinois University School of Medicine, Springfield, IL	Ph.D.	12/2007	Pharmacology
University of Miami, Miller School of Medicine, Miami, FL	Post-doc	12/2012	Neurology

A. Personal Statement

My expertise is in the field of sympathetic modulation in cerebral circulation as it relates to ischemia. I have discovered that surgical sympathetic interruption may have positive functional outcomes after ischemia. My contributions to the Evelyn F. McKnight Brain Institute involve the investigation of sympathetic function as it relates to ischemia in young and aged brain in hopes to develop novel therapies. I have dedicated over 10 years to investigate cerebral vasculature with focus on sympathetic innervations to the brain. Attenuation but not enhancement of the sympathetic nervous system projections to the brain is actually beneficial via maintaining cerebral blood flow, promoting neuronal survival and functional recovery after cardiac arrest. Investigating the function of the sympathetic nervous system after cardiac arrest in the brain can lead to novel therapies to prevent ischemic brain injury by defining the role of the sympathetic nervous system important in cerebral blood flow regulation and neuroprotection.

1. **Lin, H.W.**, Gresia, V.L., Stradecki, H.M., Alekseyenko, A., Dezfulian, C., Neumann, J.T., Dave, K.R. & Perez-Pinzon, M.A. (2014). Protein kinase c delta modulates endothelial nitric oxide synthase after cardiac arrest. *J Cereb Blood Flow Metab*, 34(4), 613-620. PMID: PMC3982078
2. **Lin, H.W.**, Saul, I., Gresia, V.L., Neumann, J.T., Dave, K.R. & Perez-Pinzon, M.A. (2014). Fatty acid methyl esters and solutol HS 15 confers neuroprotection after focal and global cerebral ischemia. *Transl Stroke Res*, 5(1), 109-117. PMID: PMC3948321
3. **Lin, H.W.** & Perez-Pinzon, M.A. (2013). The role of fatty acids in the regulation of cerebral vascular function and neuroprotection in ischemia. *CNS and Neurological Disorders-Drug Targets*, 12(3), 316-324. PMID: 23469852
4. **Lin, H.W.**, Liu, C.Z., Cao, D., Chen, P.Y., Chen, M.F., Lin, S.Z., Mozayan, M., Chen, A.F., Premkumar, L.S., Torry, D.S. & Lee, T.J. (2008). Endogenous methyl palmitate modulates nicotinic receptor-mediated transmission in the superior cervical ganglion. *Proc Natl Acad Sci U S A*, 105(49), 19525-19530. PMID: PMC2596137

B. Positions and Honors

Positions and Employment

- 1995 - 1999 Undergraduate Research Assistant, University of Wisconsin-Madison, Zoology Research Center, Madison, WI
- 1998 - 1999 Assistant Grants Officer, Madison Area Technical College, Madison, WI
- 1998 - 1999 Minority Youth Career Awareness Project Assistant Coordinator, Madison Area Technical College, Madison, WI
- 2001 - 2007 Graduate Research Assistant, Southern Illinois University School of Medicine, Department of Pharmacology, Springfield, IL
- 2007 - 2012 Postdoctoral Research Associate, University of Miami Miller School of Medicine, Department of Neurology, Miami, FL
- 2013 - present Research Assistant Professor, University of Miami Miller School of Medicine, Department of Neurology, Miami, FL

Honors and Professional Activities

- 2005 Guest Lecturer, Tzu Chi University, School of Medicine, Department of Neurology, Hualien Taiwan
- 2008 Young/New Investigator Travel Award at the "Brain Energy Metabolism and Blood Flow Conference", Gordon Conference
- 2009 Invited speaker, Cerebral Ischemia Research Group, University of Miami Miller School of Medicine, Miami, FL
- 2009 Invited speaker, Department of Physiology and Biophysics, University of Miami Miller School of Medicine, Miami, FL
- 2009 Invited judge for the Florida-Georgia Louis Stokes Alliance for Minority Participation Expo, Miami, FL
- 2010 Invited speaker, Minisymposium on Live Cell Imaging, University of Miami Miller School of Medicine, Miami, FL
- 2010 Recipient of the 4th annual American Heart Association-Philips Resuscitation Fellowship Award, Presented at the Resuscitation Science Symposium, Chicago, IL
- 2011 Invited speaker, Cerebral Ischemia Research Group, University of Miami Miller School of Medicine, Miami, FL
- 2011 Invited speaker, The Miami Project to Cure Paralysis, University of Miami Miller School of Medicine, Miami, FL
- 2011 Reviewer for the Journal of Clinical and Experimental Cardiology
- 2012 Invited speaker and chair of the organizing committee, presentation entitled: "Investigating the Cerebral Vasculature. 2012 Past, Present, and Future." Presented at the "The 3rd International Conference of Stem Cells and Regenerative Medicine and 2012 Tzu Chi University Symposium on Biomedicine, Technology, and Humanity", Hualien, Taiwan
- 2012 Reviewer for CNS & Neurological Disorder: Drug Target
- 2013 Reviewer for Neurological Research, Translational Stroke Research, PLoS One
- 2013 Editorial Board member: Neurological Research and Therapy
- 2014 Reviewer for Journal of Cerebral Blood Flow Metabolism, International Journal of Molecular Sciences, Stroke, Scientific Reports (Nature Publishing Group), Neuroscience, Nitric Oxide: Biology and Chemistry
- 2014 Invited speaker, presentation entitled: "Benefits of sympathetic nervous system attenuation in brain ischemia." Pharmacology and Physiology, International Scientific Congress, Kuala Lumpur, Malaysia.
- 2014 Invited speaker, presentation entitled: "Sympathetic Modulation During Ischemia: A Potential Approach." Evelyn F. McKnight Research Seminar Series, University of Miami, Miami, FL.
- 2015 Grant Peer Review: AHA Peer Review Committee: Basic Cell Genetics and Epigenetics 2
- 2015 Invited speaker, presentation entitled: "Palmitic and stearic acid methyl esters as potential vasodilators and neurotransmitters." Journées Chevreul Lipids and Brain III, French Society for the Study of Lipids and SCI, Paris, France.
- 2015 Invited speaker, presentation entitled: "Sympathetic modulation in cerebral ischemia." Department of Systems Medicine, University of Rome Tor Vergata. Rome, Italy.

2015

Chair of the Oral Session: Cerebral Ischemia: Functional Recovery at the XXVIIth International Symposium on Cerebral Blood Flow, Metabolism and Function & XIIth International Conference – Brain 2015, Vancouver, Canada.

Professional Memberships

2007 - present American Heart Association
2008 - present Society for Neuroscience
2012 - present The American Society for Pharmacology and Experimental Therapeutics

C. Contribution to Science

1. I currently study the connection between the sympathetic chain and the brain as it relates to cerebral circulation and nerve innervation in cerebral blood vessels. Little is known regarding sympathetic regulation in the brain. Under ischemic conditions *in vitro* and *in vivo* from the sympathetic nervous system, I discovered that palmitic acid methyl ester is a novel vasodilator and stearic acid methyl ester is a potent neuroprotectant. I am actively investigating the physiological relevance as well as potential drug targets for the treatment against ischemia.
 - a. Lee, R.H.C., Goyanes Vasquez, J.J., Couto e Silva, A., Klein, D.D., Valido, S.E., Chen, J.A., Lerner, F.M., Neumann, J.T., Wu, C.Y., **Lin, H.W.** (2015). Fatty acid methyl esters as a potential therapy against cerebral ischemia. *Oilseeds & fats Crops and Lipids*. (**In press**)
 - b. **Lin, H.W.**, Saul, I., Gresia, V.L., Neumann, J.T., Dave, K.R. & Perez-Pinzon, M.A. (2014). Fatty acid methyl esters and solutol HS 15 confers neuroprotection after focal and global cerebral ischemia. *Transl Stroke Res*, 5(1), 109-117. PMID: PMC3948321
 - c. Lee, R.H.C., Wilkins, C.S., Couto e Silva, A., Valido, S.E., Wu, C.Y., **Lin, H.W.** (2014) Fatty Acids in Vascular Health. In: Lucas F. Porto (Ed.), *Palmitic Acid: Occurrence, Biochemistry and Health Effects* (1st ed.). Hauppauge, NY: Nova Science Publishers.
 - d. **Lin, H.W.** & Perez-Pinzon, M.A. (2013). The role of fatty acids in the regulation of cerebral vascular function and neuroprotection in ischemia. *CNS and Neurological Disorders-Drug Targets*, 12(3), 316-324. PMID: 23469852
 - e. **Lin, H.W.**, Liu, C.Z., Cao, D., Chen, P.Y., Chen, M.F., Lin, S.Z., Mozayan, M., Chen, A.F., Premkumar, L.S., Torry, D.S. & Lee, T.J. (2008). Endogenous methyl palmitate modulates nicotinic receptor-mediated transmission in the superior cervical ganglion. *Proc Natl Acad Sci U S A*, 105(49), 19525-19530. PMID: PMC2596137

2. In addition to the contributions described above, my colleagues and I previously studied protein kinase C (PKC) as it relates to cerebral ischemia. Modulation of specific PKC isoforms during ischemia can prove useful to revive cerebral blood flow and provide better functional outcomes. My colleagues and I discovered that there is a delicate balance between PKC activation and repression during ischemia as it relates to cerebral blood flow and metabolism. I was the lead author in most of these studies.
 - a. **Lin, H.W.**, Gresia, V.L., Stradecki, H.M., Alekseyenko, A., Dezfulian C., Neumann, J.T., Dave, K.R. & Perez-Pinzon, M.A. (2014). Protein kinase c delta modulates endothelial nitric oxide synthase after cardiac arrest. *J Cereb Blood Flow Metab*, 34(4), 613-620. PMID: PMC3982078
 - b. **Lin, H.W.**, Della-Morte, D., Thompson, J.W., Gresia, V.L., Narayanan, S.V., DeFazio, R.A., Raval, A.P., Saul, I., Dave, K.R., Morris, K.C., Si, M.L. & Perez-Pinzon, M.A. (2012). Differential effects of delta and epsilon protein kinase C in modulation of post-ischemic cerebral blood flow. *Adv Exp Med Biol*, 737: 63-69. PMID: PMC4086166
 - c. **Lin, H.W.**, Thompson, J.W., Morris, K.C. & Perez-Pinzon, M.A. (2011). Signal Transducers and Activators of Transcription (STATs)-mediated mitochondrial neuroprotection. *Antioxid Redox Signal*, 14(10), 1853-1861. PMID: PMC3078497
 - d. **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. (2010). Derangements of post-ischemic cerebral blood flow by protein kinase C delta. *Neuroscience*, 171(2), 566-576. PMID: PMC2981031

- e. DeFazio, R.A., Raval, A.P., **Lin, H.W.**, Dave, K.R. & Perez-Pinzon, M.A. (2009). GABA synapses mediate neuroprotection after ischemic and Epsilon PKC preconditioning in the rat hippocampal slice cultures. *J Cereb Blood Flow Metab*, 29(2), 375-384. PMID: PMC2696173

Complete List of Published Work in MyBibliography:

<http://www.ncbi.nlm.nih.gov/myncbi/browse/collection/44325827/?sort=date&direction=ascending>

D. Research Support

Ongoing Research Support

13SDG1395001413 Lin (PI) 1/1/2013- 12/31/2016
National Scientist Development Grant from American Heart Association
Title: The Role of Fatty Acid Methyl Esters on Cerebral Blood Flow Following Cardiac Arrest
The goal of this study is to study fatty acid methyl esters as in cerebral ischemia.
Role: (PI)

5R01NS073779-03 Dave (PI) 3/01/12 – 12/31/16
Title: Increased cerebral ischemic injury by repeated hypoglycemic episodes in diabetes.
The goal of this study is to study cerebral ischemia under hypoglycemic conditions.
Role: Co-Investigator

R01NS056072 Dietrich (PI) 9/01/14 – 03/01/19
Title: Cyclic Nucleotide Regulation in Traumatic Brain Injury
The goal of this study is to study cyclic nucleotide regulation in traumatic brain injury.
Role: Co-Investigator

Completed Research Support

14BFSC17690007 Sacco (PI) 4/1/2014 – 4/1/2015
American Stroke Association-Bugher Foundation Centers for Excellence in Stroke Collaborative Research for Regeneration, Resilience and Secondary Prevention, Ralph S. Sacco (PI)
The goal of this study is to investigate the concept of exercise as it relates to stroke.
Role: Co-Investigator

R01 NS45676-05 Pérez-Pinzón (PI) 6/01/07- 5/31/15
Title: Mechanisms of Neuroprotection against Cardiac Arrest
The goal of this study is to investigate protein kinase C as it relates to cardiac arrest.
Role: Co-Investigator

10POST4340011 Lin (PI) 7/1/2010- 6/30/2012
Postdoctoral Research Fellowship from American Heart Association (AHA)-Philips
Title: Protein Kinase C Delta Exacerbates Post-ischemic Cerebral Blood Flow Derangements After Cardiac Arrest
The goal of this study is to investigate protein kinase C as it relates to cardiac arrest.
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: **Teshamae S. Monteith, M.D.**

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

POSITION TITLE: **Assistant Professor 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.*)

1. INSTITUTION AND LOCATION	2. DEGREE 3. (if applicable)	5. Completion Date 6. MM/YYYY 7.	8. FIELD OF STUDY 9.
Florida International University, Miami, FL	BS	12/98	Biology
University of Miami Miller School of Medicine, Miami, FL	MD	05/04	Medicine
Albert Einstein-Montefiore Medical Center, NY, NY	Intern	06/05	Internal Medicine
New York University School of Medicine, NY, NY	Residency	06/08	Neurology
Thomas Jefferson University School of Medicine, Philadelphia, PA	Fellowship	06/09	Headache
University of California, San Francisco, CA	Fellowship	06/11	Headache

A. Personal Statement

My research focus has been on headache disorders, migraine in particular, and the cross section between migraine and vascular risk factors and stroke outcomes. As a collaborator for the McKnight Brain Institute, I aim to investigate cognitive impairment in subjects with headache disorders. I have a secondary interest in understanding the impact of obesity, metabolic disorders, and dietary factors on migraine and cognition.

B. Positions and Honors

POSITIONS AND EMPLOYMENT

Traineeship:

2004-2005	Intern	Montefiore Medical Center, Bronx, New York
2005-2008	Neurology Resident	New York University, New York, NY
2008-2009	Headache Fellowship	Thomas Jefferson University, Philadelphia, PA
2009-2011	Headache Fellowship	University of California, San Francisco, San Francisco, CA

Academic Appointments:

2011-Present	Assistant Professor of Clinical Neurology	Department of Neurology, University of Miami School of Medicine, Miami, FL
--------------	---	--

OTHER EXPERIENCE AND PROFESSIONAL MEMBERSHIPS

Ad Hoc Reviewer for the Professional Journals: Headache, European Journal of Neurology, Cephalalgia.

Memberships:

1996-	American Academy of Neurology
2008-	American Headache Society
2008-	American Academy of Neurology Brain PAC Founder's Club
2008	New York State Neurological Society
2008	National Headache Foundation
2009	Pennsylvania Neurological Society
2009-	International Headache Society
2013-	Florida Society of Neurology, board member
2014-	International Association for the Study of Pain

HONORS

1993	Florida International University Tuition Scholarship, Miami, FL
1994	National Institutes of Health, Minority Biomedical Research Support Program
1998	AMSA Outstanding Commitment Award, Minority Committee Chairman
1998	Florida International University Honors Program
2000	Leonard Miller School of Medicine at the University of Miami Tuition Award
2001	McClelland Brown Trust Rotary Scholarship Award
2006	American Neurological Association Resident's Program Scholarship
2007	National Headache Foundation Travel Award
2008	American Headache Society /Merck US Human Health Scholarship Award
2010	Palatucci Co-Advocate of the Year Award, American Academy of Neurology
2013	Harold G. Wolff Lecture Award, presented at the American Headache Society meeting
2014	Doctor of Excellence, Leaders in Healthcare Network
2014	Fellow, American Headache Society
2015	South Florida, Top Black Educator, Legacy Magazine

C. Contribution to Science

- I have made significant contributions to the understanding of migraine pathophysiology and vascular complications. Through PET imaging during nitroglycerin triggered migraine attacks, our group determined several brain regions that were activated before migraine pain was experienced during the premonitory phase. This critical study was awarded the Wolff award for the key finding that confirmed migraine as a central brain disorder as opposed to a peripheral nerve disorder. The findings have implications for targeted drug approaches.
 - Maniyar FH, Sprenger T, Monteith T, Schankin C, Goadsby PJ. Brain activations in the premonitory phase of nitroglycerin-triggered migraine attacks. *Brain*. 2014;137(Pt 1):232-41
 - Maniyar FH, Sprenger T, Monteith T et al. The premonitory phase of migraine - what can we learn from it? *Headache*. 2015; 55(5):609-20.
- Through a NINDS funded supplement award to promote health related diversity research, our study findings have contributed a better understanding of the impact of migraine on silent brain lesions, cardiovascular risks and vascular outcomes through analysis of the multi-ethnic cohort from the Northern Manhattan Study. We found that compared to people without migraine, those with migraine (confirmed by International Classification of Headache Disorders-2 criteria) had a 2-fold increased odds of subclinical brain infarction (adjusted odds ratio [OR], 2.1; 95% confidence interval [CI], 1.0 - 4.2). These results were confirmed in a diverse older cohort with a high burden of cardiovascular risk factors such as hypertension. However, the association between migraine and silent brain infarction was independent of sociodemographic and cardiovascular factors. In a study accepted to *Neurology*, I also found that the impact of migraine on stroke differed among smokers and non-smokers which is consistent with other studies. Further work is needed to determine the role of lifestyle intervention, genetics, and vascular risk reduction in improving migraine complications such as stroke and other vascular disorders.
 - Monteith T, Gardener H, Rundek T et al. Migraine and risk of stroke in older adults: Northern Manhattan Study *Neurology*. 2015; 85:1-7.

- b. Monteith TS, Gardener H, Rundek T, Dong C, Mitsuhiro Y, Elkind M, DeCarli C, Sacco R, Wright C. Migraine, White Matter Hyperintensities, and Subclinical Brain Infarction in a Diverse Community: The NOMAS Study. Stroke. 2014; 45(6):1830-2.

Complete List of Published Work:

http://www.researchgate.net/profile/Teshamae_Monteith/publications

D. Research Support

Ongoing Research Support

A Phase 3 Randomized, Double-Blind, Placebo-Controlled Study of LY2951742 in Patients with Episodic Cluster Headache. Eli Lilly. Site PI, 2015.

Completed Research Support

The Relationship between Migraine, Subclinical Brain Lesions, and Biomarkers of Subclinical Cardiovascular Disease in a Tri-Ethnic Region: Supplement to Promote Diversity in Health-Related Research (R37 NS 29993) – NINDS PI, 2011-2015.

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: Carlos T. Moraes	POSITION TITLE <u>Professor</u>
eRA COMMONS USER NAME cmoraes	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
Escola Paulista de Medicina, Sao Paulo, Brazil	B.Sc.	1983	Biomedical Sciences
Escola Paulista de Medicina, Sao Paulo, Brazil	M.Sc.	1987	Molecular Biology
Department of Genetics and Development, Columbia University	M.A.	1991	Genetics & Development
Department of Genetics and Development, Columbia University	Ph.D.	1993	Genetics & Development

A. Personal Statement

My independent group at the University of Miami was established in 1993 and one of its main focus in the last decade has been the study of nuclear-mitochondrial communication, the pathogenesis of mitochondrial diseases, the development of genetic treatments and the role of mitochondrial dysfunction in age-related degenerative processes. The association with the McKnight Institute had a major impact on our studies on neurodegeneration and Alzheimer's disease.

B. Positions and Honors.

PROFESSIONAL APPOINTMENTS

2014 - Esther Lichtenstein Endowed Chair in Neurology

2005 - Professor (Tenured). Dept. of Neurology, University of Miami, Miami, FL.

1998 – 2005 Associate Professor (Tenured). Dept. of Neurology, University of Miami, Miami, FL.

1993 – 1998 Assistant Professor. Dept. of Neurology, University of Miami, Miami, FL.

1992 – 1993 Postdoctoral Research Fellow. Dept. of Neurology, Columbia University, New York, NY.

AWARDS AND OTHER PROFESSIONAL ACTIVITIES:

2005 Provost Award for Scholarly Activity, University of Miami

2002 - 2006 NIH Scientific Review Panel Member (GHD)

2010- 2013 NIH Scientific Review Panel Member (NOMD)

2007- Present Scientific Advisory Committee member, Muscular Dystrophy Association

2005- Present	Scientific Advisory Committee member, United Mitochondrial Disease Foundation
2009- Present	Chair, Scientific Advisory Committee, United Mitochondrial Disease Foundation
1999 - 2004	Scientific Advisory Committee member, Muscular Dystrophy Association
1995 - 1999	PEW Scholar in the Biomedical Sciences
1997	National Eye Institute Committee on "Development of a National Plan for Vision Research
1997	National Heart, Lung, and Blood Institute Scientific Review Committee for RFA: HL-96-013
1998	Chemistry and Related Sciences Special Emphasis Review Panel (NIH).
1998	Molecular Cytology Special Emphasis Panel (NIH).

C. Contribution to Science

4. I became involved with mitochondrial genetics during my Ph.D. Working with Drs. Salvatore DiMauro and Eric Schon at Columbia University, we were the first to show that mtDNA deletions were associated with ocular myopathy. We were also the first to show how mtDNA deletions are generated and how they segregate. Besides mtDNA deletions, we also identified several pathogenic mtDNA point mutations and described a new genetic abnormality, namely a mtDNA depletion, caused by defects in the nuclear genome.
 - a. **Mitochondrial DNA deletions in progressive external ophthalmoplegia and Kearns-Sayre syndrome. Moraes. C.T.,** DiMauro, S., Zeviani, M., Lombes, A., Shanske, S., Miranda, A. F et al., *New England Journal of Medicine*, 320: 1 293-1299 (1989).
 - b. **Molecular analysis of the muscle pathology associated with mitochondrial DNA deletions. Moraes, C. T.,** Ricci, E., Petruzzella, V., Shanske, S., DiMauro, S., Schon, E.A. and Bonilla, E. *Nature Genetics*, 1: 359-367 (1992).
 - c. **A mitochondrial tRNA anticodon swap associated with a muscle disease. Moraes. C.T.,** Ciacci, F., Bonilla, E., Ionascescu, V., Schon, E.A., and DiMauro, S. *Nature Genetics*, 4:284-287 (1993).
 - d. **Mitochondrial DNA depletion with variable tissue expression: A novel genetic abnormality in mitochondrial diseases. Moraes. C.T.,** Shanske, S., Trishler HJ., Aprille, J.R., Andreetta, F., Bonilla, E., Schon, E.A. and DiMauro, S. *American Journal of Human Genetics*, 48: 492-501 (1991).

5. As an independent investigator, I continued to study mitochondrial diseases, but became interested in the co-evolution of nuclear and mitochondrial genomes. Using cross-species transmitochondrial (xenomitochondrial) cybrids we were able to determine the timing of evolutionary divergency for functional interaction between these genomes. We showed that although the nucleus of a human cell could maintain a functional mtDNA from chimpanzee or gorilla, it could not do so with orangutan or other species of primates (old world, new world, lemurs). However, even human-Chimp xenomitochondrial cybrids had a defect in complex I, showing how co-evolution shaped these interactions. These findings are important to better understand how mutations in the mtDNA cause disease. They may not be obviously deleterious for the function of the enzyme, but may disrupt critical interactions with nuclear counterparts.
 - a. **Expanding the functional human mitochondrial DNA database by the establishment of primate xenomitochondrial cybrids.** Lesley Kenyon and **Carlos T. Moraes.** *Proceedings of the National Academy of Sciences USA* 94:9131-9135 (1997).
 - b. **Human xenomitochondrial cybrids. Cellular models of mitochondrial complex I deficiency.** Antoni Barrientos, Lesley Kenyon and **Carlos T. Moraes.** *J Biol Chem*, 273:14210-7 (1998).
 - c. **Cytochrome c Oxidase Assembly in Primates is Sensitive to Small Evolutionary Variations in Amino Acid Sequence.** Antoni Barrientos, Stefan Müller, Runu Dey, Johannes Wienberg and **Carlos T. Moraes.** *Molecular Biology and Evolution*, 17: 1508-1519 (2000)
 - d. **Fast Adaptive Co-evolution of Nuclear and Mitochondrial Subunits of ATP Synthetase in Orangutan.** Maria Pilar Bayona-Bafaluy, Stefan Müller, **Carlos T. Moraes.** *Mol. Biol. Evol.* 22:716-

6. In the early-mid 2000, I decided to create mouse models of mitochondrial disease, as the pathogenesis studies and development of therapies would require them. We created conditional knockout models of defects in complexes IV, III and I, as well as a model of mtDNA depletion by expressing restriction endonucleases targeted to mitochondria. These models have been shared to multiple groups and are deposited at Jackson laboratories. They have been used in our lab to study the role of mitochondrial oxidative phosphorylation defects in neurodegenerative diseases and to test therapies.
- Mice lacking COX10 in skeletal muscle recapitulate the phenotype of progressive mitochondrial myopathies associated with cytochrome c oxidase deficiency.** Francisca Diaz, Christine K. Thomas, Sofia Garcia, Dayami Hernandez and **Carlos T. Moraes**. *Hum. Mol. Genet.* 14: 2737–2748 (2005).
 - Cytochrome c Oxidase Deficiency in Neurons Decreases both Oxidative Stress and Amyloid Formation in a Mouse Model of Alzheimer’s Disease.** Hirokazu Fukui, Francisca Diaz, Sofia Garcia and **Carlos T. Moraes**. *Proc Natl. Acad. Sci. USA* 104 :14163–14168 (2007).
 - Striatal Dysfunctions Associated with Mitochondrial DNA Damage in Dopaminergic Neurons of a Mouse Model of Parkinson’s Disease.** Alicia M. Pickrell, Milena Pinto, Aline Hida and **Carlos T. Moraes**. *The Journal of Neuroscience*;31:17649-58 (2011).
 - A defect in the mitochondrial Complex III, but not Complex IV, triggers early ROS dependent damage in defined brain regions.** Francisca Diaz, Sofia Garcia, Kyle R. Padgett and **Carlos T. Moraes**. *Human Molecular Genetics*, 21:5066-77 (2012)
7. My interest in developing therapies to mitochondrial diseases led us to explore the role of increased mitochondrial biogenesis in mitochondrial myopathies. We found that overexpression of PGC-1 α in muscle counteracted the deleterious effect of an OXPHOS defect in mice. Moreover, we showed that some drugs, such as bezafibrate could partially mimic this effect. This work opened a new area of investigation, where increase in mitochondrial biogenesis was analyzed in several disorders suspected to have a mitochondrial component.
- Activation of the PPAR/PGC-1 α pathway prevents a bioenergetic deficit and effectively improves a mitochondrial myopathy phenotype.** Tina Wenz, Francisca Diaz, Bruce M. Spiegelman and **Carlos T. Moraes**. *Cell Metabolism* 8:249-56 (2008)
 - PGC-1 α / β induced expression partially compensates for respiratory chain defects in cells from patients with mitochondrial disorders.** Sarika Srivastava, Francisca Diaz, Luisa Iommarini, Karine Aure, Anne Lombes and **Carlos T. Moraes**. *Human Molecular Genetics* 18:1805-12. (2009)
 - Increased muscle PGC-1 α expression protects from sarcopenia and metabolic disease during aging.** Tina Wenz, Susana G. Rossi, Richard L. Rotundo, Bruce Spiegelman and **Carlos T. Moraes**. *Proc. Natl. Acad. Sci. USA* 106:20405-20410 (2009)
 - Increase Mitochondrial Biogenesis in Muscle Improves Aging Phenotypes in the mtDNA Mutator Mouse.** Lloye M. Dillon, Sion L. Williams, Aline Hida, Jacqueline D. Peacock, Tomas A. Prolla, Joy Lincoln and **Carlos T. Moraes**. *Human Molecular Genetics*, 21:2288-97 (2012).
8. We also developed a genetic approach to treat mtDNA diseases. Shortly, we used mitochondria-targeted restriction endonucleases that could digest exclusively a specific mtDNA haplotype. In heteroplasmic cells, it leads to a reduction in the mutant mtDNA load and restoration of OXPHOS activity. We showed this approach to be effective in vivo, using several viral vectors to deliver the mitoRestriction Endonuclease. More recently, we adapted TALENs to this approach (mitoTALENs), which overcomes the limitation of few sites recognition posed by the bacterial endonucleases.
- Rapid Directional Shift of Mitochondrial DNA Heteroplasmy in Animal Tissues by a Mitochondrially-Targeted Restriction Endonuclease.** Maria Pilar Bayona-Bafaluy, Bas Blits, Brendan Battersby, Eric A. Shoubridge, and **Carlos T. Moraes**. *Proc. Natl. Acad. Sci. USA* 102: 14392–14397 (2005).
 - Manipulation of mtDNA heteroplasmy in all striated muscles of newborn mice by AAV9-mediated delivery of a mitochondria-targeted restriction endonuclease.** Bacman SR, Williams

- SL, Duan D, **Moraes CT**. *Gene Ther.*;19:1101-6 (2012).
- c. **Specific elimination of mutant mitochondrial genomes in patient-derived cells by mitoTALENs**. Sandra R. Bacman, Siôn L. Williams, Milena Pinto, Susana Peralta and **Carlos T. Moraes**. *Nature Medicine*, 19:1111-3. (2013).
- d. **Selective Elimination of Mitochondrial Mutations in the Germline by Genome Editing**. Pradeep Reddy, Alejandro Ocampo, Keiichiro Suzuki, Jinping Luo, Sandra R. Bacman, Sion L. Williams, Atsushi Sugawara, Daiji Okamura, Yuji Tsunekawa, David Lam, Nuria Monsterrat, Concepcion Rodriguez Esteban, Ignacio Sancho-Martinez, Dolors Manau, Salva Civico, Francesc Cardellach, Maria del Mar O'Callaghan, Jaume Campistol, Huimin Zhao, Josep Maria Campistol, **Carlos T. Moraes**, Juan Carlos Izpisua Belmonte. *Cell*. 161, 459–469 (2015)

Complete List of Published Work in MyBibliography:

<http://www.ncbi.nlm.nih.gov/sites/myncbi/carlos.moraes.1/bibliography/40679402/public/?sort=date&direction=ascending>

D. Research Support.

Active

5R01EY010804-18 Moraes 12/01/94-4/30/17

NIH/NEI

"Setting the stage for the replacement of mitochondrial genes"

The objective of this project is to use mitochondria-targeted restriction endonucleases to modify mtDNA heteroplasmy. We express a mitochondria-targeted ApaLI in a mouse model of mtDNA heteroplasmy (BALB and NZB mtDNA haplotypes). ApaLI can cleave the BALB mtDNA but not the NZB mtDNA.

Role: PI

1R01NS079965-03 (Moraes, C.T.)

07/01/2012 – 05/31/2017

NIH/NINDS

"Cellular And Molecular Consequences Of Respiratory Chain Defects In Neurons"

The objective of this project is to investigate the phenotypic differences of mitochondrial encephalopathies caused by defects in different respiratory complexes. Genetically modified mice with defects in complexes I, III and IV are analyzed and compared.

1R01AG036871-02 Moraes 06/01/2010 – 05/31/2015 (no-cost extension. Competing renewal was in the 4%)

NIH/NIA

"Mitochondrial Dysfunction in Neurodegeneration and Compensatory Approaches"

The objective of this project is to investigate the effects of double-strand breaks in the mtDNA on the generation and accumulation of large deletions during aging. In certain conditions, mitochondria-targeted

restriction endonucleases can lead to the formation of mtDNA deletions. We are attempting to study the functional significance of these low levels of mtDNA deletions in aging.

Role: PI

1R21ES025673-01 (Moraes, CT and Caicedo, DA) 05/01/2015 – 04/30/2017

NIH/NIEHS

“Imaging mitochondrial signaling in B-cells ectopically implanted in the eye”

The objective of this grant is to study mitochondrial signaling using targeted fluorescent biosensors. Western blot is used to assess expression of Biosensors.

Role: Co-PI

UMDF (Moraes, C. T.) 09/01/2014-09/01/2016

Developing Specific Nucleases to Eliminate Mutant mtDNA

The objective of this project is to develop mitoTALEN against common mtDNA mutations and test delivery by adenovirus.

Role: PI

The Muscular Dystrophy Association (Moraes, C. T.) May/1/14-April/30/17

Reducing the levels of mtDNA mutations by mitochondrial nucleases

Develop Adenovirus vectors to deliver mitoTALENS

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: **Miguel A. Perez-Pinzon, PhD, FAHA**

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

POSITION TITLE: **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
University of Panama	B.Sc.	1983	Biology
University of Miami (RSMAS)	M.Sc.	1987	Marine Biology
University of Miami (RSMAS/Neurology)	Ph.D.	1991	Neuroscience
New York University	Postdoc	1992	Neurophysiology
Stanford University	Postdoc	1993	Neuroscience

A. Personal Statement

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 Scheingberg (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 until 2005. I am a Professor of Neurology and Neuroscience and I am Vice-Chairman 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 a stroke. My research focuses on the areas of synaptic, vascular and mitochondrial dysfunction that ensue following cerebral ischemia. Over the last 19 years, my laboratory has investigated the signaling pathways that lead to neuroprotection against ischemia following ischemic preconditioning (IPC). Our goal is to develop new therapies for pre- and post-treatment in stroke and cardiac arrest patients. Our center uses a large number of techniques that include imaging, electrophysiology, behavior and molecular biology techniques.

B. Position and Honors

Positions and Employment

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)
2000 – 2003	NIH-NINDS BDCN-3 Study Section reviewer
2001 – 2006	Associate Professor, Department of Neurology, University of Miami School of Medicine.
2004 – 2008	Brain 2 American Heart Association Grant Reviewer
2005 – present	Director of Cerebral Vascular Disease Center, University of Miami, Miller School of Medicine, Miami, FL
2006 – 2010	NIH-NINDS BINP Study Section
2006 – present	Professor, Department of Neurology, University of Miami Miller School of Medicine, Miami, FL
2007 – 2008	International Stroke Conference Program Committee: Co-Chair–Experimental Mechanisms and Models.
2007 – 2010	Associate Chair for Basic Science, Department of Neurology, University of Miami Miller School of Medicine, Miami, FL
2008 – 2010	International Stroke Conference Program Committee: Chair–Experimental Mechanisms and Models.
2010 – present	Vice-Chair for Basic Science, Department of Neurology, University of Miami Miller School of Medicine, Miami, FL

- 2012-13 Co-Chair of the Program Committee for the International Society of Cerebral Blood Flow and Metabolism (Brain 13), Shanghai, China
- 2014 NIH-NINDS BINP Study Section Ad-hoc member
- 2014 Member of the Program Committee for the International Society of Cerebral Blood Flow and Metabolism (Brain 15), Vancouver, Canada

Honors, Awards, and Professional Societies

- 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, University of Miami, Miami, FL
- 1991 Invited speaker at the Society for Experimental Biology in Birmingham, U.K.
- 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
- 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)

C. Contribution to Science

1. 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. 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., 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
 - b. 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
 - c. Dave, K. R., Bhattacharya, S. K., Saul, I., DeFazio, R. A., Dezfalian, 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). PMID:21789211
 - d. Dave, K. R., DeFazio, R. A., Raval, A. P., Torracco, 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
 - e. Perez-Pinzon, M. A., Xu, G. P., Born, J., Lorenzo, J., Busto, R., Rosenthal, M. & Sick, T. J. Cytochrome C is released from mitochondria into the cytosol after cerebral anoxia or ischemia. *J Cereb Blood Flow Metab* 19, 39-43, (1999). PMID:9886353
2. 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.

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 (2015). PMID:26159789

- a. 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
 - b. 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
 - c. DeFazio, R. A., Raval, A. P., Lin, H. W., Dave, K. R., Della-Morte, D. & Perez-Pinzon, M. A. GABA synapses mediate neuroprotection after ischemic and epsilon PKC preconditioning in rat hippocampal slice cultures. *J Cereb Blood Flow Metab* 29, 375-384, (2009). PMID:18957990
 - 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
3. Another 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. Dezfulian, C., Alekseyenko, A., Dave, K. R., Raval, A. P., Do, R., Kim, F. & Perez-Pinzon, M. A. Nitrite therapy is neuroprotective and safe in cardiac arrest survivors. *Nitric Oxide* 26, 241-250, (2012). PMID:22484664
 - d. 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
 - e. 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

Complete List of Published Work in My Bibliography:

<http://www.ncbi.nlm.nih.gov/sites/myncbi/miguel.perez-pinzon.1/bibliographay/40678659/public/?sort=date&direction=ascending>

D. Research Support

Ongoing Research Support

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 (Project Leader – Perez-Pinzon):** Enriched Environment, Exercise And Neurotherapeutics To Enhance Functional Recovery Following A Stroke

5R01NS073779-04 **Dave, Kunjan (PI) 3/1/12-12/1/16**

Increased cerebral ischemic injury by repeated hypoglycemic episodes in diabetes.

The long-term goal of this project is to improve neurological health of diabetics by decreasing the severity and incidence of cerebral ischemia in diabetics.

Completed Research Support (last 3 years)

None.

BIOGRAPHICAL SKETCH

NAME Alberto R. Ramos, MD	POSITION TITLE Assistant Professor of Neurology
eRA COMMONS USER NAME (credential, e.g., agency login) ARAMOS1	

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)	MM/YY	FIELD OF STUDY
University of Puerto Rico	BS	05/1999	Natural Sciences
Universidad Central del Caribe, PR. CUM LAUDE	MD	05/2003	Medical Doctor
Jackson Memorial Hospital-U. of Miami	Residency	06/2007	Neurology
Miami VA Health Care System-U. of Miami	Fellowship	06/2008	Sleep Medicine
University of Miami, Miller School of Medicine	MSPH	08/2012	Epidemiology

A. Personal Statement

Dr. Alberto Ramos' research focus is on sleep, aging and cerebrovascular disease. He was the recipient of a diversity research supplement grant in Health Related Research. This NIH/NINDS grant to the ongoing Northern Manhattan Study, studied the relationship between sleep and risk factors for stroke. Dr. Ramos was the site-principal investigator for the *Sueño study: Sleep Patterns as a Risk Factor for Disease in the Hispanic Community Health Study* – Field Center at the University of Miami. An NHLBI funded ancillary study to the Hispanic Community Health Study/Study of Latinos that evaluates sleep patterns and cardiovascular risk. Dr. Ramos is also the recipient of Mentored Translational Research Scholars Program (K12) from the Clinical Translational Institute (CTSI) at the Miller School of Medicine. The K12 study focused on cerebral hemodynamics as an early marker of cerebrovascular risk in sleep apnea in the Hispanic Community Health Study/Study of Latinos.

1. **Ramos AR**, Azizi A, Dib SI. Obstructive sleep apnea and stroke: links to health disparities. *Sleep Health: Journal of the National Sleep Foundation* 2015 (in press)
2. **Ramos AR**, Gangwisch J. Is Sleep Duration a Risk Factor for Stroke? *Neurology* 2015 17; 84:1066-1067. PMID:25716359
3. **Ramos AR**, Dib S, Koch S. Risk for Sleep Apnea among Caribbean Hispanics, non-Hispanic blacks and non-Hispanic whites with ischemic strokes. *Sleep Breath* 2014; 18:165-8. PMID:23771345
4. **Ramos AR**, Dib SI, Wright CB. Vascular Dementia. *Curr Transl Geriatr Exp Gerontol Rep* 2013; 2:188–195.
5. Wallace WK, **Ramos AR**, Rundek T. Sleep Disorders and Stroke. *Int J Stroke* 2012; 7:231-42. PMID:22336145
6. Dib S, **Ramos A**, Wallace D, Rundek T. Sleep and Stroke. *Periodicum Biologorum* 2013;114:369-75

B. Positions and Honors

Positions

2006-07	Administrative Chief Resident-Neurology, University of Miami/Jackson Memorial Hos., Miami, FI
2007-09	Staff Physician; Neurology Service, Miami VA Healthcare System, Miami, FI
2008-09	Instructor, Miller School of Medicine, University of Miami, Miami, FI
2009	Assistant Professor of Clinical Neurology, Miller School of Medicine, Miami, FI
2010	Co-Director, Sleep Medicine Program, Miller School of Medicine, Miami, FL

Honors

2003	Alpha Omega Alpha. Universidad Central Del Caribe, School of Medicine, PR
2007	Clinical Neuroscience Prize, Neurology Residency program, U. of Miami. Miami, FL
2008	Faculty Development Award-American Neurological Association.
2010-2014	Who's who in America
2010-2014	America's Top Physician, Consumer's Research Council of America.
2011	Distinguished Judge. Department of Otolaryngology, Miller School of Medicine. Miami, FL.
2012	NIH/American Academy of Sleep Medicine Young Investigators forum travel award.
2013	Scholar, Program to Increase Diversity among Individuals Engaged in Health-Related Research (PRIDE), NHLBI-New York University, NY.
2013	Fellow, American Academy of Sleep Medicine
2015	Diversity Leadership Development Program-American Academy of Neurology
2015	Peer Mentor, Programs to increase Diversity among individuals Engaged in Health Related Research (PRIDE), NHLBI-New York University, NY.
2015	Travel Award, U13 Conference Series: Sleep, Circadian Rhythms, and Aging: New Avenues for Improving Brain Health, Physical Health and Functioning. Supported by the National Institutes of Aging and the American Geriatric Society

C. Contribution to Science

My sleep research program investigates the health disparities and associations between poor sleep, cerebrovascular disease and neurocognitive function in epidemiological studies. I was initially evaluated the associations between subclinical cerebrovascular disease in a multiethnic cohort of the Northern Manhattan study. Along with my colleagues, we identified associations between snoring, sleep duration and daytime sleepiness with measures of subclinical vascular disease. This helped us identify race-ethnic differences and mechanisms by which sleep disruption may increase the risk of stroke.

1. **Ramos AR**, Dong C, Rundek T, Elkind ESV, Boden-Albala B, Sacco RL, Wrigth CB. Sleep Duration is associated with White Matter Hyperintensity Volume in Older Adults: The Northern Manhattan Study. *J Sleep Res* 2014; 23:524-30. PMID: 25040435
2. **Ramos AR**, Jin A, Rundek T, Russo C, Homma S, Elkind M, Sacco RL, Di Tullio MR. Relation between Long Sleep and Left Ventricular Mass from a Multi-Ethnic Elderly Cohort. *Am J Cardiol* 2013; 112:599-603. PMID: 23711813
3. **Ramos AR**, Cabral D, Lee DJ, Sacco RL, Rundek T. Cerebrovascular Pulsatility in Patients with Sleep Disordered Breathing. *Sleep Breath* 2013; 17:723-6. PMID: 22773271
4. **Ramos AR**, Wohlgemuth WK, Dong C, et al. Race-ethnic differences of sleep symptoms in an elderly multi-ethnic cohort: The Northern Manhattan Study. *Neuroepidemiology* 2011; 37:210-5. PMID:22123526
5. **Ramos AR**, Cabral D, Lee DJ, Sacco RL, Rundek T. Cerebrovascular Pulsatility in Patients with Sleep Disordered Breathing. *Sleep Breath* 2013; 17:723-6. PMID: 22773271
6. **Ramos-Sepulveda A**, Wohlgemuth W, Gardener H, Lorenzo D, Dib S, Wallace DM, Nolan B, Boden-Albala B, Elkind MS, Sacco RL, Rundek T. Snoring and insomnia are not associated with subclinical atherosclerosis in the Northern Manhattan Study. *Int J Stroke*. 2010; 5:264-8. PMID:20636708

My research on sleep health disparities led to collaborations with the investigators of the Hispanic Community Health Study/Study of Latinos (HCHS/SOL). I am a co-investigator of this large multicenter observational study of 16,415 Hispanic/Latinos in the US, which obtained sleep and its sleep ancillary study (Sueño) with the goal of identifying the prevalence and risk factors for diseases (e.g., stroke, sleep apnea) and to determine the role of health disparities in their development. The following publications shows the prevalence and determinants of sleep apnea with established vascular risk factors, along with novel associations between sleep disorders

determined with subclinical vascular disease, neurocognitive function, diet and other health outcomes in Hispanic/Latinos.

7. Cespedes EM, Hu FB, Redline S, Rosner B, Alcantara C, Cai J, Hall MH, Loredo JS, Mossavar-Rahmani Y, **Ramos AR**, Reid KJ, Shah NA, Sotres-Alvarez D, Zee PC, Wang R, Patel SR. Comparison of Self-Reported Sleep Duration with Actigraphy: Results from the Hispanic Community Health Study/ Study of Latinos Sueño Ancillary Study. *Am J of Epidemiology* 2015 (in press)
8. Mossavar-Rahmani Y, Jung M, Patel SR, Sotres-Alvarez D, Arens R, **Ramos A**, Redline S, Rock CL, Van Horn L. Eating behavior by sleep duration in the Hispanic Community Health Study/Study of Latinos. *Appetite*. 2015 95:275-284 PMID:26189885
9. Patel SR, Sotres-Alvarez D, Castañeda SF, Dudley KA, Gallo LC, Hernandez R, Medeiros EA, Penedo FJ, Mossavar-Rahmani Y, **Ramos AR**, Redline S, Reid KJ, Zee PC. Social and Health Correlates of Sleep Duration in a US Hispanic Population: Results from the Hispanic Community Health Study/Study of Latinos. **Sleep**. 2015 Jun 11. pii: sp-00591-14. PMID:26085298
10. Cespedes EM, Dudley KA, Sotres-Alvarez D, Zee PC, Daviglius ML, Shah NA, Talavera GA, Gallo LC, Mattei J, Qi Q, **Ramos AR**, Schneiderman N, Espinoza-Giacinto RA, Patel SR. Joint associations of insomnia and sleep duration with prevalent diabetes: The Hispanic Community Health Study/Study of Latinos (HCHS/SOL). *J Diabetes*. 2015 May 7. doi: 10.1111/1753-0407.12308. PMID: 25952169
11. Patel SR, Weng J, Rueschman M, Dudley KA, Loredo JS, Mossavar-Rahmani Y, Ramirez M, **Ramos AR**, Reid K, Seiger AN, Sotres-Alvarez D, Zee PC, Rui Wang, R. Reproducibility of a Standardized Actigraphy Scoring Algorithm for Sleep in a US Hispanic/Latino Population. *Sleep*. 2015 Mar 4. pii: sp-00708-14. PMID: 258456
12. Shah N, Allison M, Teng V, Wassertheil-Smoller S, Sotres-Alvarez D, **Ramos AR**, Zee P, Criqui M, Yaggi H, Gallo L, Redline S, Kaplan R. Sleep Apnea is Independently Associated with Peripheral Arterial Disease in the Hispanic Community Health Study/Study of Latinos. *Arterioscler Thromb Vasc Biol*. 2015 PMID:25657310
13. Redline S, Sotres-Alvarez D, Loredo 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; 189:335-44. PMID:24392863

Other publications:

14. **Ramos AR**, Tarraf W, Rundek T, Redline S, Wohlgemuth WK, Loredo JS, Sacco RL, Lee DJ, Arens R, Lazalde P, Choca JP, Mosely T, Gonzalez, HM. Obstructive Sleep Apnea and Neurocognitive Function among Hispanics/Latinos. *Neurology* 2015;84:391-398.PMID:2554030
15. Sanders AE, Essick GK, Beck JD, Cai J, Beaver S, Finlayson TL, Zee PC, Loredo J, **Ramos AR**, Singer RH, Jimenez MC, Redline S. Periodontitis and Sleep-disordered Breathing in the Hispanic Community Health Study/ Study of Latinos. *SLEEP*. 2014 PMID:25669183
16. **Ramos AR**, Wallace DM, Pandi-Perumal SR, Williams NJ, Castor C, Sevick MA, McFarlane SI, Girardin Jean-Louis G. Associations between sleep disturbances and diabetes mellitus among blacks with metabolic syndrome: results from the Metabolic Syndrome Outcome Study (MetSO). *Ann Med*. 2015 Apr 9:1-5.

17. Seixas A, **Ramos AR**, Gordon-Strachan GM, Fonseca VA, Zizi F, Jean-Louis G. Relationship between Visual Impairment, Insomnia, Anxiety/Depressive Symptoms among Russian Immigrants. *J Sleep Med Disord.* 2014;1. pii: 1009.PMID:26015992
18. **Ramos AR**, Wallace DM, Williams NJ, Spence DW, Pandi-Perumal SR, Zizi F, Jean-Louis G. Association between visual impairment and sleep duration: analysis of the 2009 National Health Interview Survey (NHIS). *BMC Ophthalmol* 2014 1; 14:115. PMID:25274449
19. **Ramos AR**, Dong C, Elkind MSV, 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 15; 9:669-673. PMID: 23853560
20. Shafazand S; Wallace DM; Vargas SS; Del Toro Y; Dib S; Abreu AR; **Ramos A**; Nolan B; Baldwin CM; Fleming L. Sleep disordered breathing, insomnia symptoms, and sleep quality in a clinical cohort of US Hispanics in South Florida. *J Clin Sleep Med* 2012; 8:507-514. PMID:23066361
21. Wallace DM, Shafazand S, **Ramos AR**, et al. Insomnia characteristics and clinical correlates in Operation Enduring Freedom/Operation Iraqi Freedom veterans with post-traumatic stress disorder and mild traumatic brain injury: An exploratory study. *Sleep Med.* 2011; 12:850-9. PMID:21925943
22. Reidy L, Nolan B, **Ramos AR**, Walls HC, Steele BW. Zolpidem Urine Excretion Profiles and Cross-Reactivity with ELISA(®) Kits in Subjects Using Zolpidem or Ambien(®) CR as a Prescription Sleep Aid. *J Anal Toxicol.* 2011; 35:294-301. PMID: 21619724
23. Liewluck T, Ferreira MA, Reyes-Iglesias Y, **Ramos AR**. Restless legs syndrome as an initial manifestation of metastatic conus medullaris lesion. *Mov Disord.* 2009. 15; 24:2294-6. PMID:19795474

D. Research Support

1. Sleep apnea and cerebral hemodynamics: The Hispanic Community Health Study.
National Institutes of Health, Clinical Translational Institute at the Miller School of Medicine, University of Miami, Miami, FL. Mentored Translational Research Scholars Program (K12) 5KL2TR000461-02. Role: scholar. 75% effort time. Aims: To evaluate the cerebral hemodynamics as an early marker of cerebrovascular risk in participants with sleep apnea and controls.

Completed:

1. Supplements to Promote Diversity in Health-Related Research-Stroke Incidence and Risk Factors in a Tri-Ethnic Region PI- Ralph L. Sacco; Agency: NIH/NINDS; Type: R37 (Javits Award): 2R01 (NS 29993). Supplement Grant for Alberto R. Ramos: Period 06.01.09-05.31.12. Aims: To investigate the associations between sleep symptoms and sub-clinical vascular disease in a prospective cohort of 3298 community subjects in the Northern Manhattan Study.
2. Sueño: Sleep patterns as a risk factor in the Hispanic Community Health Study.
PI: S. Patel.; Agency: NIH/ NINDS; Type RO1: HL098297.
Role: Site PI/Co-investigator. 10% effort time. Period 07.1.2011-04.31.2014. Aims: To determine the cardiovascular consequences of abnormal sleep patterns in Hispanics.

E. Other Support

1. National Institutes of Health/National Institute of Minority Health and Health Disparities-Loan Repayment Program. Two year extension, 08/2014-07/2016.
2. National Institutes of Health/National Institute of Minority Health and Health Disparities-Loan Repayment Program. One year extension, 08/2013-07/2014.

3. National Institutes of Health/National Institute of Minority Health and Health Disparities-Loan Repayment Program. One year extension, 08/2012-07/2013.
4. National Institutes of Health/National Institute of Minority Health and Health Disparities-Loan Repayment Program. Period 08/2010- 07/2012.

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 Ami P. Raval		POSITION TITLE Research Assistant 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 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. 07/1994 to 11/2000
- Assistant scientist: University of Miami, U.S.A. 9/1/2003 – 12/31/2006
- Research Assistant Professor: University of Miami, U.S.A. 2/1/2006 - Present
- 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 2013-Present

Honors, Awards, and Professional Societies:

- 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

- Member of the Society for Neuroscience.
- Member of the Society for Cerebral Blood Flow & Metabolism.

C. Contribution to Science

1. 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.

- 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.
- 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)
- 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)
- 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.

2. 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.

- 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.
- 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
- Raval AP****, Saul I, Dave KR, DeFazio1 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)
- Raval AP****, Bramlett H, Perez-Pinzon MA. Estrogen preconditioning protects the hippocampal CA1 against ischemia. *Neuroscience*. 2006; 141(4):1721-30.

3. 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 17 β -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. **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
- b. **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
- c. **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.
- d. **Raval AP****. Nicotine addiction causes unique detrimental effects on female brain. *Journal of Addictive Diseases. Review.* 2011; 30:149–158

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* 2015; In press

Complete List of Published Work in My Bibliography:

<http://www.ncbi.nlm.nih.gov/pubmed/?term=raval+ap>

D. Active Support

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

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)

Completed Research Support (past 3 years):

Florida Department of Health#09KN-14

07/1/11-06/30/14

Intra-arterial mesenchymal stem cell delivery in a canine model of acute ischemic stroke.

Principal Investigator: Dr. Dileep Yavagal

Role: Co-investigator (5% effort)

American Heart Association- Grant-in-aid

AHA # 11GRNT7370069

7/1/11- 6/30/2013

Nicotine inhibits estrogen-mediated synaptic plasticity after cerebral ischemia in female rat.

The major goal of this project is to study the effects of chronic nicotine usage on synaptic functions in female rats. There is no scientific/ financial overlap between NIH-R01 application under consideration and the funded AHA-grant-in-aid.

Role: Dr. Raval, PI, % efforts 25%

University of Miami Specialized Center Of Research on Addiction & Health in Women,
Adolescents (UM-SCOR)

Children &

10/1/2011-3/31/2013

Nicotine inhibits estrogen-mediated synaptic plasticity after cerebral ischemia in female rat

Role: PI, no % efforts

University of Miami, Stanley J. Glaser Foundation Award
UM 700852

6/1/11 - 12/31/12

Nicotine impairs hippocampal mitochondrial function in female rat.

This is a seed funding from University of Miami to generate pilot data for future federal funding. The major goal of this project is to study the effects of chronic nicotine exposure on mitochondrial function in hippocampus of female rats.

Role: Dr. Raval, PI, no % efforts

American Heart Association- Scientist Development Grant (National center)
AHA # 0730089N

1/1/11-12/31/11

Estrous cyclicity and mechanism of neuroprotection after cerebral ischemia.

The major goal of this project was to study the effects of endogenous estrogen fluctuations on neuroprotection against cerebral ischemia in normal cyclic rats.

Role: Dr. Raval, PI, % efforts 39%

Florida Department of Health
#07KN-10

7/1/07-6/30/10

Inhibitory effects of nicotine on estrogen-induced natural hippocampal neuroprotection against ischemia

The major goal of this project was to study the effects of chronic nicotine usage and female sex hormones on cerebral ischemic outcomes.

Role: Dr. Raval, PI, % efforts 50%

NIH/NINDS

1R01NS054147-01A1

Dr. Pérez-Pinzón, P.I.

7/06/06- 5/31/10

Mitochondria and Cerebral ischemia: intracellular signaling

The major goal of this project was to study the mechanisms by which ϵ PKC protect neuronal mitochondria whereas δ PKC promotes cell death after cerebral ischemia.

Role: Dr. Raval, Co-investigator % efforts 6%

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 and Public Health Sciences, Director of Clinical Translational Research Division, University of Miami Miller School of Medicine (UMMSM)**

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 am dedicated to mentoring and research as a part of the McKnight research program at the University of Miami (UM). As a Vice Chair of Clinical Research and Director of the Clinical Translational Research Division in Neurology, and a PI of two NIH/NINDS R01 grants and Co-I of several R01s I have been providing research environment and research training in vascular neurology and epidemiology for many graduate and post-graduate trainees over the course of my career. I am also a program Director of a UM Miller School of Medicine MS in Clinical Translational Investigations. I am a Training Director of the NINDS StrokeNet and NeuroNext (1 trainee/year) and Miami AHA Bugher Stroke Center (2 trainees/year). I also have a NINDS K24 training grant that allows protected time for research and mentorship. 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, 14 completed their MD, PhD, MS or MPH degrees during my mentorship and obtained NIH grants or other awards. I have been a productive investigator with over 270 publications with extensive collaborations with various research teams at Columbia University on large NIH-funded population based studies (NOMAS, INVEST, CABLE, PHPT, U01 eMERGE) and Albert Einstein in NY. I am a collaborator and site investigator of the large international stroke genetic and atherosclerosis projects and consortia (NINDS SiGN, ISGC, PROG-IMT). I was recently awarded a 3-year AHA Mentor grant to mentor 2 trainees nationally for 3 years.

These four peer reviewed publications highlight my experience and qualifications:

1. Luca CC, **Rundek T**. Parkinsonism, small vessel disease, and white matter disease: Is there a link? *Neurology*. 2015;85(18):1532-3. PMID: 26446067
2. Tietjen GE, **Rundek T**. Migraine and cryptogenic stroke: The clot thickens. *Neurology*. 2015;85(17):1436-7.
3. Gardener H, Wright CB, **Rundek T**, Sacco RL. Brain health and shared risk factors for dementia and stroke. *Nat Rev Neurol*. 2015;11(11):651-7.
4. Tiozzo E, Youbi M, Dave K, Perez-Pinzon M, **Rundek T**, Sacco RL, Loewenstein D, Lewis JE, Wright CB. Aerobic, Resistance, and Cognitive Exercise Training Poststroke. *Stroke*. 2015;46(7):2012-6.
5. **Rundek T**, Brown DL. Socioeconomic status and subclinical atherosclerosis: are we closing disparity gaps? *Stroke*. 2014;45(4):948-9. PMID: 24578211
6. Gordon-Perue G, **Rundek T**. Are prehospital stroke scales better than a coin toss at predicting acute stroke? *Neurology*. 2014;82(24):2154-5. PMID: 24850489
7. **Rundek T**, Sacco RL. Comment: New models of successful academic mentoring. *Neurology* 2011; 77(7):688.

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, Univ. of Miami, Miami, FL
2011-	Professor of Neurology (with tenure)	Miller School of Medicine, Univ. of 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, Univ. of Miami, Miami, FL
2010-	Vice Chair, Clinical Translational	Miller School of Medicine, Univ. of Miami, Miami, FL
2014-	Director, MS Clinical Translational	Miller School of Medicine, Univ. of 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. Epidemiology of stroke and atherosclerosis. Over the past 20 years I have pursued research in stroke epidemiology. The central findings from this research include the discovery of novel risk stroke 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 and contributed significantly to the literature on PFO in CVD. Our group was the first to report that atorvastatin reduces the serum coenzyme Q10 levels linking it to muscle pain. I am a strong believer in team science and many of my research products are the results of multiple collaborations between various national and international research teams and institutions.

1. **Rundek T**, Gardener H, Xu Q, Goldberg R, Wright C, Boden-Albala B, Disla N, Paik M, Elkind MSV, Sacco RL. Insulin Resistance and Risk of Ischemic Stroke Among Nondiabetic Women from the Northern Manhattan Study. **Arch Neurol.** 2010;67:1195-200. PMC2954671
2. **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. PMC2737546
3. **Rundek T**, Sacco RL. Outcome following stroke. In "Stroke- Pathophysiology, Diagnosis, and Management". Editors: J.P. Mohr, D.W. Choi, J.C. Grotta, B. Weir, P.A. Wolf; Fourth edition, Churchill Livingstone, Elsevier Inc.; Chapter 2: 58-67, 2011.
4. **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; 61:889-892. PMC15210526

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 sleep breathing disorders, vascular cognitive impairment, memory loss and dementia. I have been an active member of IAC (Intersocietal Accreditation Committee), the largest US accreditation body that sets the standards for performance of clinical ultrasound, CT/MRI and cardiac Echo. I have been an advocate for advancing quality and access to clinical ultrasound in medicine.

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. PMC3738011
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. PMC2831775
3. Lorenz MW, Polak JF, Kavousi M, Mathiesen EB, Völzke H, Tuomainen TP, Sander D, Plichart M, Catapano AL, Robertson CM, Kiechl S, **Rundek T**, Desvarieux M, Lind L, Schmid C, DasMahapatra P, Gao L, Ziegelbauer K, Bots ML, Thompson SG; **PROG-IMT Study Group**. Carotid intima-media thickness progression to predict cardiovascular events in the general population (the PROG-IMT collaborative project): a meta-analysis of individual participant data. *Lancet*. 2012;379(9831):2053-62. PMC3918517
4. Den Ruijter HM, Peters SA, Anderson TJ, Britton AR, Dekker JM, Eijkemans MJ, Engström G, Evans GW, de Graaf J, Grobbee DE, Hedblad B, Hofman A, Holewijn S, Ikeda A, Kitagawa K, Kitamura A, Koffijberg H, Lonn EM, Lorenz MW, Mathiesen EB, Nijpels G, Okazaki S, O'Leary DH, Polak JF, Price JF, Robertson C, Rembold CM, Rosvall M, **Rundek T**, Salonen JT, Sitzer M, Stehouwer CD, Wittteman JC, Moons KG, Bots ML. Common carotid intima-media thickness measurements in cardiovascular risk prediction: a meta-analysis. *JAMA*. 2012;308(8):796-803. PMC4523149

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-investigator 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.

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. PMC2692936
2. Dong C, Della-Morte D, Wang L, Cabral D, Beecham A, McClendon MS, Luca CC, Blanton SH, Sacco RL, **Rundek T**. Association of the sirtuin and mitochondrial uncoupling protein genes with carotid plaque. *PLoS One*. 2011;6(11):e27157. PMC3210138
3. Battey TW, Valant V, Kassis SB, Kourkoulis C, Lee C, Anderson CD, Falcone GJ, Jimenez-Conde J, Fernandez-Cadenas I, Pare G, **Rundek T**, James ML, Lemmens R, Lee TH, Tatlisumak T, Kittner SJ, Lindgren A, Mateen FJ, Berkowitz AL, Holliday EG, Majersik J, Maguire J, Sudlow C, Rosand J; International Stroke Genetics Consortium. Recommendations from the international stroke genetics consortium, part 2: biological sample collection and storage. *Stroke*. 2015;46(1):285-90. PMC4276505
4. Meschia JF, Arnett DK, Ay H, Brown RD Jr, Benavente OR, Cole JW, de Bakker PI, Dichgans M, Doheny KF, Fornage M, Grewal RP, Gwinn K, Jern C, Conde JJ, Johnson JA, Jood K, Laurie CC, Lee JM, Lindgren A, Markus HS, McArdle PF, McClure LA, Mitchell BD, Schmidt R, Rexrode KM, Rich SS, Rosand J, Rothwell PM, **Rundek T**, Sacco RL, Sharma P, Shuldiner AR, Slowik A, Wassertheil-Smoller S, Sudlow C, Thijs VN, Woo D, Worrall BB, Wu O, Kittner SJ; NINDS SiGN Study. Stroke Genetics Network (SiGN) study: design and rationale for a genome-wide association study of ischemic stroke subtypes. *Stroke*. 2013;44(10):2694-702. PMCID: PMC4056331

Complete List of Published Work in MyBibliography:

<http://www.ncbi.nlm.nih.gov/pubmed/?term=rundek>

<http://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:

Ongoing Research Support

Novel Factors for Unexplained Phenotypes of Subclinical Carotid Atherosclerosis NIH/NINDS R01 NS 065114 (no cost extension)

PI: T. Rundek

07.01.10-06.30.16

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.

Genetic Determinants of Extreme Phenotypes of Subclinical Atherosclerosis NIH/NINDS K24 NS 062737 (no cost extension)

PI: T. Rundek

09.30.09-08.31.16

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.

Stroke Incidence and Risk Factors in a Tri-Ethnic Region NIH/NINDS R37 NS 029993-11

PI: RL. Sacco; T. Rundek, Co-Investigator

02.01.03-01.31.20

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.

Family Study of Stroke Risk and Carotid Atherosclerosis NIH/NINDS R01 NS 40807

PI: RL. Sacco; T. Rundek, Co-Investigator

05.01.02-09.30.17

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.

University of Miami: Network of Excellence in Neuroscience Clinical Trials (NeuroNEXT) NIH/NINDS U10 NS 077423

PI: M. Benatar, R.L. Sacco; T. Rundek, Co-Investigator

09.30.11-08.31.18

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.

Ischemic Stroke Genetics

NIH/NINDS U01 The NINDS International Stroke Genetics Consortium Study

PI: S. Kittner, U Maryland; T. Rundek, Site PI

04.01.10-3.31.16

This is a GWAS, which will greatly advance the field of ischemic stroke genetics by establishing a large 11-study collaboration of unique scale to bring together the world's leading clinician-scientists in stroke genetics.

The Albert Einstein Study Program Project in Aging NIH/NIA 2P01 AG003949-26

PIs: Lipton, Derby; Albert Einstein, NY; T. Rundek, PI of TCD Core Laboratory

07.1.11-

06.30.16

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.

Oral Infections, Carotid Atherosclerosis and Stroke (INVEST) NIH/NIDCR R01 DE 13094

PI: M. Desvarieux; T. Rundek, Co-Investigator

06.15.06-05.31.17

This cohort study will examine the effect of chronic periodontal disease and inflammation as a risk factor for stroke and carotid atheroma progression.

FGF-23 and the Risk of Stroke and Cognitive Decline

NIH/NHLBI R01 HL108623-01A1

PI: C. Wright; T. Rundek, Co-Investigator

12.01.12-11.30.16

We anticipate that the results of this study, in concert with our ongoing projects on FGF23 in more advanced CKD, will rapidly set the stage for randomized controlled trials.

Stroke Prevention/Intervention Research Program in Hispanics

NIH/NINDS U54 NINDS SPIRP U54NS081763

PI: RL Sacco; T. Rundek, PI of Core C and PI of Supplement- Stroke Outcome in Women 01.01.13-12.31.17

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

Miami Regional Coordinating Center for NINDS Stroke Trials Network

NIH/NINDS U10 NS086528

PI: J Romano; T. Rundek, Co-Investigator

09.30.13-07.31.18

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.

Mechanisms of Early Recurrence in Intracranial Atherosclerotic Disease (MyRIAD)

NIH/NINDS R01 NS084288-01A1

PI: J Romano; T. Rundek, Co-Investigator

04.01.14-03.31.19

The objective of this proposal is to determine the mechanisms and predictors of stroke in patients with symptomatic Intracranial Atherosclerotic Disease.

Hispanic Community Health Study-Study of Latinos (HCHS-SOL) Miami Field Center

NIH/NHLBI N01-HC65234

PI: N. Schneiderman; T. Rundek, Adjudication Core investigator

06.01.14-05.31.19

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.

AHA-ASA/Bugher Foundation Center of Excellence in Stroke Collaborative Research

AHA14BFSC17690000

PI: RL. Sacco; T. Rundek, Training Director

04.01.14-03.31.18

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.

NCRP Winter 2015 Mentor / AHA Mentee Award

AHA 15MM26340000

PI: T. Rundek, Mentor

07.01.15-06.30.18

This awards supports Dr. Rundek's mentorship activities for 2 AHA fellows (from John Hopkins & UT Huston).

Prior Research Support (prior 5 years)

Genetic Determinants of Subclinical Carotid Disease; NIH/NINDS R01 NS 047655

PI: T. Rundek

01.01.04-12.31.11

This was a cross-sectional study evaluating potential candidate genes related to carotid IMT and distensibility in the Northern Manhattan Study cohort.

Gene-Smoking Interactions and Atherosclerosis; KN01 James & King Biomedical Research

PI: C. Dong; T. Rundek, Co-Investigator

09.01.11-08.31.14

The major goal of this project is to identify genetic variants that modify the effect of smoking on the development of atherosclerosis and the risk of clinical vascular diseases.

Primary Hyperparathyroidism: Non-Classical Manifestations; NIH/NIDK R01 DK 66329

PI: S. Silverberg; T. Rundek, Co-Investigator

7.01.05-06.30.11

The main objective of this study was to determine whether there was structural and functional evidence of increased vascular stiffness or cardiovascular calcification in patients with mild asymptomatic PHPT.

Aortic, Cardiovascular Disease and Silent Brain Infarcts; NIH/NINDS R01 NS 36286

PI: M. Di Tullio; T. Rundek: Co-Investigator

7.01.05-06.30.11

The objective of this study was to investigate cardiac sources of silent brain infarcts and cerebral white matter disease.

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 will 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, University of Miami. My clinical translational research interests include epidemiology, diagnosis, prevention, genetic, and treatment studies of stroke, cognitive impairment, and other cardiovascular conditions. I have an extensive research track record in stroke clinical trials and disparities research. I have successfully applied and managed large collaborative research programs at Columbia University and the University of Miami. For the past 23 years, I have been the PI of the Northern Manhattan Study, a NINDS-funded community-based, epidemiologic cohort study designed to evaluate the determinants of stroke and cognitive impairment among an elderly, multi-ethnic, urban population living in northern Manhattan. This study also includes a separate NINDS-funded project, the Family Study, to evaluate genetic determinants of atherosclerosis. I am PI of the NINDS U54 Stroke Prevention and Intervention Research Program to support the Florida Puerto Rico Stroke Registry and reduce stroke disparities, and founding PI of the NY Columbia Collaborative Specialized Program in Translational Research in Acute Stroke. I continue to lead and engage in large preventive trials and national and international consortia sponsored by industry and NIH. I have published extensively with over 570 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 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, and have lectured extensively at national and international conferences. 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. I am dedicated to improving efficiency in the design and implementation of randomized trials as co-PI for our Neuro-NEXT and Stroke-NET regional coordinating centers for NINDS trials. As former president of the American Heart Association and president-elect of the American Academy of Neurology, I have been and continue to be fully committed to advancing scientific collaborations and building partnerships for translational 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

Academic Appointments:

89-97	Assistant Professor of Neurology & Public Health (Epidemiology) in the Sergievsky Center
97-02	Associate Professor of Neurology & Public Health (Epidemiology) (with tenure)
03-07	Professor of Neurology & Epidemiology, Columbia University, College of Physicians and Surgeons, Mailman School of Public Health, and the Sergievsky Center (with tenure)
07-	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

Honors:

1982	Alpha Omega Alpha	2001	Fellow of the American Heart Association
1998	American Neurological 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

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 AAN, Vice President
2013-15	AAN, President-elect

C. Contribution to Science

C.1. 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-PI 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, Öunpuu 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.2. Health Disparities As Principal Investigator for both a 23-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**, Kargman DE, Gu Q, Zamanillo MC. Race-ethnicity and determinants of intracranial atherosclerotic cerebral infarction: the Northern Manhattan Stroke Study. **Stroke** 1995;26:14-20
2. **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
3. **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
4. 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

C.3. 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.

C.4. Epidemiology of stroke. Over the past 30 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 PMID: PMC2812026

C.5. Genetic contribution to atherosclerosis and stroke. As Principal Investigator of a family study for the past 10 years, I have been investigating the genetic contributions to carotid disease. Through this work, extensive data for quantitative traits in family linkage studies, genome wide association studies, fine-mapping studies, and extreme phenotypes for carotid atherosclerosis and other cardiovascular traits has been evaluated. The results of these investigations are now contributing novel observations for future targeted therapies and prevention of CVD.

1. Juo SH, Lin HF, Rundek T, Sabala EA, Boden-Albala B, Park N, Lan MY, **Sacco RL**. Genetic and Environmental Contributions to Carotid Intima-Media Thickness and Obesity Phenotypes in the Northern Manhattan Family Study. **Stroke** 2004;35:2243-7
2. **Sacco RL**, Blanton SH, Slifer S, Beecham A, Glover K, Gardener H, Wang L, Sabala E, Juo SH, Rundek T. Heritability and linkage analysis for carotid intima-media thickness: the Family Study of Stroke Risk and Carotid Atherosclerosis. **Stroke**. 2009; 40:2307-12. PMID: PMC2737512.
3. Wang L, Di Tullio MR, Beecham A, Slifer S, Rundek T, Homma S, Blanton SH, **Sacco RL**. A comprehensive genetic study on left atrium size in Caribbean Hispanics identifies potential candidate genes in 17p10. **Circ Cardiovasc Genet**. 2010; 3:386-92. PMID: PMC2923674
4. Dong C, Beecham A, Slifer S, Wang L, Blanton SH, Wright CB, Rundek T, **Sacco RL**. Genomewide linkage and peakwise association analyses of carotid plaque in Caribbean Hispanics. **Stroke**. 2010; 41:2750-6. PMID: PMC3004531.

Complete List of Published Work in My Bibliography: http://www.ncbi.nlm.nih.gov/pubmed/?term=sacco_rl

D. Current Research Support

Stroke Incidence and Risk Factors in a Tri-Ethnic Region

Role: PI; Agency: NIH/NINDS; Type: R37 (formerly 2R01) (NS 29993); Period: 01.01.93-07.31.20

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.

Family Study of Stroke Risk and Carotid Atherosclerosis

Role: PI; Agency: NIH/NINDS; Type: 1R01 (NS 240807); Period: 05.01.02-08.30.17

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.

Hispanic Stroke Prevention Intervention Research Program

Role: PI; Agency: NIH/NINDS; Type: U54 (NS 081763); Period: 01.01.13-12.31.17

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

AHA/ASA Bugher Center Foundation Center of Excellence in Stroke Award

Role: Center Director; Agency: AHA Period: 04.01.14-03.31.18

Aims: To conduct two projects evaluating the effects of physical activity and cognitive training on animals and stroke survivors on cognitive recovery.

Miami Regional Coordinating Center for NINDS Stroke-NET

Role: Co-PI Agency: NIH/NINDS; Type U10 NS086528 (Romano) Period: 09.01.13-08.31.18

Aims: The goals of the Miami RCC are to implement high-quality research clinical trials that address acute stroke treatment, prevention and recovery.

NSTN National Clinical Coordinating Center Stroke NET

Role: Prevention, Co-chair, Co-I; Agency: NIH/NINDS; Type: 1U01NS086872 (Broderick) Period: 10.01.13-09.30.18

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.

Oral Infections, Carotid Atherosclerosis and Stroke

Role: Co-PI; PI: Desvarieux; Agency: NIH/NIDCR; Type: 1R01 (DE 13094); Period: 07.01.00-12.31.15

Aims: To determine the effect of chronic periodontal disease and inflammation as a risk factor for stroke and carotid atheroma progression in a subset of the NOMAS cohort.

University of Miami: Network of Excellence in Neuroscience Clinical Trials (NEXT)

Role: PI (dual); Agency: NIH/NINDS; Type: U10 (NS077423); Period: 09.30.2011-08.31.2018

Aims: The goals of this proposal are to function effectively as a Neuro-NEXT NINDS consortium trial site

Physical activity patterns via new dimension-informative cluster models

Role: Co-I; PI: Paik/Cheung; NIH/NHLBI; Type: R01 HL111195-01A1; Period: 07.01.12-06.30.16

Aims: The goals of the project are to develop new cluster analysis methods for physical activity data from questionnaire and the accelerometry, and validate utility of the identified patterns

Hispanic Community Health Study/Study on Latinos: Miami Field Center

Role: Co-I; PI: Schneiderman; Agency: NIH/NHLBI; Type: Contract; Period: 09.30.06-03.31.16

Aims: To determine the role of acculturation in the prevalence and development of disease, and to identify risk factors playing a protective or harmful role in Hispanics/Latinos.

Clinical and Translational Science Award

Role: Co-I; PI: JSzapocznik; Agency: NIH/NCRR/NIMHD; Type: UL1TR000460; Period: 07/01/12-6/30/17

Aim: To build research capacity and facilitate translational research at University of Miami.

Hispanic Secondary Stroke Prevention Initiative (HISSPI)

Role: Co-I; PI: Carrasquillo; Agency: NIH/NIMD; Type: R01MD009164; Period: 07.10.14-03.31.19

Aim: To reduce the risk for a recurrent stroke among Latinos at high risk for a second and potentially much debilitating stroke.

Prevalence and predictors of asymptomatic atrial fibrillation in the community

Role: Co-I; PI: di Tullio; Agency: NIH/NIMD; Type: R01NS083784; Period: 04.01.14-01.31.19

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.

FGF-23 and the Risk of Stroke and Cognitive Decline

Role: Co-I; PI: Wright; Agency: NIH/NHLBI; Type: R01 HL108623-01A1; Period: 03.16.12-02.29.16

Aims: To evaluate the role of FGF23 in stroke and cognitive decline in the NOMAS cohort.

Novel Factors for Unexplained Phenotypes of Carotid Atherosclerosis

Role: Co-I; PI: TRundek/SBlanton; Agency: NIH/NINDS; Type: R01 (NS 065114); Period: 07.01.10-06.30.16

Aims: This is a genetic study to help uncover genetic factors related to unexplained extreme carotid phenotypes within the Northern Manhattan Study cohort using extreme phenotypes.

BIOGRAPHICAL SKETCH

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

NAME: Xiaoyan Sun	POSITION TITLE Assistant Professor at Dept. of Neurology, University of Miami Miller School of Medicine		
eRA COMMONS USER NAME (credential, e.g., agency login)			
EDUCATION/TRAINING (<i>Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.</i>)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	MM/YY	FIELD OF STUDY
Xi'an Medical College (Present name: School of Medicine of Xi'an Jiaotong University, China)	M.D.	08/1984	Medicine
Gunma University School of Medicine (Japan)	Ph.D.	03/1996	Biochemistry/ Neuroscience

A. Personal statement

I started my medical career as a neurologist in China. I obtained my Ph.D in neuroscience in Japan. In 2012, I finished Neurology residency from Medical University of South Carolina in United States. In 2014, I completed behavioral neurology fellowship in VA Boston Healthcare System. I am a board certified neurologist and fully trained neuroscientist. I am an assistant professor in the Department of Neurology, University of Miami Miller School of Medicine.

My previous research activities were composed of basic science and clinical research. I was involved in characterizing biochemical properties of tau protein in the axonal transport and roles of amyloid protein in Alzheimer's disease in cellular and animal models. My clinical research has been involved in identifying clinical biomarkers for diagnosis of AD including plasma amyloid ELISA, ApoE 4 genotyping and neuroimaging study in Alzheimer's disease. I am one of the earliest scientists who developed amyloid ELISA. My previous research experience and current position have provided a solid foundation to study in vivo detection of pathological changes in the patients with cognitive disorders.

- 1 Beglopoulos V*, **Sun X.***, Saura R., Kim R., and Shen J. Reduced amyloid production and increased inflammatory responses in presenilin conditional knockout mice. J Biol Chem. 2004 Nov 5; 279 (45): 46907-14 (*equal contribution)
- 2 **Sun X**, Bhadelia R, Liebson E, Bergethon P, Folstein M, Zhu JJ, Mwamburi DM, Patz S, Qiu WQ. The relationship between plasma amyloid- β peptides and the medial temporal lobe in the homebound elderly. Int J Geriatr Psychiatry. 2011 Jun;26(6):593-601
- 3 **Sun X**, Steffens D.C., AU R., Folstein M., Summergrad P., Yee J., Rosenberg I., Mwamburi D.M., Qiu W.Q.. Amyloid-associated depression: a prodromal depression of Alzheimer disease? Arch Gen Psych 2008, 65: 542-50
- 4 **Sun X**, Nicholas J., Walker A., Wagner M., and Bachman D. APOE genotype in the diagnosis of Alzheimer's disease in the patients with cognitive impairment. American Journal of Alzheimer's disease and other dementia. 2012 Aug; 27 (5):315-20.
- 5 **Sun X**, Dong C, Levin B, Crocco E, Loewenstein D, Zetterberg H, Blennow K, Wright CB, and the Alzheimer's Disease Neuroimaging Initiative. APOE ϵ 4 carriers may undergo synaptic damage conferring risk of Alzheimer's disease. Alzheimer's & Dementia in revision 2015

B. Positions and Honors

Positions and Employment

1983.9-1984.8	Intern, Shanxi Provincial People's Hospital, China
1984.9-1989.6	Resident Doctor, Dept. Neurology, Qinghai Provincial People's Hospital, China
1989.7-1990.9	Attending Doctor, Dept. Neurology, Qinghai Provincial People's Hospital
1990.10-1996.3	Foreign Clinical Practitioner and Ph.D. student, Dept. Neurology, Gunma University School of Medicine, Japan
1996.5-1998.3	Postdoctoral Fellow, Dept. Medicine, UCLA, Los Angeles, CA
1998.7-2002.8	Staff Scientist, Brain Science Institute of RIKEN, Japan
2002.8-2004.7	Postdoctoral Fellow, Dept. of Neurology, Center for Neurological Disease, Brigham and Women's Hospital, Harvard University School of Medicine, Boston, MA
2004.8-2008.6	ELISA Consultant, Center for Neurological Disease, Harvard University School of Medicine, Boston, MA
2004.8-2008.6	Clinical Research Fellow, Dept. of Psychiatry, New England Medical Center and School of Nutrition Science and Policy, Tufts University, Boston, MA
2008.7-2012.6	Resident, Dept. of Neurology, Medical University of South Carolina, Charleston, SC
2012.6-2014.6	Geriatric/behavioral Neurology fellow, Boston VA Medical Center, Boston, MA
2013.8-2014.6	Assistant professor in Dept of Neurology, Boston University School of Medicine, Boston, MA
2014.10-present	Assistant professor in Dept of Neurology, University of Miami Miller School of Medicine, Miami, FL
2014.10-present	Education director for McKnight Brain Institute of University of Miami Miller School of Medicine, FL

Other Experience and Professional Memberships

1987.5	Psychometrics short course certificate, Macquarie University, Australia
2010-Present	Member of American Academy of Neurology since 2010
2012.9	Board Certified Neurologist #57885
2012-present	South Carolina Medical License # 30195
2012-present	Massachusetts Medical License # 251388
2014-present	Florida Medical License # ME121152

Honors

1987.2-1987.5	Clinical Fellowship, The Iodine Deficient Disorder (IDD) Project Between China And Australia
1990.10-1991.9	Clinical Fellowship of Neurology, Sasakawa Foundation, Japan
1992.4-1996.3	Japanese Government Scholarship for Ph.D. Course, Japan
1996.8	Travel Award 5th International Alzheimer's Disease Conference, Japan
1996-1997	Staff Incentive Award for Exceptional Performance and Valuable Contribution, Dept. Medicine, UCLA, USA
2002-2003	Sabbatical Program In Drug Discovery, HCNR of Harvard Medical School, USA
2010.5	Best Case Presentation Award, Dept. of Neuroscience, Medical University of South Carolina

C. Contribution to Science

1. Much of my effort in the research of Alzheimer's disease has been made to identify the biomarkers for the early diagnosis of Alzheimer's disease. I am one of the earliest researchers who established one of the most sensitive amyloid Sandwich ELISA in the field. By using this ELISA, my collaborators and I published more than 10 papers to address amyloid production, degradation and regulation in cellular and mouse models.

- a. **Sun X.**, Cole GM, Chu T., Xia W., Galasko D., Yamaguchi H., Frautschy SA, and Takashima A. Intracellular A-beta is increased by okadaic acid exposure in the transfected neuronal and non-neuronal cell lines *Neurobiol. of Aging* 2002; 23:195-203
 - b. **Sun X.**, Sato S., Murayama O., Murayama M., Park J.-M., Yamaguchi H., and Takashima A. Lithium inhibits amyloid secretion in the cells transfected with amyloid precursor protein C100 *Neurosci Lett* 2002; 321:61-64
 - c. Xia X., Wang P., **Sun X.**, Soriano S., Shum W.-K., Yamaguchi H., Trumbauer ME., Takashima A., Koo EH., and Zheng H. The Aspartate 257 of presenilin 1 is indispensable for mouse development and Abeta production through beta-catenin independent Mechanisms *Proc. Natl. Acad. Sci. USA* 2002; 99:8760-8765
 - d. Leissring M.A., Farris W., Chang A.Y., Walsh D.M., Wu X., **Sun X.**, Frosch M.P., Selkoe D.J. Enhanced proteolysis of beta-amyloid in APP transgenic mice prevents plaque formation, secondary pathology, and premature death. *Neuron*. 2003 Dec 18; 40(6):1087-93
 - e. Qiu W.Q., *, **Sun X.**, *, Selkoe D.J., Mwamburi D.M., Huang T., Bhadela R., Bergethon P., Scott T.M., Summergrad P., Wang L., Rosenberg I., and Folstein M. . Depression is Associated with Low Plasma Ab42 Independently of Cardiovascular Disease in the Homebound Elderly. *Int J. Ger Psych*, Nov. 6, 2006 (*equal contribution)
2. Evaluation of the different biomarkers in the early diagnosis of Alzheimer's disease is my research focus of Alzheimer's disease. Accurate diagnosis of Alzheimer's disease at the early stage of the disease potentially benefits the treatment of patient if disease-modifying drugs become available. Besides development of amyloid Sandwich ELISA, I have investigated the application of ApoE genotyping and brain MRI in the clinical diagnosis of Alzheimer's disease. I demonstrate that ApoE genotyping is useful for the patients with early onset and atypical presentation of Alzheimer's disease.
- a. **Sun X.**, Nicholas J., Walker A., Wagner M., and Bachman D. APOE genotype in the diagnosis of Alzheimer's disease in the patients with cognitive impairment. *American Journal of Alzheimer's disease and other dementia*. 2012 Aug; 27 (5):315-20.
 - b. **Sun X.**, Salat D, Upchurch K, Deason R, Kowall N, Budson A; Alzheimer's Disease Neuroimaging Initiative. Destruction of white matter integrity in patients with mild cognitive impairment and Alzheimer disease. *2014 J Investig Med*. 2014 Oct;62(7):927-33
3. Association of amyloid with cognition in Alzheimer's disease is a key question in the research of Alzheimer's disease. Two of my studies have addressed this question. One of my studies shows visual spatial memory is decreased in the presenilin 1 mutation knock-in mice. Those mice had elevated amyloid 42 in the brain extract while there is no evidence of amyloid deposition in the mice brain. This finding suggests that cognitive impairment might be associated with elevated soluble amyloid 42 in the mice brain. Another study demonstrates that the ratio of plasma amyloid 42 to amyloid 40 is correlated with memory test score in the home-bound elderly with depression.

- a. **Sun X.***, Beglopoulos V*, Mattson M, Shen J. Hippocampal Spatial Memory Impairments Caused by the Familial Alzheimer's Disease-linked Presenilin 1 M146V Mutation Neurodegenerative Dis 2005; 2:6-15
 - b. **Sun X.**, Steffens D.C., AU R., Folstein M., Summergrad P., Yee J., Rosenberg I., Mwamburi D.M., Qiu W.Q.. Amyloid-associated depression: a prodromal depression of Alzheimer disease? Arch Gen Psych 2008, 65: 542-50
4. My early work was involved in understanding the biological properties of tau protein and regulation of amyloid protein in cellular and animal models. After highly phosphorylated tau protein was found to be a component of neurofibrillary tangle in Alzheimer's disease, the physiological function of phosphorylated tau protein remained unclear. My work demonstrates that phosphorylated tau is present in peripheral nerve in rat and involved in slow axonal transport.
- a. **Sun X.**, Tashiro T., Hirai S., Yamamoto H., Miyamoto E., and Komiya Y. Preparation of tau from the peripheral nerve: Presence of insoluble low molecular weight tau with high phosphorylation Biochem. Biophys. Res. Comm. 1995; 210:338-344
 - b. Tashiro T., **Sun X.**, Tusda M., Komiya Y. Differential axonal transport of soluble and insoluble tau in the rat sciatic nerve J. Neurochem 1996; 67(4):1566-74
 - c. **Sun X.**, Tashiro T., Hirai S. and Yamaguchi H. Identification of 5.8 kDa C-terminal fragments of Alzheimer amyloid generated in the lysosomal system. Amyloid: Int.J.Exp.Clin.Invest. 1994;1:100-106

List of Some Published Work in My Bibliography:

<http://www.ncbi.nlm.nih.gov/sites/myncbi/1T3moz65ygRQD/bibliography/43901125/public/?sort=date&direction=ascending>

D. Research Support

Ongoing Research Support

R01 David Lowenstein (PI)

2015-present

Novel Detection of Early Cognitive and Functional Impairment in the Elderly

Role: Co-Investigator

Completed Research Support

Boston University Alzheimer's Disease Center Pilot grant Neil Kowall (PI)

2012-2013

Hippocampal and white matter abnormalities in older veterans with post-traumatic stress disorder or dementia: a pilot imaging study

Role: Co-Investigator

FL State fund Rosa Rademakers (PI)

2015.3-2015.6

Identification of novel AD genes and disease associated pathways through FPADS: a Florida Presenile Alzheimer's Disease Subjects registry

Role: Co-Investigator

BIOGRAPHICAL SKETCH

NAME Clinton Wright		POSITION TITLE Scientific Director, Evelyn F. McKnight Brain Institute Associate Professor of Neurology, Neuroscience, Public Health Sciences	
eRA COMMONS USER NAME (credential, e.g., agency login) WRIGHTCL			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	MM/YY	FIELD OF STUDY
George Washington University; Washington DC	B.A.	09/90	Psychology
Columbia University College of P&S; New York, NY	M.D.	05/97	Medicine
Columbia University, Mailman School of PH; New York, NY	M.S.	05/03	Epidemiology

A. Personal Statement

My research has focused on vascular disease and its relationship to age-related memory loss and cognitive disorders and the aging brain. I am a board certified vascular neurologist and a dementia specialist, and have been Scientific Director of the McKnight Brain Institute and Chief of the Division of Cognitive Disorders in the Department of Neurology at the University of Miami since 2008. In my role as Scientific Director of the UM MBI, my goal is to create the best infrastructure possible to allow intra- and extra-mural collaboration on science that advances the mission of the Institute. I am also dedicated to creating an ideal mentoring environment to allow trainees at all levels to grow into independent investigators. My approach to vascular cognitive impairment is summarized in the following papers.

1. DeCarli C, Kawas C, Morrison JH, Reuter-Lorenz PA, Sperling RA, **Wright CB**. Session II: Mechanisms of age-related cognitive change and targets for intervention: neural circuits, networks, and plasticity. *J Gerontol A Biol Sci Med Sci*. 2012 Jun;67:747-53. PMID: PMC3732094.
2. Gardener H, **Wright CB**, Rundek T, Sacco RL. Brain health and shared risk factors for dementia and stroke. *Nat Rev Neurol*. 2015. PMID: PMC26481296.

B. Positions and Honors

1997-1998	Intern, Internal Medicine.
1998-2001	Resident, Neurology, New York Presbyterian Hospital; New York, NY
2001-2003	Stroke Fellowship, Columbia University College of Physicians and Surgeons, New York, NY
2001-2003	Neuroepidemiology Fellowship, Columbia University College of Physicians and Surgeons, New York, NY
2001-2003	Neuroepidemiology NIH Training Grant (T32) awardee
2001-2008	Assistant Attending in Neurology, New York Presbyterian Hospital, New York, NY
2003-2008	Assistant Professor of Neurology, Columbia University, New York, NY
2008-present	Adjunct Associate Professor, Department of Neurology, Columbia University, New York, NY
2008-present	Associate Professor of Neurology, Neuroscience, and Epidemiology & Public Health, University of Miami, Miami, FL
2008-present	Scientific Director, Evelyn F. McKnight Brain Institute
2008-present	Chief, Division of Cognitive Disorders, Department of Neurology, University of Miami School of Medicine
2012	Chairman's Award for Teaching Excellence, Department of Neurology, University of Miami School of Medicine
2012-present	Member, Center On Aging, Department of Psychiatry & Behavioral Sciences, University of Miami School of Medicine

C. Contribution to Science

Much of my work has focused on the epidemiology and correlates of subclinical cerebrovascular damage. As a co-investigator in the population-based Northern Manhattan Study, I have been responsible for the MRI subcommittee overseeing the conduct of an imaging substudy in which 1290 clinically stroke-free participants underwent imaging. I have described the prevalence of MRI-defined infarcts, white matter hyperintensities, and other markers of subclinical cerebrovascular disease and have identified links with some of their key risk factors, with an emphasis on novel and potentially modifiable factors as well as inflammation.

1. **Wright CB**, Rundek T, Paik MC, Elkind MSV, Sacco RL. Alcohol intake, carotid plaque, and cognition. *Stroke* 2006;37:1160-1164. PMID: PMC1447604
2. **Wright CB**, Moon Y, Paik MC, Brown TR, Rabbani L, Yoshita M, DeCarli C, Sacco R, Elkind MS. Inflammatory biomarkers of vascular risk as correlates of leukoariorosis. *Stroke*. 2009;40:3466-71. PMID: 20531432, PMID: PMC3114944
3. Marcus J, Gardener H, Rundek T, Elkind MSV, Sacco RL, DeCarli C, **Wright CB**. Baseline and longitudinal increases in diastolic blood pressure are associated with greater white matter hyperintensity volume: the Northern Manhattan Study. *Stroke* 2011;42: 2639-41. PMID: PMC3189513
4. Willey JZ, Gardener H, Moon YP, Yoshita M, DeCarli C, Cheung YK, Sacco RL, Elkind MS, **Wright CB**. Lipid profile components and subclinical cerebrovascular disease in the northern Manhattan study. *Cerebrovasc Dis*. 2014;37:423-30. doi: 10.1159/000362920. PMID: PMC4142052.
5. The links between vascular risk factors, subclinical cerebrovascular damage, and cognition have also been a major focus of my research. I have established connections of silent stroke and white matter lesions with global cognition as well as domain-specific associations, including those with psychomotor speed, executive function, and memory. I am particularly interested in the effects of vascular damage on cognitive phenotypes in relation to age-related processes and Alzheimer disease.
6. **Wright CB**, Festa J, Paik MC, Schmiedigen AP, Brown TR, Yoshita M, DeCarli C, Sacco RL, Stern Y. White Matter Hyperintensities and Subclinical Infarction: Associations with Psychomotor Speed and Cognitive Flexibility. *Stroke* 2008;39:800-805. PMID: PMC2267752
7. Khatri M, Nickolas T, Moon Y, Paik MC, Rundek T, Elkind MSV, Sacco RL, **Wright CB**. Chronic Kidney Disease (CKD) associates with Cognitive Decline. *Journal of the American Society of Nephrology* 2009; 20: 2427-2432. PMID: PMC2799177
8. Siedlecki KL, Stern Y, Reuben A, Sacco RL, Elkind MSV, **Wright CB**. Construct Validity of Cognitive Reserve in a Multi-Ethnic Cohort: the Northern Manhattan Study. *Journal of the International Neuropsychological Society* 2009;15:558-69. PMID: PMC2803322
9. Siedlecki K, Rundek T, Elkind MSV, Sacco RL, Stern Y, **Wright CB**. Using contextual analyses to examine the meaning of neuropsychological variables across samples of English-speaking and Spanish-speaking older adults. *J Int Neuropsychol Soc*. 2012 Mar;18:223-33. PMID: PMC3370823
10. Vieira JR, Elkind MSV, Moon YP, Rundek T, Boden-Albala B, Paik MC, Sacco RL, **Wright CB**. The Metabolic Syndrome and Cognitive Performance: The Northern Manhattan Study. *Neuroepidemiology* 2011;37:153-9. PMID: PMC3214939
11. 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;80:1209-15. PMID: PMC3691781
12. Willey JZ, Park Moon Y, Ruder R, Cheung YK, Sacco RL, Elkind MS, **Wright CB**. Physical Activity and Cognition in the Northern Manhattan Study. *Neuroepidemiology*. 2013; 42:100-106. PMID: PMC3942085
13. Reitz C, Mayeux R; **Wright CB**. TREM2 and neurodegenerative disease. *Alzheimer's Disease Genetics Consortium*. *N Engl J Med*. 2013 Oct 17; 369(16):1564-5.
14. Economos A, **Wright CB** (corresponding), Moon YP, Rundek T, Rabbani L, Paik MC, Sacco RL, Elkind MS. Interleukin 6 plasma concentration associates with cognitive decline: the northern Manhattan study. *Neuroepidemiology*. 2013;40:253-9. PMID: PMC3725587

Complete List of Published Work in My Bibliography:

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: **Zeki Al Hazzouri, Adina**

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

POSITION TITLE: Assistant 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
American University of Beirut, Lebanon	B.S.	06/04	Biology
American University of Beirut, Faculty of Health Sciences, Lebanon	MSc	06/06	Epidemiology
University of Michigan School of Public Health, Department of Epidemiology	PhD	06/11	Epidemiology
University of California San Francisco, Department of Epidemiology and Biostatistics		10/13	Post-doctoral fellow

A. Personal Statement

Dr. Zeki Al Hazzouri is an Assistant Professor of Epidemiology in the Department of Public Health Sciences at the University of Miami. Her primary research focus pertains to how social and cardiovascular factors experienced across the lifecourse influence cognitive function, dementia and other health outcomes in old age. In her work on longitudinal determinants of cognitive aging, she focuses on social and economic disparities in minority populations. In addition to her interest in determinants of cognitive aging, she also works on determinants of stroke outcomes in minority populations. As part of her K01 award from the National Institute on Aging, she is studying clinical and subclinical cardiovascular determinants of aging and the role of structural brain markers. Dr. Zeki Al Hazzouri's research also focuses on how to use novel statistical methods to address methodological challenges associated with longitudinal studies of aging and how to derive causal estimates from observational data.

B. Positions and Honors

Positions and Employment

2013-2014 Assistant Professor of Epidemiology, Department of Epidemiology and Biostatistics, School of Medicine, University of California San Francisco.

2014-Present Assistant Professor of Epidemiology, Division of Epidemiology, Department of Public Health Sciences, University of Miami.

Honors

2008-2009 Rackham International Student Fellowship to assist international students with outstanding academic and professional promise. University of Michigan.

2009 Student Dissertation Workshop Award on Epidemiological Methods. 42nd Annual Society for Epidemiologic Research (SER) meeting, June 23, 2009 Anaheim, CA.

2010-2011 The Barbour Scholarship for women from the 'Orient' region and who are of high academic and professional caliber. Rackham Graduate School. University of Michigan.

2010 The Harburg Student Award for Excellence in Social Epidemiology. Center for Social Epidemiology and Population Health, School of Public Health. University of Michigan.

2011	RAND Summer Institute award to attend the Mini-Med workshop and the workshop on Aging. RAND Institute, Santa Monica, CA.
2012	2012 attendee of the US 10-Day Seminar on Epidemiology and Prevention of cardiovascular Disease. Tahoe City, CA.
2012	Award for "Excellence in Research on Alzheimer's and Related Disorders" from the Alzheimers' Association in Northern California and Northern Nevada.
2012	American Heart Association/American Stroke Association/ American Brain Foundation (AHA/ASA/ABF) Lawrence M. Brass, M.D. Stroke Research Postdoctoral Fellowship.

C. Contribution to Science (see my bibliography at: <http://www.ncbi.nlm.nih.gov/sites/myncbi/1-OQdGSK0wU5Q/bibliographahy/46032250/public/?sort=date&direction=descending>)

1. Early Life and cumulative Social and Psychosocial Determinants of Cognitive Aging and Dementia
 Dr. Zeki Al Hazzouri's dissertation research challenged the lifecourse framework of cognitive aging and dementia in minority populations. Using data from the Sacramento Area Latino Study on Aging, she was among the first to examine life course socioeconomic determinants of cognitive aging and dementia in Latinos. She evaluated the role of a childhood socioeconomic construct, determined by variables such as sibling mortality and parental education and occupation, along with adult and late-life socioeconomic constructs on cognitive function and dementia incidence. She also evaluated how socioeconomic mobility across the life course (upward or downward mobility) shaped these older age outcomes. Her findings suggested that greater cumulative socioeconomic disadvantage and all-time low or downward socioeconomic mobility were associated with faster cognitive decline and greater dementia incidence, compared with more advantageous lifecourse socioeconomic status. She also investigated the influence of the neighborhood's social context on trajectories of cognitive decline and the role of individual-level socioeconomic factors in mediating these contextual effects. More recently, she examined how cumulative psychosocial factors over 20 years influenced cognition and dementia risk in very old women. In her work she continues to focus on social and economic disparities in minority populations. For example, she is currently examining how economic hardship over 25 years, as determined by the federal poverty level, is associated with cognitive function in young and middle-aged white and black adults of the Coronary Artery Risk Development in Young Adults study. Dr. Zeki Al Hazzouri conducts this work with the goal of better understanding how socioeconomic and psychosocial exposures from across the lifecourse influence cognitive health of minority and vulnerable populations. For her work in this area of research, she received the Harburg Award by the University of Michigan School of Public Health as recognition for outstanding study of psychosocial and biological correlates of health.

- Zeki Al Hazzouri A**, Haan MN, Kalbfleisch J, Galea S, Lisabeth L, Aiello A. Life course socioeconomic position and incidence of dementia and cognitive impairment without dementia in older Mexican Americans: Results from the Sacramento Area Latino Study on Aging. *Am J Epidemiol* 2011; 173(10):1148-58. PMC3121319.
- Zeki Al Hazzouri A**, Haan MN, Osypuk TL, Abdou C, Ladson H, Aiello AE. Neighborhood socioeconomic context and cognitive decline among older Mexican Americans: Results from the Sacramento Area Latino Study on Aging. *Am J Epidemiol* 2011; 174 (4):423-31. PMC3159426.
- Haan MN, **Zeki Al Hazzouri A**, Aiello AE. Life course socioeconomic trajectory, nativity and cognitive aging in Mexican Americans: the Sacramento Area Latino Study on Aging. *J Gerontol B Psychol Sci Soc Sci* 2011; 66 Suppl 1: i102-i110. PMC3132761.
- Zeki Al Hazzouri A**, Vittinghoff E, Byers AL, Covinsky K, Blazer D, Diem S, Ensrud K, Yaffe K. Long term depressive symptom burden and risk of cognitive decline and dementia among very old women. *J Gerontol A Biol Sci Med Sc* 2014; 69(5):595-601. PMC3991142.

2. Determinants of cardiovascular Disease And Risk Factors, Nativity, and Acculturation

Because of the cultural characteristics of the Latino population and the modifiable nature of cardiovascular disease risk factors, Dr. Zeki Al Hazzouri has been interested in how nativity and acculturation, among other determinants, shape cardiovascular health. She has led or contributed to research evaluating the association of intergenerational education and acculturation on metabolic syndrome and cardiovascular disease risk

factors. In addition, using data from the Sacramento Area Latino Study on Aging, she created a cardiovascular risk score that predicted the 10-year risk of cardiovascular disease in Latinos, and evaluated its association with dementia incidence. She is also currently leading work on determinants of stroke outcomes in minority populations. For example, she is examining whether perceived walking speed is associated with risk of stroke in minority older adults, independent of cognitive and physical functions.

- a. **Zeki Al Hazzouri A**, Haan MN, Robinson W, Gordon-Larsen P, Clayton E, Aiello A. Associations of intergenerational education with waist circumference, metabolic syndrome, and type-2 diabetes in US Latinos. *Obesity*, 23(5): 1097-1104, 2015. PMC4414717.
- b. López L, Peralta Carmen, Lee A, Zeki Al Hazzouri A, Haan MN. Impact of Acculturation on Cardiovascular Risk Factors Among Elderly Mexican Americans. *Annals of Epidemiology* 2014; 24(10):714-9. PMC4170012.
- c. Peralta CA, Lee A, Odden M, Lopez L, **Zeki Al Hazzouri A**, Neuhaus J, Haan MN. Association between chronic kidney disease detected using creatinine and cystatin C and death and cardiovascular events in elderly Mexican Americans: the Sacramento Area Latino Study on Aging. *J Am Geriatr Soc* 2013; 61(1):90-95. PMC3545054.
- d. **Zeki Al Hazzouri A**, Haan MN, Neuhaus JM, Pletcher M, Peralta CA, Lopez L, Perez Stable EJ. Cardiovascular risk score, cognitive decline, and dementia in older Mexican Americans: The role of sex and education. *J Am Heart Assoc* 2013; 2(2). PMC3647277.

3. Subclinical and Clinical Cardiovascular Risk Factors of Cognitive Function and Dementia

Dr. Zeki Al Hazzouri leads ongoing work on how subclinical and clinical cardiovascular risk factors contribute to cognitive aging, Alzheimer disease and other dementias. She has led research, jointly funded by the American Heart Association, American Stroke Association and American Brain Foundation, evaluating the associations of biological biomarkers and subclinical cardiovascular disease with cognitive aging in diverse populations, including Latinos, African Americans, and non-Hispanic whites. For example, she showed that obesity and leptin, a biomarker of body fat, interacted in their influence on cognitive decline and development of dementia in older adult Hispanics and non-Hispanic whites – and for this work she was granted an award for “Excellence in Research on Alzheimer’s and Related Disorders” from the Bay Area Alzheimers’ Association. Recently, using data from the Coronary Artery Risk Development in Young Adults Study, she showed that intima-media thickness, a measure of atherosclerosis, was strongly associated with worse cognitive performance at a mean age of 50 years old. In addition, using data from the Cardiovascular Health Study, she is currently evaluating the effect of statin on cognitive decline while using novel causal inference methods applied to observational data. Dr. Zeki Al Hazzouri continues to examine subclinical and clinical cardiovascular risk factors in relation to cognitive aging, with a focus on structural brain markers as part of her NIA K01 award. For example, she is currently evaluating the longitudinal associations between trajectories of lipids and structural brain markers in midlife.

- a. **Zeki Al Hazzouri A**, Vittinghoff E, Sidney S, Reis J, Jacobs D, Yaffe K. Intima-Media Thickness and Cognitive Function in Stroke-Free Middle-Aged Adults: Findings From The Coronary Artery Risk Development in Young Adults Study. *Stroke*, 46(8): 2190-2196, 2015. PMC4519386.
- b. **Zeki Al Hazzouri A**, Haan MN, Deng Y, Yaffe K. Reduced heart rate variability is associated with worse cognitive performance in elderly Mexican Americans. *Hypertension* 2014; 63(1):181-7. PMC4045649.
- c. **Zeki Al Hazzouri A**, Newman AB, Simonsick E, Sink KM, Tyrrell KS, Watson N, Satterfield S, Harris T, Yaffe K, for the Health ABC study. Pulse Wave Velocity and Cognitive Decline in Elders: The Health, Aging, and Body Composition Study. *Stroke* 2013; 44(2):388-93. PMC3572783.
- d. **Zeki Al Hazzouri A**, Stone KL, Haan MN, Yaffe K. Leptin, mild cognitive impairment, and dementia among elderly women. *J Gerontol A Biol Sci Med Sci* 2013; 68(2):175-180. PMC3598359.

D. Research Support

Ongoing Research Support

University of Miami
NIH/NIA K01AG047273

04/14 – 03/19

Lifecourse cardiovascular risk, depression and cognition in black & white adults.

The goal of this grant is to examine the associations of cardiovascular risk factors with cognitive function and depressive symptoms, and the role of structural brain changes.

Role: PI

Completed Research Support

University of California San Francisco 09/13 – 06/14

Center for Aging in Diverse Communities- Pilot Grant

Race/ethnicity, life course socioeconomic factors, and cognitive performance among non-Hispanic white and African American young to middle-aged adults: findings from the Coronary Artery Risk Development in Young Adults (CARDIA) study.

The goal of this grant was to examine the role of life course socioeconomic factors, such as poverty defined by the federal poverty level and perceived economic hardship across 25 years, on cognitive performance among black and white middle-aged adults.

Role: PI

University of California San Francisco 8 KL2 TR000143-08 10/13 – 04/14

(Johnston)

NCATS

Clinical and Translational Science Institute (CTSI)

Effects of race and lifecourse cardiovascular risk on neuropsychiatric outcomes.

The goal of the CTSI KL2 career development award is to increase the number and quality of clinical and translational investigators skilled at leading multidisciplinary research teams. My role is as a KL2 Scholar, for which I receive salary support for 9 calendar months, plus research funds. The goal of my project was to evaluate the associations of cardiovascular risk factors with the risk of neuropsychiatric outcomes.

Role: KL2 scholar

American Heart Association, American Stroke Association, 01/12 – 10/13
and American Brain Foundation

Lawrence M. Brass, MD Stroke Research Fellowship

Cardiovascular risk factors for stroke and consequences of stroke among three racial/ethnic groups.

The goal of this Postdoctoral research fellowship grant was to examine subclinical measures of disease and risk factors for stroke (such as arterial stiffness and heart rate variability) in relation to cognitive function among three racial/ethnic older adult populations; Mexican Americans, African Americans and Non-Hispanic Whites.

Role: PI.

University of California San Francisco 10/11– 06/13

Center for Aging in Diverse Communities- Pilot Grant

Socioeconomic factors, metabolic and inflammatory biomarkers in relation to cognitive status in older Mexican Americans.

The goal of this grant was to examine the interplay between socioeconomic factors, inflammatory and metabolic biomarkers in predicting cognitive outcomes among older adult U.S. Hispanics.

Role: PI.

University of California San Francisco Department of 01/12 – 12/12

Psychiatry- Pilot Grant

Arterial stiffness and depressive symptoms among white and black older adults.

The goal of this grant was to examine whether arterial stiffness is associated with change in depressive symptoms over time and whether this association is different for whites and blacks.

Role: PI.