

*EVELYN F. McKNIGHT BRAIN INSTITUTE*

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Dear Trustees,

Enclosed please find a copy of the Evelyn F. McKnight Brain Institute Progress Report for 2013. We are excited to present an update on our progress addressing the mission of the McKnight Brain Research Foundation.

There are many other exciting milestones explained in our report and we look forward to seeing you here in February to review our progress in greater detail.

Wishing you a happy and healthy 2014. Should you have any questions please feel free to contact Dr. Sacco at 305-243-7519 or Dr. Wright at 305-243-1664.

Yours Sincerely,

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

Clinton B. Wright, M.D.  
Scientific Director  
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RLS/CW/KU/bd

cc: Marsha Kegley  
Hank Raatama  
Marjorie Neil

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## 1. Summary of Scientific Achievements since Last Report

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The University of Miami Evelyn F. McKnight Brain Institute (UM-MBI) has taken important strides in 2013. We have expanded its programs in ways that advance our mission of understanding and treating cognitive aging, with further development of bench science and animal models, epidemiologic research, and work with multi-site genetic consortia. In addition, the UM-MBI was awarded a prestigious center grant that includes two interventional studies with cognitive outcomes.

Drs. Perez-Pinzon, Dave, and Wright, along with trainees Jacob Neumann and Charles Cohan have advanced their study of the effects of cerebral ischemia on learning and memory and the underlying molecular mechanisms. Data from our studies in 2013 showed that significant impairment in spatial memory formation following cerebral ischemia in middle-aged rats correlated with a reduction in the number of normal hippocampus neurons and synaptic dysfunction. These important findings are highly relevant to cognitive aging, and a manuscript with co-author Dr. Carol Barnes from the University of Arizona MBI has been submitted to *Experimental Neurology*.

The cognitive component of the Northern Manhattan Study entered its 12<sup>th</sup> year of federal funding in 2013. The team was awarded two additional years of NIH support as part of the NINDS Javits prize won by the group in 2008. One of the main aims of this extension is highly relevant to the McKnight mission as we are creating regional maps of cortical thickness in about 800 NOMAS participants and segmenting white matter lesions to determine their topography using three different metrics. Other work includes a study by Dr. Wright and Collaborator Hannah Gardener on the association between an infectious burden index of exposure to several common pathogens and cognitive function. We found an association between the infectious burden index and worse cognitive performance. Dr. Wright's grant on mineral metabolism entered its second year and initial analyses have been submitted for publication and some of these data will be presented at the International Stroke Conference in February 2014.

A major development in 2013 was selection by the American Heart Association for an American Stroke Association/Bugher Foundation Center of Excellence award, one of only three given out in the U.S. This is a four-year program that contains a clinical trial to study the effects of exercise and cognitive training on cognitive outcomes after cerebral ischemia.

Our UM-MBI Clinical and Biorepository Registry entered its third year and continued to enroll. We now have 300 participants in the multi-disciplinary study, having enrolled 69 in 2013. Our source is the comprehensive memory clinic for people with cognitive complaints. The UM-MBI continues to support the biomarker and imaging research, allowing the collection of high quality cognitive and neuroimaging data. In 2013 we continued to collect cerebrospinal fluid in collaboration with Dr. Mash. McKnight trainee Agustina Rosetti continued her study of inflammation and cognitive aging as she advanced her psychology Ph.D. dissertation work under the supervision of Dr. Bonnie Levin. Dr. Noam Alperin with expert help of post-doctoral trainee Murat Bagci has begun quantitative measurements of cerebral blood flow using MRI in this sample, allowing us to advance our study of aging of the circulation and how it affects cognition.

We continue to follow participants in the Systolic Pressure Intervention Trial (SPRINT), the large multi-center NIH/NHLBI funded clinical trial to examine the effect of intensive blood pressure lowering on brain morphology and cognitive function. Participants will undergo a second MRI scan to measure longitudinal changes in brain morphology beginning late in 2014.

Dr. Czaja's CREATE Center completed the cross-site randomized PRISM trial that examined the benefits of a specially designed computer software application for a sample of 300 older adults age 65-98 years "at risk" for social isolation. The preliminary results are encouraging with respect to social support, social isolation and attitudinal outcomes. The group is currently exploring the link between individual characteristics such as cognitive abilities and outcomes that are highly relevant to successful aging.

Dr. Alberto Ramos, both a McKnight Collaborator and a Trainee, was chosen to receive a mentored K12 award that will protect his time for research and career development in the area of sleep and cognitive aging. His award supports work on an ancillary study to the large NHLBI Hispanic Community Health Study/Study of Latinos (HCHS/SOL) at the Miami field site.

We also participated in the MBRF Poster Session at the Society for Neuroscience. In addition, representatives from our McKnight Brain Institute also presented data at important national and international meetings, including the International Symposium on Cerebral Blood Flow, Metabolism and Function, Alzheimer's Association International Conference, Gerontological Society of America Annual Meeting, American Psychological Association Annual Convention, International Neuropsychological Society Annual Meeting, Cognitive Neuroscience Society Annual Meeting, International Genetic Epidemiology Society Annual Meeting, Associated Professional Sleep Societies Meeting, American Academy of Neurology, the American Neurological Association, the International Stroke Conference of the American Heart Association, the Society for Neuroscience Conference, among others (see Section 4 for further details).

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

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**Alperin N, Bagci AM**, Lam BL, Sklar E. Automated quantitation of the posterior scleral flattening and optic nerve protrusion by MRI in idiopathic intracranial hypertension. *AJNR*. 2013; 34:2354-9.

**Alperin N**, Olin C, **Bagci A**, Lee S, Adams D, Kovanlikaya I, Katzen H, Ivkovic M, Heier L, Relkin N. Low-Dose Acetazolamide Reverses Periventricular White Matter Hyperintensities in iNPH. *Neurology*. 2013. [In Press.]

**Alperin N**, Ranganathan S, Bagci AM, Adams DJ, Ertl-Wagner B, Saraf-Lavi E, Sklar EM, Lam BL. MRI evidence of impaired CSF homeostasis in obesity-associated idiopathic intracranial hypertension. *AJNR*. 2013;34:29-34.

Alsulaimani S, **Gardener H**, Elkind MS, Cheung K, **Sacco RL**, **Rundek T**. Elevated homocysteine and carotid plaque area and densitometry in the Northern Manhattan Study. *Stroke*. 2013; 44:457-61.

**Bagci AM**, Lee SH, Nagornaya N, Green BA, **Alperin N**. Automated posterior cranial fossa volumetry by MRI: applications to Chiari malformation type I. *AJNR*. 2013;34:1758-63.

**Barrientos A**, Ugalde C. I function, therefore I am: overcoming doubt about mitochondrial supercomplexes. *Cell Metab*. July 2013.18:147-9

Boot WR, Charness N, **Czaja SJ**, Sharit J, Rogers WA, Fisk AD, Mitzner T, Lee CC, Nair S. The Computer Proficiency Questionnaire (CPQ): Assessing low and high computer proficient seniors. *The Gerontologist*. [In press.]

Bourens M, Fontanesi F, Soto IC, Liu JJ, **Barrientos A**. Reactive Oxygen Species and Redox Regulation of Mitochondrial Cytochrome c Oxidase Biogenesis. *Antioxid. Redox Signal* 19:1940-52

Cao L, Molina J, Abad C, Carmona-Mora P, Oyarzo AC, **Young JI**, Walz K. Correct developmental expression levels of Rai1 in forebrain neurons is required for control of body weight, activity levels and learning and memory. *Hum Mol Genet*. 2013 Nov 11. [Epub ahead of print] PMID: 24218365

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**Crocco E**, Curiel RE, Acevedo A, **Czaja SJ**, Loewenstein DA. An evaluation of deficits in semantic cuing, proactive and retroactive interference as early features of Alzheimer's disease. *The American Journal of Geriatric Psychiatry*, June, 2013: doi:pii: S1064-7481(13)00083-3. 10.1016/j.jagp.2013.01.066. [Epub ahead of print].

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**Czaja SJ**, Loewenstein D, Schulz R, Nair SN, Perdomo D. A Videophone Psychosocial Intervention for Dementia Caregivers. *Am J of Geriatr Psychiatry*. Nov, 2013; 21:1071-81 doi: 10.1016/j.jagp.2013.02.019. Epub 2013 Jul 3.

**Dave KR**, Della-Morte D, Saul I, Prado R, **Perez-Pinzon MA**. Ventricular fibrillation-induced cardiac arrest in the rat as a model of global cerebral ischemia. *Transl Stroke Res*. 2013 Oct 1;4.

Daviaud N, Garbayo E, Lautram N, Franconi F, Lemaire L, **Perez-Pinzon M**, Montero-Menei CN. Modeling nigrostriatal degeneration in organotypic cultures, a new ex vivo model of Parkinson's disease. *Neuroscience*. 2013 Oct 23;256C:10-22.

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**Gardener H**, Goldberg R, Mendez AJ, **Wright CB, Rundek T**, Elkind MS, **Sacco RL**. Adiponectin and risk of vascular events in the Northern Manhattan Study. *Atherosclerosis*. 2013; 226:483-9.

**Gardener H, Rundek T, Wright CB**, Elkind MS, **Sacco RL**. Coffee and tea consumption are inversely associated with mortality in a multiethnic urban population. *J Nutr*. 2013;143:1299-308.

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### 3. Publication (Other)

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**Crocco, EA**, Eisdorfer, C. Research in Mental Health and Caregiving, *The Challenges of Mental Health and Caregiving*, Springer, NY, 2014.

**Czaja SJ**, Beach S, Charness N, Schulz R. (in press) Older adults and the Adoption of Healthcare Technology: Opportunities and Challenges. In A. Sixsmith & G. Gutman (eds.), *Technology for Active Aging, International Perspectives on Aging*, New York: Springer Science & Business Media Press.

**Czaja SJ**, 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).

**Dave KR**, Thompson JW, **Neumann JT**, **Perez-Pinzon MA**, **Lin HW** Neurovascular mechanisms of ischemia tolerance against brain injury. In: *Vascular Mechanisms in CNS Trauma* Springer Press Editors: Eng H. Lo, Josephine Lok, MingMing Ning, Michael J. Whalen (eds.). Springer Press 2013.

Fontanesi F, **Barrientos A**. (2013) Mitochondrial Cytochrome *c* Oxidase Assembly in Health and in Human Diseases. In *Mitochondrial disorders caused by nuclear genes. Part 3*. Wong, LJ Ed. Springer Science. pp: 239-259

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**Wright CB**, Zonderman A. What can memory tests predict about the aging brain? The freedom to recall. *Neurology* 2013; 80: 1274-5.

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#### 4. Presentations at Scientific Meetings

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Bhattacharya P, **Raval AP**, Dong C, Zhao W, Hare JM, Yavagal DR. Intra-arterial delivery of mesenchymal stem cell protects brain in a rat model of stroke. Program#/Poster#: 440.03/Y1. Neuroscience Meeting Planner. San Diego, CA. November 2013.

**Cohan CH**, **Neumann JT**, Binkert M, **Dave KR**, **Wright CB**, **Perez-Pinzon MA**. Cardiac arrest decreases hippocampal CA1 neurons, inhibits plasticity and impairs spatial memory in middle aged rats. Brain 2013 (26th International symposium on Cerebral blood flow, metabolism and function) Conference. Shanghai, China. May 2013.

**Cohan C**, **Wright CB**, **Perez-Pinzon MA**. Age-dependent decline of Protein kinase C epsilon-mediated expression of activity-regulated cytoskeleton-associated protein in the hippocampus of Fischer 344 rats. McKnight Brain Research Foundation Poster Reception and Society for Neuroscience Conference. San Diego, November 2013.

Curiel RE, **Crocco E**, Czaja SJ, Wright C, Wahlestedt C, Levin B, Loewenstein DA. A new measure for evaluation of semantic interference and semantic cuing in Alzheimer’s disease. Poster presented at the Alzheimer’s Association International Conference (AAIC), Boston, MA, July 2013.

**Czaja SJ**. Findings from the PRISM Field Trial: A Technology-Based Intervention For At Risk Older Adults. Invited Presentation. Gerontological Society of America Annual Meeting. New Orleans, LA. November 2013.

**Czaja SJ.** An Overview of the PRISM Trial and Challenges to Implementation. Invited Presentation. Gerontological Society of America Annual Meeting. New Orleans, LA. November 2013.

**Czaja SJ.** Health Literacy and Aging: Diversity and Significance. Gerontological Society of America Annual Meeting. Invited Presentation. New Orleans, LA. November 2013.

**Czaja SJ.** Understanding the Needs of LGBT Older Adults. Poster Session. Gerontological Society of America Annual Meeting. New Orleans, LA. November 2013.

**Czaja SJ.** The Good, Bad, and the Ugly: Recruitment and Retention Issues in Conducting Technology Interventions with Older Adults. Invited Presentation. Gerontological Society of America Annual Meeting. New Orleans, LA. November 2013.

**Czaja SJ.** Workplace Technologies and Older Workers: Opportunities and Challenges. Invited Presentation. WWW2013 Work, Well-Being and Wealth: Active Ageing at Work Conference. Helsinki, Finland. August 2013.

**Czaja SJ.** Older People Abilities and New Technology. Invited Presentation. Seminar on Occupational Gerontology: Aging and New Technology. University of Tampere, Finland. August 2013.

**Czaja SJ.** Designing and Implementing a Technology Intervention to Support Well-Being of Older Adults: Prism. Symposium. 121<sup>st</sup> American Psychological Association Annual Convention, Honolulu, Hawaii, July 2013.

**Czaja SJ.** Staying Connected Through On-Line Tools. Invited Presentation. Alzheimer's Association International Conference. Boston, MA. July 2013.

**Dave KR,** Dasani S, Pileggi A. Exposure of diabetic rats to recurrent hypoglycemia increases cerebral ischemic damage via enhanced post-ischemic mitochondrial dysfunction. *Brain* 2013 (26th International symposium on Cerebral blood flow, metabolism and function) Conference. Shanghai, China. May 2013.

Denny K, **Rossetti MA,** Broz M, Ruiz J, Katzen H, Sharma KR, Arheart K, Maudsley A, **Levin BE,** Govind V. MRS correlates of executive function and depression in ALS. Presented at the 41st International Neuropsychological Society Annual Meeting, Waikoloa, Hawaii. February 2013.

Denny K, **Rossetti, MA,** Katzen H, Sharma KR, Arheart K, Maudsley A, **Levin BE,** Govind V. MRS correlates of working memory and anxiety in ALS. Presented at the Cognitive Neuroscience Society Annual Meeting. San Francisco, CA. April 2013.

**Dong C, Rundek T, Wright CB,** Santigo M, Elkind MSV, **Sacco RL.** Race-Ethnic Disparities in Cardiovascular Health Behavior and Health Factor Changes: Results from the Northern Manhattan Study. Oral presentation at AHA/ASA Scientific Sessions. Dallas, Texas. November 2013.

**Dong C**, Wang L, Beecham A, Cabral D, **Wright CB**, **Blanton SH**, Zhao H, **Sacco RL**, **Rundek T**. Genetic Loci on 8q23 and 15q21 Influence the Effect of Smoking on Carotid Plaque Burden: Results from a Multiethnic Cohort Abstract(#52) The 22nd International Genetic Epidemiology Society Annual Meeting. Chicago, Illinois. September 2013.

Fuchs P, **Diaz F**, **Dave KR**. Post-ischemic mitochondrial dysfunction in brains of diabetic rats exposed to recurrent hypoglycemia. McKnight Brain Research Foundation Poster Reception and Society for Neuroscience Conference. San Diego, November 2013.

Guilliam D, Endara-Bravo A, **Ramos AR**. Narcolepsy Diagnosed in a patient with Neuromyelitis Optica without demyelinating lesions. Associated Professional Sleep Societies Meeting, Baltimore, MD. June 2013.

**Levin BE**, Rossetti MA, Llabre M, Santiago M, Elkind MS, **Rundek T**, **Sacco RL**, Yaakov AS, and **Wright CB**. Modeling metabolic syndrome and its association with cognition. Presented at the American Psychosomatic Society Annual Meeting, Miami, FL. March 2013.

**Lin HW**, Saul I, Gresia VL, Narayanan SV, **Neumann JT**, **Dave KR**, **Perez-Pinzon MA**. Fatty acid methyl esters confer neuroprotection after cerebral ischemia. Brain 2013 (26th International symposium on Cerebral blood flow, metabolism and function) Conference. Shanghai, China. May 2013.

Loewenstein DA, Curiel RE, **Crocco E**, Wright C, Wahlestedt C, Levin B, **Czaja SJ**. Prospective Memory and Early Deficits in MCI and Pre-MCI. Alzheimer's Association International Conference (AAIC), Boston, MA. July 2013.

Morris-Blanco KC, **Neumann JT**, Cohan CH, Narayanan S, **Perez-Pinzon MA**. Protein kinase C epsilon regulates mitochondrial NAD<sup>+</sup>/NADH following resveratrol and ischemic preconditioning in cortical cultures. Society for Neuroscience Conference. San Diego, November 2013.

Morris-Blanco KC, **Neumann JT**, **Perez-Pinzon MA**. Ischemic preconditioning regulates mitochondrial NAMPT via the protein kinase c epsilon-AMPK pathway in cortical cultures. Brain 2013 (26th International symposium on Cerebral blood flow, metabolism and function) Conference. Shanghai, China. May 2013.

Nahab F, Shen Q, **Wright CB**, Moreno L, Zadeh N, Pattany P. Brain MRI Morphometric Changes in Essential Tremor Versus Controls. American Academy of Neurology Meeting. San Diego, CA. March 2013.

Narayanan S, **Perez-Pinzon MA**. Role of nuclear erythroid 2-related factor 2 in ischemic preconditioning-induced neuroprotection. Brain 2013 (26th International symposium on Cerebral blood flow, metabolism and function) Conference. Shanghai, China. May 2013.

Narayanan S, **Perez-Pinzon MA**. Ischemic preconditioning and astrocyte-neuronal interactions following oxygen-glucose deprivation in neuronal cultures. Society for Neuroscience Conference. San Diego, November 2013.

**Neumann JT**, Koronowski KB, Lin HW, **Perez-Pinzon MA**. PKC epsilon preconditioning extends the time to anoxic depolarization in hippocampal slices. McKnight Brain Research Foundation Poster Reception and Society for Neuroscience Conference. San Diego, November 2013.

**Neumann JT**, **Perez-Pinzon MA**.  $\epsilon$ PKC Preconditioning reduces excitability and firing properties of CA1 hippocampal neurons. Brain 2013 (26th International symposium on Cerebral blood flow, metabolism and function) Conference. Shanghai, China. May 2013.

Pericak-Vance M, Kundle B, Kholi M, Naj A, Perry W, Hamilton K, Whithead PL, Levin B, Carney R, **Crocco E**, Wright C, Beecham G, Martin E, Wang L, Gilbert J, Haines J. Variant domain mapping in confirmed late-onset alzheimer's disease (LOAD) loci identifies multiple genomic regions with potentially functional variants. Poster presented at the Alzheimer's Association International Conference (AAIC), Boston, MA. July 2013.

**Ramos AR**, **Dong C**, Elkind MSV, Boden-Albala B, **Sacco RL**, **Rundek T**, **Wright CB**. Association between Sleep Duration and White Matter Hyperintensities: The Northern Manhattan Study. Associated Professional Sleep Societies Meeting, Baltimore, MD. June 2013.

**Raval AP**, Borges-Garcia R, Racine M, Javier Moreno W, **Perez-Pinzon MA**, Bramlett H. Periodic  $17\beta$ -estradiol pretreatment protects rat brain from cerebral ischemic damage via estrogen receptor- $\beta$ . McKnight Brain Research Foundation Poster Reception and Society for Neuroscience Conference. San Diego, CA. November 2013.

**Raval AP**, Borges-Garcia R, Racine M, Moreno W, Bramlett H, **Perez-Pinzon MA**. Periodic  $17\beta$ -estradiol pretreatment protects rat brain from cerebral ischemic damage via estrogen receptor- $\beta$ . Program# 14, McKnight Brain Research Foundation, San Diego, CA. Society for Neuroscience. November 2013.

Rossetti MA, Denny K, Widerstrom-Noga E, Katzen HL, Arheart KL, Mathew A, Adcock J, Babakhanyan I, Govind V, **Levin BE** and Maudsley AA. The relationship between thalamic metabolites, attention, and pain in mild TBI. Presented at the 41<sup>st</sup> International Neuropsychological Society Annual Meeting, Waikoloa, Hawaii. February 2013.

Shafazand, S, Wallace, DK, Vargas, S., Luca, C, Katzen, H, **Levin, BE**, and Singer, C. (2013). Sleep Quality, Duration, Insomnia Symptoms, and Risk for Sleep Disordered Breathing in Parkinson's Disease *Neurology, Suppl. 80*

Thompson JW, **Raval AP**, **Neumann JT**, **Perez-Pinzon MA**. Ischemic preconditioning increases BDNF protein expression leading to ischemic tolerance. Society for Neuroscience Conference. San Diego, November 2013.

Wright B, Lewis L, Noble J, Vonsattel JP, Khandji A, Sommerville R, **Wright CB**. Case Series: Eosinophilic Vasculitis Isolated to the Central Nervous System. American Academy of Neurology Meeting 2013. San Diego, CA. March 2013.

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

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**Alperin N**, Lee SH, Bagci AM, Sekula RF, Green BA. Association between Posterior Cranial Fossa Volumetry and CSF Flow Dynamics in Chiari Malformations Type I. Annual meeting of the Congress of Neurological Surgeons. San Francisco, CA. October 2013.

**Alperin N, Bagci**, AM, Lam BB, Sklar E. Automated Quantitation of Globe Flattening by MR Imaging in Idiopathic Intracranial Hypertension. ASNR 51st Annual Meeting. San Diego, CA. May 2013.

**Barrientos, A.** Biogenesis of the mitochondrial translation machinery and the OXPHOS complexes. Invited speaker at The Center for Molecular Medicine and Genetics (CMMG) seminar series. Wayne State University School of Medicine, Detroit, MI. December 2013.

**Barrientos, A.** Mitochondrial protein synthesis and biogenesis of the OXPHOS system. Invited speaker at the Department of Biochemistry and Biophysics, Texas A&M University Grand Rounds Series. College Station, TX. October 2013.

**Barrientos, A.** Mitochondria-independent mechanisms of NMNAT-mediated neuroprotection. Neurological Disorder Research Group (NDRG) meeting. University of Miami. March 2013.

**Crocco, E.** “Depression and Anxiety Disorders in the Older Veteran” Miami VAMC/GRECC—The Miami Area Geriatric Educational Center (MAGEC), Miami, FL. September 2013.

**Czaja SJ.** 5<sup>th</sup> Annual Health Literacy Research Conference. Invited Panel. Challenges and Future Directions for Health Literacy Research Targeting the Elderly. National Academy of Sciences. Washington, DC. October 2013.

**Czaja SJ.** Workshop: Charting a Research Agenda for Studying Internet and Social Media Use in Middle-Age and Older Adults. Panel Discussion: “Barriers and Benefits of Internet and Social Media use for Older Adults”. University of Michigan, School of Information, Ann Arbor, MI. October 2013.

**Czaja SJ.** The Potential Role of Technology in Enhancing the Health and Well-Being of Older Adults Opportunities and Challenges. Invited Lecture. John Hopkins University, School of Nursing and Center for Aging and Health, Baltimore, MD. June 2013.

**Czaja SJ.** Improving the Health and Independence of Older Adults. Invited Lecture. Columbia University Medical Center, New York, NY. June 2013.

**Czaja SJ.** The Potential of Technology Systems for Enhancing the Independence and Quality of Life for Older Adults. Distinguished Lecture. University of Maryland, Baltimore, MD. March 2013.

**Czaja SJ.** Improving the Health and Independence of Older Adults. Invited Lecture. Northwestern University, Chicago, IL. March 2013.



**Monteith, TS.** New Investigator and Trainee/Headache Excellence Tournament; International Headache Congress, Boston, MA , June 2013.

**Moraes, CT.** Mitochondrial Disease: Translating biology into new treatments. Wellcome Trust Scientific Conferences. Cambridge, UK, October 2013.

**Moraes CT.** Modifying mitochondrial genomes. Max Planck Institute for Biophysics. Bad Neuheim, Germany. October 2013

**Moraes CT.** Mitochondrial DNA damage in muscle aging. EMBO workshop on Muscle Wasting. Ancona, Switzerland. September 2013.

**Moraes CT.** Mitochondrial DNA Heteroplasmy Manipulation with mitoTALEN. United Mitochondrial Disease Foundation Annual Meeting. Orange County CA. June 2013

**Moraes CT.** Novel Genetic Approaches to Treat Mitochondrial Diseases. NHLB-Sponsored conference on mitochondrial biology. Bethesda, May 2013.

**Moraes CT.** Treating mitochondrial diseases. MDA-Sponsored Therapeutic Approaches to Muscle Diseases. Bethesda, April 2013.

**Moraes CT.** Therapeutic Approaches to Mitochondrial Diseases. Invited Seminar. Department of Pathology, University of Pittsburgh, Pittsburgh, PA. January 2013.

**Ramos, AR.** Sleep apnea and glaucoma. Glaucoma 2.0 Bed to Bedside Meeting. Bascom Palmer Eye-Institute, University of Miami. Mandarin Oriental hotel, Miami, Fl. January 26, 2013 (CME 1.0) 2013

**Ramos, AR.** Sleep health and Vascular Disease. University of Miami, Sleep Disorders Symposium. Bascom Palmer eye institute, Miami, FL. (CME 0.5) 2013.

**Ramos, AR.** Sleep and vascular disease. Nurses. Bascom Palmer Eye institute, University of Miami, Miller School of Medicine, Miami Fl. (CE 2.0) 2013.

**Sacco, RL.** Public Health and Economic Impact of Stroke and How to Solve it and Secondary Stroke Prevention: The Use of Antiplatelets and Anticoagulants, ISET Focused Symposium, Miami Beach, FL. January 2013.

**Sacco, RL.** Addressing Race and Ethnic Disparities in Stroke Prevention, East Atlantic Student Research Forum, University of Miami Miller School of Medicine, Miami, FL. February 2013.

**Sacco, RL.** It's Time to Peak: Translating Evidence and Excellence in Stroke Care, University of Florida, Gainesville, FL. May 2013.

**Sacco, RL.** NHLBI workshop titled "Using existing medical data collection systems for cardiovascular disease surveillance." Bethesda, MD. June 2013.

**Sacco, RL.** Alzheimer's Disease-Related Dementias Workshop 2013: Research Challenges and Opportunities. Natcher Auditorium, NIH Campus, Bethesda, MD. May 2013.

**Sacco, RL.** Strategies for Stroke Prevention: Update in Stroke Prevention, Lecture at JFK Medical Center, Atlantis, FL. December 2013.

**Sacco, RL.** The Heart and Brain: Ensuring a Healthy Connection, Coral Reef Medical Center Lecture Series, Key Largo, FL. April 2013.

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## **6. Awards (other)**

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Dr. Czaja received an RO1 award for NIH/NINR to test the efficacy of a technology based intervention for family caregivers of AD patients.

Dr. Czaja was named President, Division 20 (Division of Adult Development and Aging), American Psychological Association, 2013-2016

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

Dr. Czaja received the Jack A. Kraft Award for Innovation, Human Factors and Ergonomics Society, 2013.

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

Dr. Dave was awarded a local scientific advisory committee pilot grant.

Dr. Lin received a National Scientist Development Grant from American Heart Association.

Dr. Neumann was awarded a post-doctoral fellowship grant from American Heart Association

Dr. Perez-Pinzon was awarded a project as a part of American Stroke Association Bugher Foundation centers of excellence in stroke collaborative research for regeneration, resilience and secondary prevention (start date April 1, 2014).

Dr. Ramos received a K12 Scholar, Mentored Research Award, Clinical Translational Science Institute (CTSI) at the Miller School of Medicine, University of Miami.

Dr. Ramos was named a 2013 Fellow of the American Academy of Sleep Medicine.

Dr. Ramos was named as Scholar by the **Program to Increase Diversity among Individuals Engaged in Health-Related Research (PRIDE)**. New York University, NY

Dr. Sacco was appointed to the NINDS National Neurological Disorders and Stroke Advisory Council, 2013-17

Dr. Sacco was selected as Vice President of the American Academy of Neurology, 2013-15.

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## 7. Faculty

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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)

<b>Name</b>	<b>Center Role</b>	<b>Area of Expertise</b>
Noam Alperin, Ph.D.	Member	Physics (MRI)
Susan Blanton, Ph.D.	Member	Genetics
Kunjan R. Dave, Ph.D.	Member	Neurobiology
Chuanhui Dong, Ph.D.	Member	Epidemiology, biostatistics
Bonnie E. Levin, Ph.D.	Schoninger Professor	Neuropsychology
Kevin Lin, Ph.D.	Member	Neuroscience
Teshamae Monteith, M.D.*	Neurology	Headache
Tatjana Rundek, M.D., Ph.D.	Member	Epidemiology, neurology
Ralph L. Sacco, M.D., M.S.	Executive Director	Neurology, epidemiology, genetics
Clinton B. Wright, M.D., M.S.	Scientific Director	Neurology, epidemiology, cognition

<b>Name</b>	<b>Center Role</b>	<b>Area of Expertise</b>
Antonio Barrientos, Ph.D.	Collaborator	Neuroscience, genetics
Elizabeth Crocco, M.D.	Collaborator	Psychiatry
Sara Czaja, Ph.D.	Collaborator	Aging, psychology, engineering
Hannah Gardener, Sc.D.	Collaborator	Epidemiology
Kevin Lin, Ph.D.	Collaborator	Neuroscience
Carlos Moraes, Ph.D.	Collaborator	Neuroscience
Miguel Perez-Pinzon, Ph.D.	Collaborator	Neuroscience
Alberto Ramos, M.D.*	Collaborator	Sleep Medicine, Neurology
Ami P. Raval, Ph.D.	Collaborator	Neuroscience
Juan Young, Ph.D.	Collaborator	Genetics

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## 8. Trainees

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<b>Name</b>	<b>Center Role</b>	<b>Area of Expertise</b>
Ahmet Murat Bagci, Ph.D.	Postdoctoral trainee	Bio-engineering
Ashley Beecham, M.S.	Graduate Student	Genetics
Charles Cohan, B.S.	Graduate Student	Neuroscience
Teshame Monteith, M.D.	Neurology	Headache
Nooshin Nabizadeh, M.S.	Graduate student	Electrical Engineering
Jacob Neumann, Ph.D.	Postdoctoral Fellow	Neuroscience

Alberto Ramos, M.D.*	Postdoctoral trainee	Sleep Medicine, Neurology
Agustina Rosetti, M.S.	Graduate Student	Psychology
Jessica Warsch, M.D. Ph.D.	Resident	Epidemiology

\* both faculty and trainee.

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## 9. Clinical/Translational Programs

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### New Programs

Dr. Barrientos is studying the chronological life span of yeast as a model of aging of postmitotic cells such as neurons. His group is interested in the regulation of chronological life span by mitochondrial ATP production and reactive oxygen species (ROS). The data are showing that ROS can act as signaling molecules and have a positive impact on developing stress resistance and promoting longevity. In excess, ROS produce a deleterious effect and the group has observed that the modulation of chronological life span by nutritional cues (caloric restriction, interference of the TOR pathway, etc) requires mitochondrial respiration above a certain threshold, and that ROS act as signaling molecules.

Dr. Ramos began his work to evaluate cerebral hemodynamics by transcranial Doppler ultrasound in a subset of participants of HCHS/SOL as noted in the Summary. The goal is to evaluate cerebral hemodynamics as a subclinical measure of early cerebrovascular risk in relation to sleep apnea. So far he has already enrolled 40 participants in the study (projected 200 participants).

Drs. Levin and trainee student Agustina Rosetti are working with Dr. Wright as part of collaboration with the Department of Psychology to examine the relationship between inflammation, brain morphology, and cognition. The study includes a sample of elderly people enrolled in the UM-MBI Clinical and Biorepository Registry who presented to clinic with memory complaints. The study will focus on adiposity and its relationship to inflammatory markers, including molecular isoforms of adiponectin, leptin, interleukin 6, tumor necrosis factor alpha, and C reactive protein. Levels of inflammation will be correlated with performance on a battery of neuropsychological measures examining memory, attention, language, visuospatial performance and executive functions. These findings will also be correlated to total brain and hippocampal volumes as measured by MRI. Drs. Alperin and Bagci developed a method for segmentation and characterization of white matter hyperintensities to study the impact of load and location.

Dr. Rundek began operating the core laboratory for MOBILISE (Mobility Biology and Intervention Study at Einstein), a cerebral hemodynamics study of the vascular mechanisms of normal aging, MCI and dementia using transcranial Doppler (TCD) and the TCD challenge test with carbon dioxide (CO<sub>2</sub>) to test cerebral vasoreactivity and reserve. This study examines the relationship of microvascular disease and impaired cerebral vasoreactivity to mobility outcomes in older adults and is addressing an important question regarding vascular mechanisms that underlay functional disability. There were 98 participants enrolled into MOBILISE and Dr.

Rundek presented preliminary data on the associations of TCD measures of blood flow velocities in arteries of the circle of Willis with cognitive performance in participants over age 70 in the EAS cohort (52% female, mean age  $80.9 \pm 5.6$  years, mean education 15 years).

Dr. Susan Blanton completed a genome-wide association study with trainee Ashley Beecham and in collaboration with Drs. Sacco, Rundek, and Wright. Four cognitive domains, including memory, language ability, executive function, and processing speed were examined in a stratified analysis within the race-ethnic subsets of NOMAS: Hispanic, Caucasian, and African American. One of the most notable findings was an association with a single nucleotide polymorphism located within an intronic region of the Rhomboid, veinlet-like3 (*RHBDL3*) gene. This protein is an interesting candidate for future study given its prominent expression along the developing ventral neural tube and ventral forebrain. This will be followed up on in 2014.

### **Update on Existing Clinical Studies**

Processing bloods continued for the R01 entitled, “Fibroblast Growth Factor 23 and the Risk of Stroke and Cognitive Decline” (PI: Dr. Wright). To date more than 4,000 samples have been processed for plasma fibroblast growth factor 23 (FGF23), phosphate, parathyroid hormone, and cystatin C. Work is well underway with a publication on FGF23 as a risk factor for cerebral hemorrhage submitted to Neurology, an abstract on FGF23 as a correlate of carotid artery plaque accepted for the upcoming International Stroke Conference as well as a manuscript in preparation.

We now have 300 participants in the multi-disciplinary UM-MBI Clinical and Biorepository Registry, having enrolled 69 in 2013. Our source is the comprehensive memory clinic for people with cognitive complaints. In 2013 we continued to collect cerebrospinal fluid in collaboration with Dr. Mash. McKnight trainee Agustina Rosetti continued her study of inflammation and cognitive aging as she advanced her psychology Ph.D. dissertation work under the supervision of Dr. Bonnie Levin. Dr. Noam Alperin with expert help of post-doctoral trainee Murat Bagci has begun quantitative measurements of cerebral blood flow using MRI in this sample, allowing us to advance our study of aging of the circulation and how it affects cognition. Dr. Rundek continued the **Aging and Memory Brain Hemodynamic (AMBH) study** as part of our UM Memory Disorder Clinic, the prospective neuroimaging study of cerebral blood flow assessments using Transcranial Doppler (TCD) in our McKnight Memory Disorder Clinic Registry.

Dr. Ramos continued to manage SUENO (sleep habits as a risk factor in HCHS/SOL; R01 HL098297) as the Miami site-PI. SUENO is an ancillary study to study sleep and its relation to cognitive function and cardiovascular disease in HCHS/SOL. The study plans to recruit more than 2,000 participants with the goal of defining the predictors of abnormal sleep with actigraphy (a wristwatch-like device that records movement and can be used to infer sleep from awake states).

Dr. Levin has continued her collaboration with Drs. Andrew Maudsley and Varan Govind from Radiology using magnetic resonance spectroscopy (MRS) to examine alterations in brain metabolites associated with select cognitive and behavioral changes commonly found in the aging process. In one study, they are focusing on the association between metabolic changes in

the mediodorsal nucleus and its projections to the pre-frontal cortex and subjective reports of pain, affective distress and working memory in a sample of middle aged and elderly adults following a traumatic brain injury. This work demonstrates the utility of using MRS to examine brain metabolites that cannot be detected by conventional MRI.

We completed 91 follow up cognitive assessments during the past year in the Northern Manhattan Study (NOMAS). Trainees Nooshin Nabizadeh (graduate student) and Murat Bagci (post-doctoral fellow), under the supervision of Dr. Noam Alperin and Dr. Wright are creating regional maps of cortical thickness in 800 NOMAS participants and also segmenting white matter lesions in a way that allows us to determine their topography using three different metrics. The focus of this work is age-related cognitive problems. These methods are also being applied in the McKnight Memory Disorders Clinic Registry.

The NOMAS group continued work as part of the Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) Consortium, completing a genome-wide association study on several phenotypes, including MRI-defined brain infarcts, White Matter Hyperintensity Volume, Hippocampal Volume, and Intra-Cranial Volume. The results of these analyses in the Caucasian individuals from the Northern Manhattan Study (NOMAS) were shared with the CHARGE Consortium, and a meta-analysis of the NOMAS results with results from other cohorts within the CHARGE Consortium is currently underway.

We are also leading a sub-study of the genetics of White Matter Hyperintensity Volume, with a particular focus on Hispanics. We are conducting a joint genome-wide association study with the Hispanic individuals from both NOMAS and the Washington Heights Inwood and Columbia Aging Project (WHICAP). In an exploratory analysis the association between the cognitive domains and carotid intima-media thickness has also been done. We found carotid intima-media thickness to be inversely associated with the memory domain, independent of demographic and vascular risk factors. This work will be presented at the 2<sup>nd</sup> International Conference on Heart and Brain during February 2014.

During the past year, we have continued our collaboration with Dr. Sara Czaja of the UM Center on Aging (COA). Dr. Czaja has continued to focus on understanding the implications of age-related changes in cognition for everyday functioning and independence. She has developed new techniques for assessing function using technological tasks. Drs. Wright, Czaja, and others are working together on a project to assess subtle declines in function related to memory problems.

As mentioned above, the Cerebrovascular Research Lab continued the collaboration with Dr. Carol Barnes with our animal behavior core to study the effects of cerebral ischemia on cognitive decline with an important publication now submitted. The project involves inducing cerebral ischemia in rats of different ages, including aged rats, in order to study the interaction of aging and cerebral ischemia on cognitive decline. We have focused on how histological and electrophysiological alterations after cerebral ischemia affect cognitive processes. We completed a study to characterize changes in hippocampal cell survival, synaptic plasticity, and spatial memory in a middle-aged (9 month-old) rodent model. Data from our studies in 2013 showed that significant impairment in spatial memory formation following cerebral ischemia in middle-

aged rats correlated with a reduction in the number of normal hippocampus neurons and synaptic dysfunction. As noted above, this work has been submitted to Experimental Neurology.

Dr. Carlos Moraes continues his work on the role of mitochondrial dysfunction in aging. His lab has developed novel genetically modified mice that can be induced to damage mitochondrial DNA in specific tissues and organs, allowing studies of effects of aging. They have also studied how increases in mitochondrial biogenesis can have anti-aging effects, particularly in post-mitotic tissues such as muscle and brain. This translational work may lead to novel biomarkers and treatments to counter the effects of aging and age-related cognitive loss.

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## 10. Technology Transfer

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- Patent applications  
No Patents have been applied for or received
- Revenue generated from technology  
Not applicable

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## 11. Budget Update

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- Status of matching funds (see attached).
- Existing budget (see attached).
- Projected budget for coming year (see attached).
- Extramural funding:
  - ❖ FGF-23 and the Risk of Stroke and Cognitive Decline  
Source: National Heart Lung and Blood Institute  
Principal Investigator: Clinton Wright  
2013 budget: 370,065
  - ❖ Memory Disorder Clinic  
Source: Florida Department of Elder Affairs  
Principal Investigators: Elizabeth Crocco, Clinton Wright  
2013 budget: \$250,000
  - ❖ Systolic Pressure Intervention Trial  
Source: Wake Forest University (sub-contract)  
Principal Investigator: Clinton Wright  
2013 budget: \$ 73,296

- ❖ Independent Scientist Award  
Source NINDS (K02NS059729)  
Principal Investigator: Clinton Wright, MD MS  
2013 budget: \$ 126,198
  
- ❖ Stroke Incidence and Risk Factors in a Tri-ethnic Region  
Source: NIH, NINDS (R01 NS029993)  
Principal Investigator: Ralph Sacco MD MS  
2013 budget: \$ 1,911,673
  
- ❖ Genetic Determinants of Extreme Phenotypes of Subclinical Atherosclerosis  
Source: NIH, NINDS (K24 NS062737)  
Principal Investigator: Tatjana Rundek  
2013 budget: \$ 203,429
  
- ❖ Role of Fatty Acid Methyl Esters on Cerebral Blood Flow  
Source: American Heart Association  
Principal Investigator: Hungwen “Kevin” Lin  
2013 budget: \$ 75,000
  
- ❖ Mechanisms of Neuroprotection Against Cardiac Arrest  
Source: NIH, NINDS (R01 NS045676)  
Principal Investigator: Miguel Perez-Pinzon  
2013 budget: \$ 316,514
  
- ❖ Ischemic Preconditioning: Mechanisms of Neuroprotection  
Source: NIH, NINDS (R01NS034773)  
Principal Investigator: Miguel Perez-Pinzon  
2013 Budget: \$365,774
  
- ❖ Improving the Functional Outcomes in Older Adults with Schizophrenia  
Source: NIH, NIA (5R21 AG041740)  
Principal Investigator: Sara Czaja, Ph.D.  
2013 Budget: 144,585
  
- ❖ Center for Research and Education on Aging and Technology  
Source: NIH, NIA (P01 AG017211)  
Principal Investigator: Sara Czaja, Ph.D.  
2013 Budget: 1,646,080



- ❖ A Tailored Technology Intervention for Diverse Family Caregivers of AD Patients  
Source: NIH, NINR (R01 NR014434)  
Principal Investigator: Sara Czaja, Ph.D.  
2013 Budget: 482,892
  
- ❖ HCHS/SOL Sleep patterns as a Risk Factor for Disease in the Hispanic Community  
Source: Brigham and Women's Hospital  
Principal Investigator: Alberto Ramos  
2013 budget: \$ 127,796
  
- ❖ Increased Cerebral Ischemic Injury by Repeated Hypoglycemic Episodes in Diabetes  
Source: NIH, NINDS (R01 NS073779)  
Principal Investigator: Kunjan Dave  
2013 budget: \$ 290,676
  
- ❖ Gene-Smoking Interactions and Atherosclerosis  
Source: Florida Biomedical Research Program  
Principal Investigator: Chuanhui Dong  
2013 budget: \$ 112,500

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## 12. Educational programs focusing on age related memory loss

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### Scientific

The Schoninger Neuropsychology Program continued to teach and train post-doctoral fellows, interns, graduate and undergraduate students. The Post Doctoral Training Program has three full time fellows. The Neuropsychology Practicum supports 5 upper level graduate students from the Department of Psychology. There is also a year-long internship rotation that supports 2 Psychology Interns from the Mailman Center for Child Development. Current teaching activities include: weekly case supervision with each trainee, group supervision, and Neuropsychology rounds. In addition, this year an intensive three-credit course was offered to upper level graduate students.

Our Memory Disorders Clinic trains students at all levels through exposure to patients and caregivers. A multidisciplinary team from neurology, psychiatry, and neuropsychology provide teaching. Medical students, graduate neuropsychology students and post-doctoral fellows, and geriatric psychiatry fellows are an integral part of the clinic and assist with cognitive and clinical evaluations.

Our 2013 UM-MBI Seminar Series continued to bring scientists together:

<b>Speaker</b>	<b>Area of Expertise</b>	<b>Title</b>
Matthew Harms, MD	Neurology	“C9ORF72 ALS-FTD: Current understanding and future challenges”
Claes Wahlestedt, M.D., Ph.D.	Psychiatry	“RNA and Neurology”
Alberto Ramos, M.D., MSPH, FASM	Neurology	“Obstructive sleep apnea and cerebral hemodynamics”
Corneliu Luca, MD, PhD	Movement Disorders	“Modulation of dysfunctional gait networks in Parkinson’s disease”
Ritobrato Datta, PhD.	Neuroscience	“Visual Brain Index: A multimodality imaging based scoring system to quantify brain alteration in the blind.”
Hong Jiang, MD, PhD	Neuro-ophthamology	Ocular microvascular function in Alzheimer's disease
Christer Nordstedt, MD, PhD	Neuroscience	“Alzheimer’s Disease: The End of the Beginning”
Dr. Jodi Warman Chardon, MSc, MD, FRCPC	Neurogenetics	“Neurogenetics in Neuromuscular Disorders: How advances in genetic testing will change patient management”
Xiaoxiao Bai, PhD.	Neurology & Bioengineering	“Multimodal neuroimaging: application in epilepsy and cognitive impairment”

### **Public**

An important contribution to the UM-MBI effort is a new program developed by Dr. Czaja to provide a Certificate in Gerontology. The purpose of the University of Miami Center on Aging’s Certificate Program is to provide education and training about the aging process and to increase availability of qualified providers to serve our community’s aging population.

The annual Miami Brain Fair was held on Saturday, March 23, 2013 at the downtown Miami Science Museum and a very successful community educational event. As usual, the event

educated the public about neuroscience, to promote brain/spinal cord injury prevention, provided teaching opportunities for neuroscientists at all career stages, and developed a network within the neuroscience community for the Miami Society for Neuroscience (SFN) Chapter. The event was attended by 2,800 people and more than half were children. This event was free to the public.

Drs. Wright and Crocco carried out educational programs about age-related memory loss and other forms of cognitive decline for local seniors and senior centers and retirement communities.

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

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The MRI Standardization Working Group has been actively working on a proposal to the MBRF and an update on the progress of this group will be sent under separate cover. However, we are planning a cross-Institute study that will leverage the strengths of each and provide a unique opportunity for a McKnight study large enough to recruit enough of the oldest old to be able to measure variability in function, with a focus on normal cognitive aging, cerebrovascular disease, and other factors that are important for older adults to maintain their independence.

We have continued to collaborate with Dr. Gene Alexander, using voxel-based morphometry to examine regional differences in brain volume in relation to blood pressure and hypertension. We have a manuscript in preparation and data from this collaboration were presented at the Inter-Institutional Meeting hosted by the UAB MBI.

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### **14. Collaborative Programs with non-McKnight Institutes, Institutions, and Research Programs**

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Our collaboration with Columbia University allows the Northern Manhattan Study (NOMAS) to continue to follow its stroke-free cohort for vascular events and deaths. In addition, the sub sample of 1,290 participants that underwent neuropsychological testing continues to come in for the second evaluation (see Section 9 – Update). We have begun collaborations with Richard Mayeux at Columbia as well and with the CHARGE consortium, a group that includes investigators from Europe and the United States and a number of academic institutions.

Dr. Rundek initiated a study in collaboration with the Albert Einstein Study Program Project in Aging, funded by NIA (2P01 AG003949).

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

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We plan to respond to the recently announced joint NIA/MBRF RFA-AG-14-016, Plasticity and Mechanisms of Cognitive Remediation in Older Adults.

McKnight MRI Working Group proposal as discussed above, and details to follow under separate cover.

Continue work on the UM-MBI Registry, examining cerebral hemodynamics using transcranial Doppler with the help of Dr. Rundek, and new MRI methods for quantitating blood flow with the help of Dr. Alperin.

Initiation of the American Stroke Association/Bugher Foundation Center of Excellence award in April 2014. This is a four-year program that contains both a clinical trial to study the effects of exercise and cognitive training on cognitive outcomes after cerebral ischemia, and a project with translational potential involving an animal model that uses the interventions of exercise and enriched environment, in combination with dietary supplements, to improve cognitive outcomes.

We will continue work on aging and cerebral ischemia using our cardiac arrest model in 18 months old rats. Our work will include cognitive and behavioral studies in young and old rats and will also correlate these deficits with changes in electrophysiological characteristics in the rat hippocampus. We will also attempt to obtain healthy slices from 18 month-old rats for electrophysiological recordings.

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**16. Endowment Investment Results**

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Please see attached report.

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

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No funds were used for prohibited purposes. See attached report.

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**18. Do you recommend any modification to the Gift Agreement?**

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We do not request any modifications to the Gift Agreement.

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

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Yes, all activities during the report period furthered the Purpose of the Gift.

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**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?**

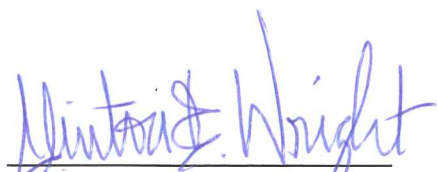
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A significant loss to the program was the departure of Dr. Richard Isaacson, who left the UM-MBI having been Education Director since 2008. We are aware of the value the MBRF places on education and the positive reception Dr. Isaacson's work received. We have continued to educate members of the UM scientific community with our McKnight Research Seminars and have also educated the public through the highly successful Brain Fair at the Miami Science Museum and through a number of educational lectures given by members and collaborators of the Institute, including memory screenings at senior centers, forums for caregivers, and other programs. We are committed to finding a highly qualified person to fill the role of Education Director and have been actively searching and interviewing candidates with the hope of having a new faculty member join the Institute sometime in 2014.


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

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Clinton B. Wright, M.D. M.S.  
Scientific Director

January 14, 2014  
Date

  
Ralph L. Sacco, M.D. M.S.  
Executive Director

January 14, 2014  
Date

McKnight053113

Summary

Evelyn F. McKnight Center for Age-Related Memory Loss  
at the Miller School of Medicine  
Market Value Analysis  
May 31, 2013

McKnight Contribution	\$5,000,000
UM Match	2,530,864
Transfers from Other University Funds	1,110,302
Investment Return	2,935,642
Distributions for Spending	(2,925,948)
5/31/13 Endowment Balance	<u>\$8,650,860</u>
Unmatched Balance	<u>\$2,469,136</u>

Mcknight  
Budget vs Actual (for FY14 June 1, 2013 - May 31,2014)

					<u>Budget</u>	<u>Actual as of 12/31/2013</u>	<u>Projected at Yr End</u>	<u>Variance to Budget</u>
<b>Revenue</b>					570,000.00	504,776.90	570,000.00	-
McKnight Project Clinical and Clinical Research Program								
<b>Personnel</b>								
<b><u>Subtotal Faculty Salary and CFB</u></b>					183,357	97,333	184,072	(715)
<b>Faculty</b>	<b>Role In Project</b>	<b>Effort</b>	<b>CFB Rate</b>					
Clinton Wright, MD	Scientific Director	14%	20.80%	33,383.19	25,944.14	49,011.90	(15,628.71)	
Ralph Sacco, MD	Executive Director	7%	20.80%	40,088.90	11,289.19	34,497.77	5,591.13	
Fatta Nahab	Imaging	4%	20.80%					
Noam Alperin	Radiology	5%	26.20%					
Susan H. Blanton	Genetics	5%	26.20%					
Bonnie Levin, PHD (Schoninger)	Neuropsychology	30%	26.20%					
Heather Katzen	Neuropsychology	5%	26.20%					
Kunjan Dave	Basic Science	5%	26.20%					
<b><u>Subtotal Staff Salary and CFB</u></b>					288,593	164,512	288,938	(345)
<b>Staff</b>	<b>Role in Project</b>							
Ahmet Bagci	Radiology	19%	42.00%					
Madiley Broz	Neuropsychology	30%	42.00%					
Sharlett Anderson (Replace Broz)	Neuropsychology	48%	42.00%					
Digna Cabral	Administrative Support	15%	42.00%					
Charles Cohan	Med Grad Student	100%	0.00%					
Maria Mendoza-Puccini	Clinical Research Coordinator	90%	42.00%					
Nooshin Nabizadeh	Teaching Assistant	100%	0.00%					
Isabel Saul	Research Support Specialist	30%	42.00%					
Maria Rosetti	Grad Student	50%	0.00%					
Ida Babakhanyan	Neuropsychology	100%	42.00%					
Hui Chao Lee	Research Asst/Technician	50%	42.00%					
<b>Total Personnel</b>					<b>471,950</b>	<b>261,846</b>	<b>473,010</b>	<b>(1,060.12)</b>
<b><u>Non Personnel Expenses</u></b>								
Communcations				3,469.56	2,232.82	3,914.82	(445.26)	
Consulting and Other Outside Services				6,000.00	5,000.00	5,000.00	1,000.00	
Internal UM Services Provided				35,000.00	450.81	35,000.00	-	
Supplies				6,550.00	6,047.03	10,206.82	(3,656.82)	
Travel				6,000.00	876.95	1,170.91	4,829.09	
Equipment & Furniture				1,200.00	39.53	67.77	1,132.23	
Other *				39,830.69	1,119.49	41,629.82	(1,799.13)	
<b><u>Total Non Personnel Expenses</u></b>					<b>98,050</b>	<b>15,767</b>	<b>96,990</b>	<b>1,060.12</b>
<b>Grand Total Expenses</b>					570,000	277,612	570,000	0.00
<b>Net Operating Income</b>					-	227,165	0.00	0.00

\*Cost Share for Dr. Sacco, Fall Grad Tuition, Spring Grad Tuition, Dues & Membership, Postage, Freight, Printing, HIHG Biorepository

Mcknight  
 Budget For FY15 June 1, 2014 - May 31,2015

				<u>Budget</u>
<b><u>Revenue</u></b>				<b>574,617.52</b>
McKnight Project Clinical and Clinical Research Program				
<b><u>Personnel</u></b>				
<b><u>Subtotal Faculty Salary and CFB</u></b>				<b>218,117.44</b>
<u>Faculty</u>	<u>Role In Project</u>	<u>CFB Rate</u>	<u>Effort</u>	
Clinton Wright, MD	Scientific Director	20.80%	16%	40,990.85
Ralph Sacco, MD	Executive Director	20.80%	5%	35,114.94
TBA	Educational Director	20.80%	20%	48,320.00
Noam Alperin	Radiology	26.20%	5%	12,509.46
Bonnie Levin, PHD (Schoninger)	Neuropsychology	26.20%	30%	67,076.69
Gustavo Rey	Neuropsychology	26.20%	5%	9,465.00
Kunjan Dave	Basic Science	26.20%	5%	4,640.50
<b><u>Subtotal Staff Salary and CFB</u></b>				<b>289,770.52</b>
<b><u>Staff</u></b>	<b><u>Role in Project</u></b>			
Ahmet Bagci	Radiology	42.00%	20%	19,434.97
Sharlett Anderson	Neuropsychology	42.00%	30%	14,534.15
Digna Cabral	Administrative Support	42.00%	10%	9,543.47
Charles Cohan	Med Grad Student	0.00%	100%	27,810.00
Maria Mendoza-Puccini	Clinical Research Coordinator	42.00%	90%	70,503.12
Nooshin Nabizadeh	Teaching Assistant	0.00%	100%	27,810.00
Isabel Saul	Research Support Specialist	42.00%	30%	28,562.16
Maria Rosetti	Grad Student	0.00%	50%	11,667.84
Ida Babakhanyan	Neuropsychology	42.00%	100%	51,191.06
Hui Chao Lee	Research Asst/Technician	42.00%	50%	28,713.76
<b>Total Personnel</b>				<b>507,887.96</b>
<b><u>Non Personnel Expenses</u></b>				
Communcations				3,469.56
Internal UM Services Provided				29,000.00
Supplies				10,890.00
Travel				5,000.00
Equipment & Furniture				7,000.00
Conference & Registration				1,000.00
Other				10,370.00
<b><u>Total Non Personnel Expenses</u></b>				<b>66,729.56</b>
<b>Grand Total Expenses</b>				<b>574,617.52</b>
<b>Net Operating Income</b>				<b>(0.00)</b>



## **Faculty**

Noam Alperin, Ph.D.

Susan Blanton, Ph.D.

Kunjan R. Dave, Ph.D.

Chuanhui Dong, Ph.D.

Bonnie E. Levin, Ph.D.

Hung-Wen Lin, Ph.D.

Teshamae S. Monteith, M.D.

Alberto Ramos, M.D.

Tatjana Rundek, M.D., Ph.D.

Ralph L. Sacco, M.D., M.S.

Clinton B. Wright, M.D., M.S.

**BIOGRAPHICAL SKETCH**

Provide the following information for the Senior/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 Noam Alperin, PhD		POSITION TITLE	
eRA COMMONS USER NAME (credential, e.g., agency login) nalperin		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.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	MM/YY	FIELD OF STUDY
Tel-Aviv University, Israel	B.Sc.	10/80	Physics
Hebrew University, Jerusalem		8/83	Medicine
University of Chicago, Chicago, IL	Ph.D.	8/92	Medical Physics
University of Chicago, Chicago, IL	Postdoctoral	10/94	MRI

**A. Personal Statement: N/A**

**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, Uni. 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. Selected Peer-reviewed Publications (Selected from 48 peer-reviewed publications)**

**Most relevant to the current application**

1. **Alperin N**, Vikingstad EM, Gomez-Anson B, Levin DN. Hemodynamically independent analysis of cerebrospinal fluid and brain motion observed with dynamic phase contrast MRI. *Magnetic resonance in medicine* : official journal of the Society of Magnetic Resonance in Medicine / Society of Magnetic Resonance in Medicine. 1996;35(5):741-54
2. **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.
3. **Alperin N**, Lee SH. (2003). PUBS: Pulsatility based segmentation of lumens conducting nonsteady flow. *Magnetic Resonance in Medicine*, 49:934–944.
4. **Alperin N**, **Lee SH**, Sivaramakrishnan A, Hushek SG. Quantifying the effect of posture on intracranial physiology in humans by MRI flow studies. *Journal of magnetic resonance imaging* : JMRI. 2005;22(5)
5. **Alperin N**, Mazda M, Lichtor T, **Lee SH**. From Cerebrospinal Fluid Pulsation to Noninvasive Intracranial Compliance and Pressure Measured by MRI Flow Studies. *Current Medical Imaging Reviews*. 2006;2:117-29

6. **Tain RW, Alperin N.** Noninvasive intracranial compliance from MRI-based measurements of transcranial blood and CSF flows: indirect versus direct approach. *IEEE transactions on bio-medical engineering.* 2009;56(3):544-51
7. Alperin N, Bagci A, Lee S.H, Eftimov L, Ertl-Wagner B. Comparison between Total CBF Values Measured by ASL and Phase Contrast Over Increased Range of CBF Values. *Proc of ISMRM 2010;* 4080
8. Tain RW, Bagci AM, Lam BL, Sklar EM, Ertl-Wagner B, **Alperin N.** Determination of cranio-spinal canal compliance distribution by MRI: Methodology and early application in idiopathic intracranial hypertension. *J Magn Reson Imaging.* 2011 Dec;34(6):1397-404. doi: 10.1002/jmri.22799. Epub 2011 Oct 3.
9. **Alperin N,** Ranganathan S, **Bagci AM,** Adams DJ, Ertl-Wagner B, Saraf-Lavi E, et al. MRI Evidence of Impaired CSF Homeostasis in Obesity-Associated Idiopathic Intracranial Hypertension. *AJNR American journal of neuroradiology.* 2012. Epub 2012/07/07.
10. Koerte I, Haberl C, Schmidt M, Pomschar A, Lee S, Rapp P, **Alperin N,** Ertl-Wagner B. Inter- and intrarater reliability of blood and cerebrospinal fluid flow quantification by phase-contrast MRI. *J Magn Reson Imaging.* 2013 Jan 31. doi: 10.1002/jmri.24013.
11. Ranganathan S, Lee SH, Checkver A, Sklar E, Lam BL, Danton GH, **Alperin N.** Magnetic Resonance Imaging Finding of Empty Sella in Obesity related Idiopathic Intracranial Hypertension is Associated with Enlarged Sella Turcica. *Neuroradiology.* 2013 May 25.
12. Tain RW, **Alperin N.** Intracranial pressure dynamics are not linked to aqueductal cerebrospinal fluid stroke volume. *J Appl Physiol.* 2013 Jun; 114(11):1645.
13. Pomschar A, Koerte I, Lee S, Laubender RP, Straube A, Heinen F, **Alperin N.** MRI evidence for altered venous drainage and intracranial compliance in mild traumatic brain injury. *PloS one.* 2013;8(2):e55447.
14. Bagci AM, Lee SH, Nagornaya N, Green BA, **Alperin N.** Automated posterior cranial fossa volumetry by MRI: applications to Chiari malformation type I. *Ajnr.* 2013;34(9):1758-63.
15. **Alperin N,** Bagci AM, Lam BL, Sklar E. Automated quantitation of the posterior scleral flattening and optic nerve protrusion by MRI in idiopathic intracranial hypertension. *Ajnr.* 2013;34(12):2354-9.
16. **Alperin N,** Ranganathan S, Bagci AM, Adams DJ, Ertl-Wagner B, Saraf-Lavi E, Sklar EM, Lam BL. MRI evidence of impaired CSF homeostasis in obesity-associated idiopathic intracranial hypertension. *Ajnr.* 2013;34(1):29-34.
17. Gutierrez J, Sultan S, Bagci A, Rundek T, **Alperin N,** Elkind MS, Sacco RL, Wright CB. Circle of Willis Configuration as a Determinant of Intracranial Dolichoectasia. *Cerebrovascular diseases.* 2013;36(5-6):446-53.
18. Gutierrez J, Bagci A, Gardener H, Rundek T, Ekind MS, **Alperin N,** Sacco RL, Wright CB. Dolichoectasia Diagnostic Methods in a Multi-Ethnic, Stroke-Free Cohort: Results from the Northern Manhattan Study. *J Neuroimaging.* 2013.
19. **Alperin N,** Oliu C, Bagci A, Lee S, Adams D, Kovanlikaya I, Katzen H, Ivkovic M, Heier L, Relkin N. Low-Dose Acetazolamide Reverses Periventricular White Matter Hyperintensities in iNPH. *Neurology.* 2013;In Press.

#### **Additional recent publications of importance to the field (in chronological order)**

1. Raksin P, **Alperin N,** Surapaneni S, Lichtor T. (2003). Noninvasive Intracranial Compliance and Pressure from Dynamic MR Imaging of Blood and CSF Flows: Review of Principles, Implementation, and Other Noninvasive Approaches. *Neurosurg. Focus,* 14 (4); 1:8.
2. Sivaramakrishnan A, **Alperin N,** Surapaneni S, Lichtor T. (2004). Evaluating the Effect of Decompression Surgery on CSF Flow and Intracranial Compliance in Patients with Chiari Malformation Using MRI Flow Studies. *Neurosurgery,* 55(6):1344-50; discussion 1350-1.
3. Ford MD, **Alperin N,** Lee SH, Holdsworth DW, Steinman DA. (2005) Characterization of volumetric flow rate waveforms in the normal internal carotid and vertebral arteries. *Physiological Measurements,* 26(4):477-88.
4. Lichtor T, Egofske P, **Alperin N.** (2005). Noncommunicating cysts and cerebrospinal fluid flow dynamics in a patient with a Chiari I malformation and syringomyelia. *Spine,* 15;30(12):1466-72
5. **Alperin N,** Sivaramakrishnan A, Lichtor T. (2005). Magnetic resonance imaging-based measurements of cerebrospinal fluid and blood flow as indicators of intracranial compliance in patients with Chiari malformation. *Journal of Neurosurgery,* 103(1):46-52.

6. **Alperin N**, Lee S, Sivaramakrishnan A, Hushek S. (2005). Quantifying the Effect of Posture on Intracranial Physiology in Humans by MRI Flow Studies. *Journal of Magnetic Resonance Imaging*. 22(5):591-6.
7. Tain RW, Ertl-Wagner B, **Alperin N**. (2009). Influence of the compliance of the neck arteries and veins on the measurement of intracranial volume change by phase-contrast MRI. *Journal of Magnetic Resonance Imaging*, 30(4):878-83.
20. Wåhlin A, Ambarki K, Birgander R, **Alperin N**, Malm J, Eklund Assessment of craniospinal pressure-volume indices. *AJNR Am J Neuroradiol*. 2010 Oct;31(9):1645-50. Epub 2010 Jul 1
21. Teng PY, Bagci AM, **Alperin N**. Automated prescription of an optimal imaging plane for measurement of cerebral blood flow by phase contrast magnetic resonance imaging. *IEEE Trans Biomed Eng*. 2011 Sep;58(9):2566-73. Epub 2011 Jun 13.
22. Tain and RW, **Alperin N**. (2009). Noninvasive Intracranial Compliance From MRI-Based Measurements of Transcranial Blood and CSF Flows: Indirect vs. Direct Approach. *IEEE Trans Biomed Eng*, 56(3):544-51.

## D. Research Support

### Ongoing Research Support

**R01 NS052122 PI: Alperin**

08/01/07-01/31/14

Development and Early Clinical Evaluation of Noninvasive MRI Measurement of ICP

The goal of the study is to implement an MRI-based measurement of intracranial compliance and pressure (MR-ICP) in the clinical setup of Arnold Chiari Malformations and evaluate the role of intracranial compliance in the pathophysiology of this relatively common but poorly understood neurological problem.

**NASA NNX14AB51G PI: Alperin**

12/01/2013- 11/30/2014

Retrospective Analyses of MR Imaging of CSF Dynamics Pre and Post Space Flight

Microgravity-induced elevated intracranial pressure (ICP) is currently thought to be the cause of Visual Impairment Intracranial Pressure (VIIP) syndrome. The cause for ICP elevation in-flight has not yet been established. Current investigations of the VIIP syndrome focus on the vascular and interstitial cephalad fluid redistribution. An overlooked component is a potential cephalad cerebrospinal fluid (CSF) shift that is the focus of this study. The proposed study will utilize specialized MRI sequences, collected on 7 short-duration and 10 long-duration crewmembers, to assess CSF hydrodynamics and vascular hemodynamics to quantify CSF dynamics related physiological parameters.

### Completed Research Support

**R41 NS46185 PI: Alperin**

05/28/05-04/30/08

Noninvasive ICP: Reduction to practice

This proposal aims to make the MR-ICP method more widely available for use in Radiology by developing a user friendly software tool for MRI technologists. Role: PI

## BIOGRAPHICAL SKETCH

Provide the following information for the Senior/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 Blanton, Susan Halloran.	POSITION TITLE Associate Professor		
eRA COMMONS USER NAME (credential, e.g., agency login) Shblanton			
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
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

Not Applicable

### 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-present	Assoc Professor, Dr. John T. Macdonald Foundation Department of Human Genetics, University of Miami Leonard M. Miller School of Medicine, Miami, Florida
2012-present	Executive Director, John P. Hussman Institute for Human Genomics University of Miami Leonard M. Miller School of Medicine, Miami, Florida

#### Other Experience and Professional Memberships

1990-1995	Member, Tuberos 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	Special emphasis panel, NINDS
2005-2007	Ad Hoc, NINDS study section NST
2007-2011	Member, NINDS study section NST
2008-present	Editorial Board, Journal of Biomedicine and Biotechnology
2008	Reviewer, March of Dimes
2011	NCBDDD, Fragile X/Rare Disorders special emphasis panel

#### 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

### C. Selected Peer-reviewed Publications (Selected from 143 peer-reviewed publications)

#### Recent publications of importance to the field (in chronological order)

1. **Blanton SH**, Burt A, Stal S, Mulliken J, Garcia E, Hecht JT. Family-based study shows heterogeneity of susceptibility locus on chromosome 8q24 for nonsyndromic cleft lip and palate. *Birth Defects Research Part A: Birth Defects Res A Clin Mol Teratol.* 2010 Apr;88(4):256-259. PMID: PMC2861347.
2. Sirmaci A, Erbek S, Price J, Huang M, Duman D, Cengiz FB, Bademci G, Tokgoz-Yilmaz S, Hismi B, Ozdag H, Öztürk B, Kulaksizoglu S, Yildirim E, Kokotas H, Grigoriadou M, Petersen MB, Shahin H, Kanaan M, King MC, Chen ZY, **Blanton SH**, Liu XZ, Zuchner S, Akar N, Tekin M. A Truncating Mutation in SERPINB6 is Associated with Autosomal Recessive Non-Syndromic Sensorineural Hearing Loss. *Am J Hum Genet.* 2010 May 14;86(5):797-804. PMID: PMC2869020.
3. Della-Morte D, Beecham A, Boden-Albala B, Slifer S, McClendon MS, Rundek T, **Blanton SH**, Sacco RL. Genetic linkage of serum homocysteine in Dominican families: the family study of stroke risk and carotid atherosclerosis. *Stroke.* 2010 Jul;41(7):1356-62. PMID: PMC2914470.
4. 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 Aug;3(4):386-92. PMID: PMC2923674.
5. Kumar A, Maheswara RD, Prabhakaran VC, Shetty JS, Murthy GJ, **Blanton SH**. A homozygous mutation in LTBP2 causes isolated microspherophakia. *Hum Genet.* 2010 Oct;128(4):365-71.
6. **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.* 2010 Nov;47(6):574-7. PMID: PMC3039881.
7. Dong C, Beecham A, Slifer S, Wang L, **Blanton SH**, Wright CB, Rundek T, Sacco RL. Genomewide Linkage and Peakwide Association Analyses of Carotid Plaque in Caribbean Hispanics. *Stroke.* 2010 Dec;41(12):2750-6. PMID: PMC3004531.
8. Dong C, Beecham A, Slifer S, Wang L, McClendon MS, **Blanton SH**, Rundek T, Sacco RL. Genome-wide linkage and peak-wide association study of obesity-related quantitative traits in Caribbean Hispanics. *Hum Genet.* 2011 Feb; 129(2):209-19. PMC Journal-In Process.
9. 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 OLR1 Gene and Carotid Plaque. *Stroke.* 2011 Mar;42(3):588-92. PMID: PMC3042493.
10. 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 Apr;42(4):889-96. PMID: PMC3116444.
11. Dong C, Beecham A, Wang L, Slifer S, Wright CB, **Blanton SH**, Rundek T, Sacco RL. Genetic loci for blood lipid levels identified by linkage and association analyses in Caribbean Hispanics. *J Lipid Res.* 2011 Jul;52(7):1411-9. PMID: PMC3122911.
12. Kuo F, Gardener H, Dong C, Cabral D, Della-Morte D, **Blanton SH**, Elkind MS, Sacco RL, Rundek T. Traditional Cardiovascular Risk Factors Explain the Minority of the Variability in Carotid IPlaque. *Stroke.* 2012 Jul;43(7):1755-60. PMID: PMC3383876.
13. Della-Morte D, Beecham A, Rundek T, Wang L, McClendon MS, Slifer S, Blanton SH, Di Tullio MR, Sacco RL. A Follow-Up Study for Left Ventricular Mass on Chromosome 12p11 Identifies Potential Candidate Genes. *BMC Med Genet.* 2011 Jul 26;12:100. PMID: PMC3199748.
14. Della-Morte D, Beecham A, Dong C, Wang L, McClendon MS, Gardener H, **Blanton SH**, Sacco RL, Rundek T. Association between variations in coagulation system genes and carotid plaque. *J Neurol Sci.* 2012 Dec 15;323(1-2):93-8. doi: 10.1016/j.jns.2012.08.020. PMID: PMC3483411 [Available on 2013/12/15].

15. Wang L, Rundek T, Beecham A, Hudson B, **Blanton SH**, Zhao H, Sacco RL, Dong C. Genome-Wide Interaction Study Identifies RCBTB1 as a Modifier for Smoking Effect on Carotid Intima-Media Thickness. *Arterioscler Thromb Vasc Biol.* 2013 Nov 7. [Epub ahead of print].

#### D. Research Support

##### Ongoing Research Support

**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

**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

**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.

**1 R01 DC009645-01A2-02** (Tekin, M)

06/01/10-05/31/15

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

**1R01NS065114-04** (Tatjana Rundek, Susan Blanton)

07/01/10-06/30/15

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: Co-Principal Investigator

(Dong, C)

07/01/11-06/30/14

James and Esther King Biomedical Research

*"Gene-Smoking Interactions and Atherosclerosis"*

Role: Collaborator

**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: Principle Investigator

**1R01 DC012836-01** (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** (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

**Completed Research Support (last three years)**

**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

**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 dominate retinitis pigmentosa.

Role: PI on subcontract

**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

**5R01HD043342-05** (Hecht) PI – University of Texas

09/29/06-07/31/11

**5R01HD043342-05** (Hecht) PI – University of Texas (Admin Supp)

08/01/09-07/31/11

NIH-NICHHD

*“Genetic Studies of Clubfoot” (ITEV)*

*“Genetic Studies of Clubfoot Administrative Support” (ITEV)*

To map the genes for clubfoot

Role: PI on Subcontract

**5R01HD051804-05** (Werler)

08/01/06-05/31/11

NIH-NICHHD

*“Maternal Vasoactive Exposures and Rise of Clubfoot”*

The purpose of this grant is to confirm previously reported linkages in clubfoot.

Role: PI on subcontract

**No number** (Hecht) – UTHSC

01/01/07-12/31/10

Shriner’S Hospital for Crippled Children

*“Gene Studies in Idiopathic Talipes Equinovarus (ITEV) (Clubfoot)”*

The purpose of this grant is to evaluate the role of genes in candidate pathways in the development of club foot.

Role: Consultant



**BIOGRAPHICAL SKETCH**

Provide the following information for the Senior/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 Kunjan R. Dave		POSITION TITLE <b>Research Associate Professor</b>	
eRA COMMONS USER NAME (credential, e.g., agency login) <b>KRDAVE</b>			
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
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, USA.	Post doc	2000-2003	Neurology

**A. Personal Statement**

NA.

**B. Positions and Honors****Professional experience:**

- Research Associate Professor (2013 - ) Department of Neurology, Univ. of Miami School of Medicine, Miami, USA.
- Research Assistant Professor (2006 - 2013) Department of Neurology, Univ. of Miami School of Medicine, Miami, USA.
- Assistant Scientist (2003 - 2006) Department of Neurology, Univ. of Miami School of Medicine, Miami, USA.
- 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 research paper "Effect of Aluminium-induced Alzheimer-like condition on oxidative energy metabolism in rat liver, brain and heart mitochondria," for the year 1999-2000.
- Received "Hari Ohm Ashram Prerit Shri Bhaikaka Inter-University Smarak Trust" Award, Sardar Patel University, Vallabh Vidyanagar, Gujarat, India for research paper "Paracetamol hepatotoxicity and microsomal function." for the 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:**

- Member Society for Neurosciences.

### C. Selected Peer-reviewed Publications

\* First two authors contributed equally to the work.

- 1) **Dave KR**, Della-Morte D, Saul I, Prado R, Perez-Pinzon MA. Ventricular fibrillation-induced cardiac arrest in the rat as a model of global cerebral ischemia. *Transl Stroke Res.* 2013 Oct 1;4(5).
- 2) Thompson JW, **Dave KR**, Saul I, Narayanan SV, Perez-Pinzon MA. Epsilon PKC Increases Brain Mitochondrial SIRT1 Protein Levels via Heat Shock Protein 90 following Ischemic Preconditioning in Rats. *PLoS One.* 2013 Sep 13;8(9):e75753.
- 3) Thompson JW, **Dave KR**, Young JI, Perez-Pinzon MA. Ischemic preconditioning alters the epigenetic profile of the brain from ischemic intolerance to ischemic tolerance. *Neurotherapeutics.* 2013 Oct;10(4):789-97.
- 4) Neumann J.T., Cohan C.H., **Dave K.R.**, Wright C.B., Perez-Pinzon M.A. Global Cerebral Ischemia: Synaptic and Cognitive Dysfunction. *Curr Drug Targets.* 2013 Jan 1;14(1):20-35.
- 5) **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.* 2011;6(7):e22057.
- 6) **Dave K.R.**, Tamariz J., Desai K.M., Brand F.J., Liu A., Saul I., Bhattacharya S.K., Pileggi A. Recurrent hypoglycemia exacerbates cerebral ischemic damage in streptozotocin-induced diabetic rats. *Stroke.* 2011, 42:1404-11.
- 7) **Dave K.R.**, Defazio R.A., Raval A.P., Dashkin O., Saul I., Iceman K.E., Perez-Pinzon M.A., Drew K.L. Protein kinase C epsilon activation delays neuronal depolarization during cardiac arrest in the euthermic arctic ground squirrel. *J Neurochem.* 2009, 110:1170-9.
- 8) \* 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.* 2009, 159, 993-1002.
- 9) \* **Dave K.R.**, Anthony Defazio R, Raval A.P., Dashkin O., Saul I., Iceman K.E., Perez-Pinzon M.A., Drew K.L. Protein kinase C epsilon activation delays neuronal depolarization during cardiac arrest in the euthermic arctic ground squirrel. *J Neurochem.* 2009, 110, 1170-9.
- 10) **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.
- 11) \* **Dave, K.R.**, R. Prado, A.P. Raval, K.L. Drew, M.A. Perez-Pinzon, The arctic ground squirrel brain is resistant to injury from cardiac arrest during euthermia, *Stroke*, 37:1261-1265, 2006
- 12) \* Raval A.P., **K.R. Dave**, M.A. Perez-Pinzon, Resveratrol mimics ischemic preconditioning in the brain, *J Cereb Blood Flow Metab*, 26:1141-7, 2006.
- 13) \* **Dave, K.R.**, C. Lange-Asschenfeldt, A.P. Raval, R. Prado, R. Busto, I. Saul, M.A. Perez-Pinzon, Ischemic preconditioning ameliorates excitotoxicity by shifting glutamate/gamma-aminobutyric acid release and biosynthesis, *J Neurosci Res.*, 82:665-673, 2005
- 14) \* Raval, A. P., **K.R. Dave**, R. Prado, L.M. Katz, R. Busto, T.J. Sick, M.D. Ginsberg, D. Mochly-Rosen, M.A. Perez-Pinzon, 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
- 15) \* **Dave, K.R.**, A.P. Raval, R. Prado, L.M. Katz, T.J. Sick, M.D. Ginsberg, R. Busto, M.A. Perez-Pinzon, Mild cardiopulmonary arrest promotes synaptic dysfunction in rat hippocampus. *Brain Res*, 1024:89-96, 2004

#### 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

3R01NS034773-11S1 Dr. Pérez-Pinzón, P.I. 1/1/2011 – 6/30/2013  
NIH/NINDS

Ischemic preconditioning: mechanisms of neuroprotection

The major goal of this project is to study the mechanisms by which ischemic preconditioning promotes protection.

Role: Co-investigator

Univ. of Miami SAC 2013-13 Dr. Dave, PI 01/2013 – 01/2014

Red blood cell microparticles (RMPs) to reduce bleeding following hemorrhagic stroke.

The major goal of this project is to determine efficacy of RMPs in reducing bleeding in a rat model of hemorrhagic stroke.

Role: Principal Investigator

**BIOGRAPHICAL SKETCH**

Provide the following information for the Senior/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 Dong, Chuanhui		POSITION TITLE	
eRA COMMONS USER NAME (credential, e.g., agency login) CHDONG07		Research 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)	MM/YY	FIELD OF STUDY
Tongji Medical University, Wuhan, China	M.D.	07/84	Preventive Medicine
Hubei Medical University, Wuhan, China	M.A.	06/89	Epidemiology
Shanghai Medical University, Shanghai, China	Ph.D.	07/98	Molecular Epidemiology
Karolinska Institute, Stockholm, Sweden	Post-Doc	12/00	Genetic Epidemiology
University of Pennsylvania, Philadelphia	Post-Doc	10/03	Statistical Genetics

**A. Personal Statement**

N/A

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

1984-1986 Teaching Assistant, Dept. of Epidemiology, Hubei Medical University, Wuhan, China  
 1989-1995 Instructor, Clinical Epidemiology, Dept. of Epidemiology, Hubei Medical University, Wuhan, China  
 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- Research Assistant 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  
 2002-2006 Member, American Association for Cancer Research  
 2006-2007 Statistical Design and Analysis Committee for QRRO, American College of Radiology

**C. Selected Peer-reviewed Publications** (Selected from 70 peer-reviewed publications in international Journals and 25 in national journals)

- Dong C.,** Wang S., Li W.D., Zhao H., Price R.A. (2003). Interacting genetic loci in chromosome regions 20q and 10q influence extreme human obesity. *Am J of Hum Genet*, 72(1): 115-124. PMID:12478478
- Dong C.,** Li W.D., Li D., Zhao H., Price R.A. (2005). Interaction between obesity-susceptibility loci in chromosome regions 2p25-p24 and 13q13-q21. *Eur J of Hum Genet*, 13(1): 102-108. PMID:15470360
- Dong C.,** Li W.D., Geller F., Lei L., Li D., Gorlova O.Y., Hebebrand J., Amos C.I., Nicholls R.D., Price R.A. (2005). Possible Genomic Imprinting of Three Human Obesity-Related Genetic Loci. *Am J Hum Genet*, 76(3): 427-437. PMID:15647995

4. Wong M.L., **Dong C.**, Maestre-Mesa J., Licinio J. (2008). Polymorphisms in inflammation-related genes are associated with susceptibility to major depression and antidepressant response. *Mol Psychiatry*, 13(8):800-812. PMID:18504423
5. **Dong C.**, Wong M.L., 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
6. Licinio, J., **Dong, C.**, Wong, M.L. (2009). Novel sequence variations in the brain-derived neurotrophic factor gene and association with major depression and antidepressant treatment response. *Archive of General Psychiatry*. 66(5):488-497. PMID:19414708
7. **Dong C.**, Beecham A., Slifer S., Wang L., Blanton S., Wright C.B., Rundek T., Sacco R.L. (2010). Genome-wide linkage and peak-wide association analyses of carotid plaque in Caribbean Hispanics. *Stroke*, 41(12):2750-2756. PMID: 20966410
8. **Dong, C.**, Beecham, A., Slifer, S., McClendon, M.S., Wang, L., Blanton, S.H., Rundek, T., Sacco, R.L. (2011). Linkage and association of obesity related-quantitative traits with genes on chromosome 1q43 in Caribbean Hispanics. *Human Genetics*, 129(2):209-19. PMID: 21104097
9. **Dong C.**, Beecham A., Wang L., Slifer S., Blanton S.H., Wright C.B., Rundek T., Sacco R.L. (2011). Genetic loci for blood lipid levels identified by linkage and association analyses in Caribbean Hispanics. *J Lipid Res*, 52(7):1411-1419, 2011. PMID: 21558551
10. **Dong, C.**, Della-Morte, D., Wang, L., Cabral, D., Beecham, A., McClendon, M.S., Luca, C.C., Blanton, S.H., Sacco, R.L., Rundek, T. (2011) Association of the Sirtuin and Mitochondrial Uncoupling Protein Genes with Carotid Plaque. *PLoS One*, 6(11): e27157. PMID: 22087257
11. **Dong, C.**, Beecham, A., Wang, L., Blanton, S.H., Rundek, T., Sacco, R.L. (2012) Follow-up association study of linkage regions reveals multiple candidate genes for carotid plaque in Dominicans. *Atherosclerosis*. 223(1):177–183. PMID: 22503546
12. Wang, L., Beecham, A., Zhuo, D., **Dong, C.**, Blanton, S.H., Rundek, T., Sacco, R.L. (2012). Fine Mapping Study Revealed Novel Candidate Genes for Carotid Intima-Media Thickness in Dominicans. *Circ Cardiovasc Genet*. 5(2):234-41. PMID:22423143
13. **Dong, C.**, Rundek T., Wright, C.B., Anwar, Z., Elkind, M.S.V., Sacco, R.L. (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(24):2975-84. PMID: 22619283
14. Wong ML, **Dong C**, Andreev V, Arcos-Burgos M, Licinio J., (2012). Prediction of susceptibility to major depression by a model of interactions of multiple functional genetic variants and environmental factors. *Mol Psychiatry*. 17(6):624-33. PMID: 22449891
15. Wang, L., Rundek, T., Beecham, A., Hudson, B., Blanton, S.H., Zhao, H., Sacco, R.L., **Dong, C.** Genome-Wide Interaction Study Identifies RCBTB1 as a Modifier for Smoking Effect on Carotid Intima-Media Thickness. *Arterioscler Thromb Vasc Biol*. 2013 Nov 7. [Epub ahead of print]. PMID: 24202307

#### D. Research Support

##### Ongoing Research Support

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.

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

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

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

NIH/NINDS, 1U54NS081763, Ralph Sacco (PI)                                  2013-2017  
Hispanic stroke prevention intervention research program  
Role: Co-investigator/Statistician

1R01 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

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 2012-2015  
Role: Biostatistician

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  
Role: Co-investigator/Biostatistician

**Completed Research Support (within the last three years):**

2R01NS040807                  Ralph Sacco (PI)                                  09/09-08/11  
Family study of stroke risk and carotid atherosclerosis  
To investigate genes influencing carotid atherosclerosis through linkage and association studies.  
Role: Statistician

1U01NS069208                  Kittner Steven(PI)                                  07/10-06/13  
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

R21MH084814                  Drenna G Waldrop-Valverde (PI)                                  05/09-04/11  
Health literacy, cognitive and social determinants of HIV appointment attendance  
Role: Statistician

5R01DA018066                  Drenna G Waldrop-Valverde (PI)                                  08/05-07/10  
HIV+Drug Users: Neurocognitive Aspects of ARV Adherence  
To identify contributors to poor treatment adherence in HIV+Drug Users.  
Role: Statistician

K24RR017365                  Ma-Li Wong (PI)                                  07/03-05/10  
Pharmacogenetics of Antidepressant Drugs  
To identify genetic variants associated with antidepressant response.  
Role: Statistician

**BIOGRAPHICAL SKETCH**

Provide the following information for the Senior/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, PhD		POSITION TITLE Professor of Neurology and Psychology	
eRA COMMONS USER NAME (credential, e.g., agency login) bonnie_levin			
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
Georgetown University Temple University	BS PhD	1974 1983	Psychology Psychology

**Positions and Honors**

**EMPLOYMENT:**

- 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, Department of Neurology, University of Miami
- 2011- Professor, Department of Neurology

**AWARDS AND OTHER PROFESSIONAL EXPERIENCE:**

- 1974-Cum Laude, Georgetown University; Psi Chi Honor Society
- 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, Neuropsychology Review, Neuropsychology and Cognition
- Alexandria and Bernard Schoninger Endowed Professorship in Neurology, 2009

**C. Selected Publications:**

1. Papapetropoulos, S. Katzen, H., Schrag, A., Singer, C., Scanlon, B. K., Nation, D. Guevara, A. & Levin, B.E. A questionnaire-based (UM-PDHQ) study of hallucinations in Parkinson's disease. BMC Neurology, 8,21-29.
2. Nation, DA, Katzen, HL, Scanlon, B.E., Papapetropolis, S, Duncan R, Rodriguez, RA, Singer, C, Levin, BE. Defining subthreshold depression in Parkinson's disease, International Journal of Geriatric Neuropsychiatry, 2009, 24 (9) 937-943.
3. Levin, BE. Behavioral/Neuropsychological outcomes and quality of life endpoints, Woodbury KM, Coull BM (eds) Clinical Trials in Neurosciences. Frontiers of Neurology and Neuroscience. Basel, Karger, 2009 (25) ; 78-92
4. Papapetropoulos, S., Katzen, H., Scanlon, B., Guevera, A., Singer, C., & Levin, B. (2010). Objective quantification of neuromotor symptoms in Parkinson's disease: implementation of a portable, computerized measurement tool. Parkinson's Disease, Vol. 2010. Article ID 760196, 6 pages, 2010. doi:10.4061/2010/760196
5. Katzen, H., Myerson, C., Papapetropoulos, S., Nahab, F., Gallo, B. & Levin, B. (2010). Multi-modal hallucinations and cognitive function in Parkinson's disease. Dementia and Geriatric Cognitive Disorders, 30 (1):51-56.
6. Katzen, H., Ravdin, L.D., Assuras, S., Heros, R., Kaplitt, M., Schwartz, T. H., Fink, M., Levin, B.E., & . Relkin, N.R. (2011). Post-shunt cognitive and functional improvement in idiopathic Normal Pressure Hydrocephalus (iNPH). Neurosurgery, 68(2): 416-419.
7. 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 (in press)
8. Geldmacher, DS, Levin BE, Wright CB. Characterizing healthy samples for studies of normal cognitive aging. Front. Ag. Neurosci., 4:6, 2012
9. Scanlon, B. K., Levin, B. E., Nation, D. A., Katzen, H. L., Guevara-Salcedo, A., Singer, C., & Papapetropoulos, S. (in press). An accelerometry-based study of lower and upper limb tremor in Parkinson's disease. Journal of Clinical Neuroscience.
10. Robertson, ED, DeFazio, A., Barnes, CA., Alexander, GE., Bizon, JL., Bowers, D., Foster, TC., Glisky, EL, Levin, BE, Ryan, L., Wright, CB., Geldmacher, DS. Challenges and opportunities for characterizing cognitive aging across species. Front.Ag, Neurosci., 4:6, 2012
11. Nahab, F., Levin, BE. Characterizing the Spectrum of Volition in Psychogenic Movement Disorders.
12. Psychogenic Movement Disorders and other Conversion Disorders. M. Hallett (Ed) Cambridge University Press (in press)
13. Assuras, S., Levin , BE. Special considerations for the neuropsychological interview of older adults. In L. Ravdin and H. Katzen (eds) Handbook on the Neuropsychology of Aging and Dementia. New York, Springer Publishing, 2012
14. Levin BE. Dementia. In MD Gellman and JR Turner (eds). Encyclopedia of Behavioral Medicine. Springer Science and Business Media, New York, 2012 (in press)
15. Levin, B.E., Katzen,H.L., Maudsley, A., Post, J., Myerson, C., Govind, V., Nahab, F., Scanlon, B., & Mittel, A. Whole-brain Proton MR Spectroscopic Imaging in Parkinson's Disease. [published online ahead of print December 10 2012. Journal of Neuroimaging, 2012.
16. Nahab FB, Levin B. Deception. In: Hallett M, Cloninger CR, Fahn S, Halligan P, Jankovic J, Lang AE, Voon V, eds. Psychogenic Movement Disorders and Other Conversion Disorders. Cambridge University Press 2012.

**Abstracts relevant to the proposed project:**

- Rossetti, M. A., Denny, K., Widerstrom-Noga, E., Katzen, H.L., Arheart, K.L., Mathew, A., Adcock, J., Babakhanyan, I., Govind, V., Levin, B.E and Maudsley A.A. (2013, February). The relationship between thalamic metabolites, attention, and pain in mild TBI. Presented at the 41<sup>st</sup> International Neuropsychological Society Annual Meeting, Waikoloa, Hawaii.



Program Director/Principal Investigator (Last, First, Middle): Levin, Bonnie E.

Levin, B.E., Rossetti, M.A., Llabre, M., Santiago, M., Elkind, M.S., Rundek, T., Sacco, R.L., Yaakov, A.S., and Wright, C.B. (2013, March). Modeling metabolic syndrome and its association with cognition. Presented at the American Psychosomatic Society Annual Meeting, Miami, FL.

Denny, K., Rossetti, M. A., Katzen, H., Sharma, K. R., Arheart, K., Maudsley, A., Levin, B., Govind, V. (2013, April). MRS correlates of working memory and anxiety in ALS. Presented at the Cognitive Neuroscience Society Annual Meeting. San Francisco, CA.

Denny, K., Rossetti, M. A., Broz, M., Ruiz, J., Katzen, H., Sharma, K. R., Arheart, K., Maudsley, A., Levin, B., Govind, V. (2013, February). *MRS correlates of executive function and depression in ALS*. Presented at the 41st International Neuropsychological Society Annual Meeting, Waikoloa, Hawaii.

#### **D. Research Support**

##### **Completed:**

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 in the order listed on Form Page 2. Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Lin, Hung Wen		POSITION TITLE Research Assistant Professor of Neurology	
eRA COMMONS USER NAME (credential, e.g., agency login) Hungwenlin			
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
Univ of Wisconsin – Madison, WI	BS	1999	Biochemistry
Southern Illinois Univ School of Medicine, Springfield, IL	PhD	2007	Pharmacology
Univ of Miami Miller Sch of Medicine, Miami, FL	Post-Doc	2007-2012	Neurology

**A. Personal Statement**

NA

**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 4<sup>th</sup> 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 3<sup>rd</sup> 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, Journal of Clinical and Experimental Cardiology
- 2013 Reviewer for Neurological Research, Translational Stroke Research, PLoS One
- 2013 Editorial Board member: Neurological Research and Therapy

### Patent

1. Endogenous Methyl Palmitate Modulates Nicotinic Receptor-Mediated Transmission in the Superior Cervical Ganglion. U.S. Provisional Patent filed Nov. 14, 2008, U.S. Prov. Pat. #61/199,297, **Hung Wen Lin** and Tony Jer-Fu Lee are named inventors.

### Professional Memberships

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

### C. Peer-Reviewed Publications

#### Most relevant to the current application (selected from 17 publications)

1. Neumann JT, Cohan CH, Dave KR, Alekseyenko A, Binkert M, Stransky K, **Lin HW**, Barnes CA, Wright CB, Perez-Pinzon MA. (2013) Effect of cardiac arrest on cognitive impairment and hippocampal plasticity in middle-aged rats. **(to be submitted)**
2. **Lin HW**, Gresia VL, Stradecki HM, Alekseyenko A, Dezfalian C, Neumann JT, Dave KR, Perez-Pinzon MA. (2013) Protein kinase c delta modulates endothelial nitric oxide synthase-mediated hypoperfusion after cardiac arrest. *J Cereb Blood Flow Metab.* **(In Press)**
3. **Lin HW**, Saul I, Gresia VL, Neumann JT, Dave KR, Perez-Pinzon MA. (2013) Fatty acid methyl esters and solutol HS 15 confers neuroprotection after focal and global cerebral ischemia. *Transl Stroke Res.* (epub ahead of print)
4. **Lin HW**, Della-Morte D, Thompson JW, Gresia VL, Narayanan SV, DeFazio RA, Raval AP, Saul I, Dave KR, Morris KC, Si ML, Perez-Pinzon MA (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: 22259083
5. Della-Morte D, Raval AP, Dave KR, **Lin HW**, Perez-Pinzon MA (2011) Post-ischemia activation of protein kinase C epsilon protects the hippocampus from cerebral ischemic injury: possible alterations in cerebral blood flow. *Neurosci. Lett.* 487:158-162. PMCID: PMC3004991
6. **Lin HW**, DeFazio RA, Della Morte D, Thompson JW, Narayanan SV, Raval AP, Saul I, Dave KR, Perez-Pinzon MA (2010) Derangements of post-ischemic cerebral blood flow by protein kinase C delta. *Neuroscience* 171:566-576. PMCID: PMC2981031
7. DeFazio RA, Levy S, Morales CL, Levy RV, Dave KR, **Lin HW**, Abaffy T, Watson BD, Perez-Pinzon MA, Ohanna V (2010) A protocol for characterizing the impact of collateral flow after distal middle cerebral artery occlusion. *Trans. Stroke Res.* 2:122-127. PMCID: PMC3095390
8. **Lin HW**, Liu CZ, Cao D, Chen PY, Chen MF, Lin SZ, Mozayan M, Chen AF, Premkumar LS, Torry DS, Lee TJ (2008) Endogenous methyl palmitate modulates nicotinic receptor-mediated transmission in the superior cervical ganglion. *Proc. Natl. Acad. Sci. U S A* 105:19525-19530. PMCID: PMC2596137

**Additional recent publications of importance to the field** (in chronological order)

1. Della Morte D, Abete P, Gallucci F, Scaglione A, D'Ambrosio D, Gargiulo G, De Rosa G, Dave KR, **Lin HW**, Cacciatore F, Mazzella F, Uomo G, Rundek T, Perez-Pinzon MA, Rengo F (2008) Transient ischemic attack before non-lacunar stroke in the elderly. J. Stroke Cerebrovasc. Dis. 17:257-262. PMCID: PMC2676578
2. DeFazio RA, Raval AP, **Lin HW**, Dave KR, Perez-Pinzon MA (2009) GABA synapses mediate neuroprotection after ischemic and epsilon PKC preconditioning in the rat hippocampal slice cultures. J. Cereb. Blood Flow Metab. 29: 375-384. PMCID: PMC2696173
3. Dave KR, Bhattacharya SK, Saul I, DeFazio RA, DeZfulian C, **Lin HW**, Raval AP, Perez-Pinzon MA (2011) 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. PMCID: PMC3137627
4. **Lin HW**, Thompson JW, Morris KC, Perez-Pinzon MA (2011) Signal transducers and activators of transcription (STATs)-mediated mitochondrial neuroprotection. Antioxid. Redox. Signal. 14: 1852-1861. PMCID: PM3078497
5. Morris KC, **Lin HW**, Thompson JW, Perez-Pinzon MA (2011) Pathways for ischemic cytoprotection: role of sirtuins in caloric restriction, resveratrol and ischemic preconditioning. J. Cereb. Blood Flow Metab. 31:1003-1019. PMCID: PMC3070983
6. **Lin HW**, Yoshida T, Rundek T (2012) Letter by Lin HW et al. regarding article, "Nitric oxide scavenging of red blood cell microparticles and cell-free hemoglobin as a mechanism for the red cell storage lesion". Circulation 125: e384. PMID: 22354984
7. **Lin HW**, Perez-Pinzon MA (2013) The role of fatty acids in the regulation of cerebral vascular function and neuroprotection in ischemia. CNS Neurol. Disord. Drug Targets 12: 316-324. PMID: 23469852

**D. Research Support**

National Scientist Development Grant from American Heart Association 01/01/13- 12/31/16  
The Role of Fatty Acid Methyl Esters on Cerebral Blood Flow Following Cardiac Arrest  
P.I.: Hung Wen Lin

**R01 NS045676** NIH/NINDS 06/01/07- 05/31/15  
Mechanisms of Neuroprotection against Cardiac Arrest  
Role: Co-investigator

**R01 NS073779** NIH/NINDS 03/01/12 - 12/31/16  
Increased Cerebral Ischemic Injury by Repeated Hypoglycemic Episodes in Diabetes  
Role: Co-investigator

**There is no scientific overlap between current or proposed projects**

**Completed Research Support**

**T32 NS007459** NIH/NINDS 08/01/09- 07/31/10  
Training Program in CNS Injury and Repair  
Role: Investigator

**10POST4340011** American Heart Association (AHA)-Philips 07/1/10- 06/30/12  
Protein Kinase C Delta Exacerbates Post-ischemic Cerebral Blood Flow Derangements after Cardiac Arrest  
P.I.: Hung Wen Lin

**BIOGRAPHICAL SKETCH**

Provide the following information for the Senior/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 <b>Teshamae S. Monteith, M.D.</b>	POSITION TITLE <b>Assistant Professor of Clinical Neurology Chief, Headache Division Miller School of Medicine, University of Miami, FL</b>
eRA COMMONS USER NAME (credential, e.g., agency login)	

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
Florida International University, Miami, FL	B.S.	12/1998	Biology
University of Miami, Miller School of Medicine, Miami, FL	M.D.	05/2004	Medicine
Albert Einstein-Montefiore Medical Center	Intern	06/2005	Internal Medicine
New York University School of Medicine, NY, NY	Residency	06/2008	Neurology
Thomas Jefferson University School of Medicine	Fellowship	06/2009	Headache
University of California, San Francisco	Fellowship	06/2011	Headache

**A. Personal Statement. N/A**

**B. Positions and Honors**

**POSITIONS AND EMPLOYMENT**

**Traineeship:**

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

**Other:**

1998	Victimization Peer Educator	Florida International University, Miami, FL
1997	Laboratory Technician	Miami Dade College, Miami FL

**Academic Appointments:**

2011-Present	Assistant Professor of Clinical Neurology	Department of Neurology, University of Miami, Miami, Florida
2013-Present	Headache Fellowship Director	Department of Neurology, University of Miami Florida

**Hospital Appointments:**

2011-Present	Chief, Headache Division	Department of Neurology, University of Miami, Miami, Florida
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**OTHER EXPERIENCE AND PROFESSIONAL MEMBERSHIPS**

**Ad Hoc Reviewer for the Professional Journals:** *American Headache Society, European Journal of Neurology.*

**Memberships:**

- 1996- American Academy of Neurology
- 2008- American Headache Society (New Investigator and Trainee, section chair; Academic Center Program Directors' Committee);
- 2009- International 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 (board member)
- 2013 Florida Society of Neurology (board member)

**HONORS**

- 1993 Florida International University Tuition Scholarship, Miami, FL
- 1994 National Institute of Health, Minority Biomedical Research Support Program
- 1998 AMSA Outstanding Commitment Award, Minority Committee Chairman
- 1998 Florida International University Honor's Program
- 2000 Leonard Miller School of Medicine at the University of Miami Tuition Award
- 2001 M<sup>c</sup> Clelland 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, 2010
- 2013 Harold G. Wolff Lecture Award, presented at the American Headache Society meeting 2013

**C. Selected Peer-reviewed Publications**

**Most relevant to the current application**

1. Monteith, T.S. and ML. Oshinsky, Tension-type headache with medication overuse: pathophysiology and clinical implications. *Curr Pain Headache Rep* 2009; 13(6): 463-9.
2. Kister I, Caminero AB, Monteith TS, Soliman A, Bacon TE, Bacon JH, et al. Migraine is comorbid with multiple sclerosis and associated with a more symptomatic MS course. *The journal of headache and pain.* 2010;11(5):417-25.
3. Raymond GV, Seidman R, Monteith TS, Kolodny E, Sathe S, Mahmood A, Powers JM. Head trauma can initiate the onset of adreno-leukodystrophy. *Journal of Neurological Sciences* 2010; 70-74.
4. Monteith, TS, Sprenger T. Tension type headache in adolescence and childhood: where are we now? *Curr Pain Headache Rep* 2010; 14 (6)424-30
5. Monteith T, Goadsby PJ. Acute Migraine Therapy: New Drugs and New Approaches. *Current Treatment Options in Neurology* 2011; 13 (1): 1-14
6. Knash ME, Monteith TS, Raskin NH. A comment on brief sharp stabs of head pain and giant cell arteritis. *Headache* 2011; 51 (6): 1010.
7. Monteith, TS, Scher AI. Epidemiology and classification of post-traumatic headache: What do we know and how do we move forward? *Cephalalgia.* 2013 Aug 8. [Epub ahead of print]
8. Maniyar FH, Sprenger T, Monteith T, Schankin C, Goadsby PJ. Brain activations in the premonitory phase of nitroglycerin-triggered migraine attacks. *Brain.* 2013 Nov 25. [Epub ahead of print]
9. Monteith, TS. Borsook D. Insights and Advances in Post-traumatic Headache: Research Considerations. *Current Neurology and Neuroscience Reports.* 2014. Accepted.
10. Marmura M, Monteith TS, Anjum W et al. Olfactory acuity in episodic migraine at baseline and during attacks, *Cephalalgia* 2014. Accepted.

**D. Research Support**

**Ongoing Research Support:**

<b><i>Grant Title</i></b>	<b><i>Year</i></b>	<b><i>Funding Agency</i></b>
<b><i>Active</i></b>		
(R37 NS 29993) Monteith (PI) The Relationship between Migraine, Subclinical Brain Lesions, and Biomarkers of Subclinical Cardiovascular Disease in a Tri-Ethnic Region; Role: PI.	2011-current	NINDS Supplement to Promote Diversity in Health-Related Research.
Marmura (PI) Olfactory acuity in episodic migraine at baseline and during attacks. Role: drafting/revising the manuscript for content; analysis or interpretation of data; study concept or design.	2009-current	Merck Investigator

**Completed Research Support**

PP1471 Kister (PI) Migraine and Multiple Sclerosis; Role; Data analysis, drafting manuscript for content	2008	National Multiple Sclerosis Society
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### BIOGRAPHICAL SKETCH

Provide the following information for the Senior/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 Alberto R. Ramos, MD	POSITION TITLE Assistant Professor of Neurology
eRA COMMONS USER NAME (credential, e.g., agency login) ARAMOS1	

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

**A. Personal Statement. N/A**

**B. Positions and Honors**

**Positions**

- 2006-07 Administrative Chief Resident-Neurology, University of Miami/Jackson Memorial Hos., Miami, FL.
- 2007-09 Staff Physician; Neurology Service, Miami VA Healthcare System, Miami, FL
- 2008-09 Instructor, Miller School of Medicine, University of Miami, Miami, FL.
- 2009 - Assistant Professor of Clinical Neurology, Miller School of Medicine, Miami, FL.
- 2010- present. Co-Director, UHealth 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, for Research project during Neurology Residency. Miami, FL
- 2008 Faculty Development Award-American Neurological Association, Annual meeting.
- 2010-2012 Who's who in America
- 2010-2012 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). New York University, NY.

**C. Peer-reviewed Publications**

1. **Ramos AR**, Dib SI, Wright CB. Vascular Dementia. *Curr Transl Geriatr and Exp Gerontol Rep* 2013; 2:188–195
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(4):599-603. PMID: 23711813
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.** 2013 (in press). PMID:23771345



4. **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(7):669-73. PMID: 23853560
5. Dib S, **Ramos A**, Wallace D, Rundek T. Sleep and Stroke. *Periodicum Biologorum*. 2012;114:369-75
6. **Ramos AR**, Cabral D, Lee DJ, Sacco RL, Rundek T. Cerebrovascular Pulsatility in Patients with Sleep Disordered Breathing. *Sleep Breath*. 2013;17(2):723-6. PMID: 22773271
7. 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(5):507-514.
8. Wallace WK, **Ramos AR**, Rundek T. Sleep Disorders and Stroke. *Int J Stroke*. 2012; 7(3):231-42. PMC3387919
9. **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(3-4):210-5.
10. 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(9):850-9.
11. 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(5):294-301.
12. **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. PMC2907549
13. 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.

#### D. Research Support.

1. Sleep apnea and cerebral hemodynamics: The Hispanic Community Health Study.  
KL2 Scholar-PI: Alberto R. Ramos, Mentor: Tatjana Rundek. Agency: CTSI-Miller School of Medicine: K12 Scholar: 5KL2TR000461-02. 75% effort time. Aims: To evaluate the cerebral hemodynamics as an early marker of cerebrovascular risk in participants with sleep apnea and controls.
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. Period 07.1.2011-04.31.2014. Aims: To determine the cardiovascular consequences of abnormal sleep patterns in Hispanics.

#### Completed Research.

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.

#### E. Other Support

1. National Institutes of Health/National Institute of Minority Health and Health Disparities-Loan Repayment Program. One year extension, 08/20123-07/2014.
2. National Institutes of Health/National Institute of Minority Health and Health Disparities-Loan Repayment Program. One year extension, 08/2012-07/2013.
3. 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 Senior/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 Tatjana Rundek, MD PhD		POSITION TITLE Professor of Neurology	
eRA COMMONS USER NAME (credential, e.g., agency login) TR89XX		Director, Clinical Translational Research University of Miami Miller School of Medicine	
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	MM/YY	FIELD OF STUDY
University of Zagreb, College of Mathematics, Croatia	B.S.	09/79-06/83	Applied Mathematics
Medical School University of Zagreb, Croatia	M.D.	08/84-06/89	Medicine
Medical School University of Zagreb, Croatia	M.S.	07/89-06/91	Epidemiology/Bioinformatics
Ludwig-Maximillian University, Munich, Germany	Ph.D.	08/91-05/95	Neuroscience
Medical School University of Zagreb, Croatia	Residency	1991-1994	Neurology
Grosssharden Spital, Munich, Germany	Fellowship	1994-1995	Stroke
Columbia University, New Work	Fellowship	1998-2001	Stroke/Epidemiology

**A. Personal Statement: N/A.**

**B. Positions and Honors**

**POSITIONS AND EMPLOYMENT**

**Traineeship:**

1990-91	Medicine Internship	Clinical Hospital for Pulmonary Diseases, Zagreb, Croatia
1991-94	Neurology Residency	Grosssharden Spital Munich, Germany
1995-96	Neurosonology Post-Doctoral Fellow	Neurosonolgy Laboratory University of Ulm, Germany
1998-00	Stroke Fellow (Epidemiology)	Columbia University, New York, NY

**Academic Appointments:**

1994-96	Assistant Professor of Neurology	Department of Neurology, University of Zagreb, Croatia
1996-98	Associate Professor of Neurology	Department 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, University of Miami, Miami, FL
2011-	Professor of Neurology	Miller School of Medicine, University of Miami, Miami, FL

**Hospital Appointments:**

1994-98	Stroke Attending	Department of Neurology, University of Zagreb, Croatia
2002-07	Director, Neurosonology Laboratory	Columbia University, New York, NY
2007-	Director, Clinical Translational Research Division in Neurology	Department of Neurology, Miller School of Medicine, University of Miami, Miami, FL

**OTHER EXPERIENCE AND PROFESSIONAL MEMBERSHIPS**

**Editorial Board Member of the Professional Journals:** Stroke, Neurology, Cerebrovascular Disease, Journal of Ultrasound in Medicine, Journal of CardioMetabolic Syndrome

**Ad Hoc Reviewer for the Professional Journals:** Neuroepidemiology, Circulation, JACC, Scandinavian Journal of Rheumatology, Headache, Annals of Internal Medicine, Archives of Neurology

**Memberships:**

- 1997- American Academy of Neurology
- 1997- American Heart Association
- 1997- European Federation of Neurological Societies - Dementia Panel Delegate
- 1994- American Institute of Ultrasound in Medicine
- 1994- European Society of Neurosonology and Cerebral Hemodynamics

## HONORS

- 1997 Fulbright Award and Scholarship, Neurological Institute, Columbia University, New York, NY
- 1996 George Soros Scholarship, Neurology Seminars, University of Krems, Austria
- 1995 Humbolt Award, Neurosonology Laboratory, University of Ulm, Germany
- 2006 Nassau Women Physicians Foundation Award for Stroke Research in Women; Long Island, NY
- 2009 President, Neurosonology Community Practices of the American Institute of Ultrasound in Medicine
- 2012 Member of the Board of the Directors of the Intersocietal Accreditation Committee

## C. Selected Peer-Reviewed Publications (from 12 chapters, 28 invited articles, 209 peer-reviewed articles):

1. Della-Morte D, Cacciatore F, Salsano E, Pirozzi G, Genio MT, D'Antonio I, Gargiulo G, Palmirota R, Guadagni F, **Rundek T**, Abete P. Age-related reduction of cerebral ischemic preconditioning: myth or reality? *Clin Interv Aging*. 2013;8:1055-1061. **PMCID: PMC3817003**
2. Della-Morte D, Ricordi C, **Rundek T**. The fountain of youth: role of sirtuins in aging and regenerative medicine. *Regen Med*. 2013 Nov;8(6):681-3. **PMID: 24147522**
3. Wallace DM, Ramos-Sepulveda A, **Rundek T**. Sleep disorders and stroke. *Int J Stroke*. 2012;7(3):231-42. **PMCID: PMC3387919**
4. Kuo F, Gardener H, Dong C, Cabral D, Della-Morte D, Blanton SH, Elkind MS, Sacco RL, **Rundek T**. Traditional cardiovascular risk factors explain the minority of the variance in carotid plaque. *Stroke*. 2012; 43:1755-60. **PMCID: PMC3383876**
5. Gardener H, Sjoberg C, Crisby M, Goldberg R, Mendez A, Wright CB, Elkind MS, Sacco RL, **Rundek T**. Adiponectin and Carotid Intima-Media Thickness in the Northern Manhattan Study. *Stroke*. 2012; 43(4):1123-5. **PMCID:PMC3314722**
6. Markert MS, Della-Morte D, Cabral D, Roberts EL Jr, 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):827-32. **PMCID: PMC3226921**
7. 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. **PMCID: PMC3210138**
8. Gardener H, **Rundek T**, Markert M, Wright CB, Elkind MS, Sacco RL. Diet Soft Drink Consumption is Associated with an Increased Risk of Vascular Events in the Northern Manhattan Study. *J Gen Intern Med*. 2012;27(9):1120-6. **PMCID: PMC3514985**
9. Gardener H, **Rundek T**, Wright CB, Elkind MS, Sacco RL. Dietary sodium and risk of stroke in the Northern Manhattan study. *Stroke*. 2012;43(5):1200-5. **PMCID:PMC3347890**
10. Della-Morte D, Guadagni F, Palmirota R, Testa G, Caso V, Paciaroni M, Abete P, Rengo F, Ferroni P, Sacco RL, **Rundek T**. Genetics of ischemic stroke, stroke-related risk factors, stroke precursors and treatments. *Pharmacogenomics*. 2012;13(5):595-613. **PMCID: PMC3514985**

## D. Research Support

### Ongoing Research Support

#### **Genetic Determinants of Extreme Phenotypes of Subclinical Atherosclerosis**

**NIH/NINDS K24 NS 062737 PI: T. Rundek**

(09.30.09-08.31.14)

This is a mid career award to train young investigators in patient-oriented research, perform research on genetic factors of extreme phenotypes of subclinical atherosclerosis.

#### **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; T. Rundek, Co-Investigator** (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.

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

**PI: R.L. Sacco; T. Rundek, Co-Investigator** (05.01.02-09.30.12)

The major goal of this study is to evaluate heritability and genetic linkage of novel vascular risk factors such as carotid intima-media thickness and carotid stiffness among the families of high-risk Caribbean Hispanics.

**Univ of Miami: Network of Excellence in Neuroscience Clinical Trials (NEXT) 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 NEXT and other NINDS trial implementation at the U of Miami and to leverage existing institutional strengths to enhance NEXT consortium activities.

**Ischemic Stroke Genetics**

**NINDS U01 The NINDS International Stroke Genetics Consortium Study**

**PI: S. Kittner on behalf of ISGC, U of Maryland, Site PIs: T. Rundek, R.L. Sacco** (04.01.10-3.31.14)

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

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

**PIs: Lipton, Derby; Albert Einstein, NY, T. Rundek, PI for the TCD Core Laboratory** (07.01.11-06.30.15)

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.

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

**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.

**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 (& supplement FL-PR CReSD-W)**

**NIH/NINDS U54 NINDS SPIRP U54NS081763**

**PI: RL Sacco; T. Rundek, Co-Investigator** (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&Puerto Rico using effective and culturally appropriate methods.

**Miami Regional Coordinating Center for NINDS Stroke Trials Network U10 NINDS NS086528**

**NIH/NINDS 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.

## **Prior Research Support**

### **Genetic Determinants of Subclinical Carotid Disease**

**NIH/NINDS R01 NS 047655**

**PI: T. Rundek**

(01.01.04-12.31.10).

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

### **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.

### **Mechanisms of Stroke in Intracranial Stenosis and Stenting (MoSISS)**

**NIH/NINDS R01 (NS 069938)**

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

(04.15.10-09.30.11).

This was an ancillary study of SAMMPRIS to study the underlying mechanisms in intracranial stenosis randomized to stenting vs. best medical treatment using TCD and QMRI.

### **MESA (Multi-Ethnic Subclinical Atherosclerosis**

**NIH/NHLBI-HC**

**CU PI: S. Shea; T. Rundek, Collaborator**

(06.15.02-05.31.10)

The objective of this large NIH contract was to examine traditional and novel risk factors and markers of subclinical atherosclerosis in a large sample of individuals from multi-ethnic communities.

### **A Multicenter, Randomized, Double-Blind Placebo-Controlled Study to test the Safety and Efficacy of Lipitor (atorvastatin) in Reducing the Progression of Carotid IMT in Early Childhood SLE", The Atherosclerosis Prevention in Pediatric Lupus Erythematosus (APPLE) Study; NIH/NIAMS BAA-02;**

**PI: L.E. Schanberg, Duke; T.Rundek, Site Co-I**

(06.15.04-05.31.08).

The objective of this study was to assess the efficacy of atorvastatin in reducing carotid IMT in children with systemic lupus erythematosus.

### **Carotid Artery Distensibility and Risk of Stroke; *The Gilbert Baum Memorial Grant and the American Institute of Ultrasound in Medicine Award;***

**PI: T. Rundek**

(7.01.04-06.30.05).

The objective of this case-control study was to determine whether impaired carotid distensibility assessed by ultrasound is associated with an increased risk of stroke.

### **The Hazel K. Goddess Fund for Stroke Research in Women;**

***The Hazel K. Goddess Fund;***

**PI: T. Rundek**

(7.01.01-06.30.04).

The major goals was to determine the effects of structural and functional carotid artery wall properties in a prospective cohort study of postmenopausal women over age 55 from 3 race-ethnic groups from northern Manhattan.

### **The PACTS-HOPE Project: Premature Atherosclerosis and Cardiovascular Risk in Children: Carotid Ultrasound Sub-study; CDC;**

**PI: E. Abrams, T. Rundek: Co-Investigator**

(7.01.05-06.30.06).

The objective of this sub-study was to examine the presence of subclinical atherosclerosis in HIV positive children and its associations with increased risk of CVD in children on the AZT medication.

**BIOGRAPHICAL SKETCH**

Provide the following information for the Senior/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 <b>Ralph Lewis Sacco, MD MS</b>	POSITION TITLE <b>Chairman and Professor of Neurology, Public Health Sciences, Human Genetics, and Neurosurgery</b>
eRA COMMONS USER NAME (credential, e.g., agency login) <b>SACCORL</b>	

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
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. N/A**

**B. Positions and Honors**

- 1989-97 Assistant Professor of Neurology & Public Health (Epidemiology) in the Sergievsky Center
- 1997-02 Associate Professor of Neurology & Public Health (Epidemiology) in the Sergievsky Center (with tenure)
- 2003-07 Professor of Neurology & Epidemiology, Columbia University, College of Physicians and Surgeons, Mailman School of Public Health, and the Sergievsky Center (with tenure)
- 2007- Olemberg Family Chair in Neurological Disorders, Miller Professor of Neurology, Epidemiology and Public Health, 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          |

**Other Professional Experience**

- 1999-05 American Academy of Neurology - Clinical Research Subcommittee, Chair
- 1997-03 NINDS, Performance Safety & Monitoring Committee, VISP Trial
- 2004-06 NINDS Neurosciences Training Grant Review Group, Member
- 2002-03 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
- 2005-09 American Academy of Neurology, Board of Directors
- 2010-11 President, American Heart Association, National Board of Directors
- 2013-15 Vice President, American Academy of Neurology
- 2013-16 National Advisory Neurological Disorders and Stroke Council, NINDS

**C. Selected Peer-reviewed Publications**

1. Sacco RL, Gan R, Boden-Albala B, Lin IF, Kargman DE, Hauser WA, Shea S, Paik M. Leisure-Time Physical Activity and Ischemic Stroke Risk: The Northern Manhattan Stroke Study. **Stroke** 1998;29:380-387 PMID: 9472878
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 PMID: 9482500
3. 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 PMID: 9892451
4. 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 PMID: 11386928
5. 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 PMID: 11486097.

Program Director/Principal Investigator (Last, First, Middle): Sacco, Ralph L

6. 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 Leukoariosis. **Stroke**. 2009 Nov;40(11):3466-71.
7. 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: 19958966
8. Willey JZ, Disla N, Moon YP, Paik MC, Sacco RL, Boden-Albala B, Elkind MS, Wright CB. Early depressed mood after stroke predicts long-term disability: the Northern Manhattan Stroke Study. **Stroke**. 2010;41:1896-900.
9. Rundek T, Gardener H, Xu Q, Goldberg RB, Wright CB, Boden-Albala B, Disla N, Paik MC, Elkind MS, Sacco RL. Insulin resistance and risk of ischemic stroke among nondiabetic individuals from the northern Manhattan study. **Arch Neurol**. 2010;67:1195-200.
10. Marcus J, Gardener H, Rundek T, Elkind MS, 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 Sep;42(9):2639-41.
11. Vieira JR, Elkind MS, 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(3-4):153-9.
12. 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 Jun 19;125(24):2975-84.
13. Economos A, Wright CB, 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 Jan 24;40(4):253-259.
14. Warsch JR, Rundek T, Paik MC, Elkind MS, Sacco RL, Wright CB. Association between northern Manhattan study global vascular risk score and successful aging. **J Am Geriatr Soc**. 2013 Apr;61(4):519-24.
15. Katan M, Moon YP, Paik MC, Sacco RL, Wright CB, Elkind MS. Infectious burden and cognitive function: the Northern Manhattan Study. **Neurology**. 2013 Mar 26;80(13):1209-15.
16. Ramos AR, Dong C, Elkind MS, Boden-Albala B, Sacco RL, Rundek T, Wright CB. Association between sleep duration and the mini-mental score: the Northern Manhattan study. **J Clin Sleep Med**. 2013 Jul 15;9(7):669-73.
17. 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 Dec 3;42(2):100-106.

#### **D. Research Support**

##### **Ongoing Research Support**

##### **Stroke Incidence and Risk Factors in a Tri-Ethnic Region**

Role: PI; Agency: NIH/NINDS; Type: R37 (formerly 2R01) (NS 29993); Period: 01.01.93-03.31.15

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

##### **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 (a) to function effectively as a NEXT consortium trial site, (b) to enhance quality and efficiency of NEXT and other NINDS trial implementation at the University of Miami and (c) to leverage existing institutional strengths to enhance NEXT consortium activities.

##### **Miami Clinical and Translational Science Institute**

Role: Co-I; PI: JSzapocznik; Agency: NIH/NCRR/NIMHD; Type: UL1TR000460; Period: 06.01.13-05.31.20

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

##### **Novel Factors for Unexplained Phenotypes of Carotid Atherosclerosis**

Role: Co-I; PI: TRundek/SBlanton; Agency: NIH/NINDS; Type: R01 (NS 065114); Period: 07.01.10-06.30.15

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.

##### **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.

**Subclinical Cardiovascular Disease Study: MESA Field Center**

Role Adjudicator; Agency: NIH/NHLBI; Type: Contract (NHLBI-HC-98-08); Period:03.01.99-08.31.15

Aims: To identify subclinical predictors of atherosclerotic disease in a multi-center prospective cohort study.

**Subclinical Cardiovascular Disease Study: MESA Air**

Role: Adjudicator; Agency: NIH/NHLBI; Type: Subcontract (NHLBI-HC-83169701); Period:04.01.07-07.31.14;

Aims: The prospective study of atherosclerosis, clinical cardiovascular disease and long term exposure to ambient particulate matter and other air pollutants in a multiethnic cohort.

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

Role: Co-I; PI: Schneiderman; Agency: NIH/NHLBI; Type: Contract; Period: 10.01.07-03.31.14

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.

**Ethnic/Racial Variations of Intracerebral Hemorrhage (ERICH)**

Role: Co-I; PI; Woo; Agency: NIH/NINDS; Type: R01 (NS069763) Period: 08.01.10-07.31.15

Aims: To identify the relative importance of leading risk factors for ICH in whites among blacks and Hispanics, determine differences in outcomes, and differences in neuroimaging characteristics by race and ethnicity.

**NINDS Ischemic Stroke Genetics Consortium**

Role: Co-I; PI: Kittner; Agency; NIH/NINDS; Type: U01 (NS069208); Period: 07.01.10-06.30.14

Aims: To assemble ischemic stroke phenotypic data and DNA samples from 11 stroke studies.

**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 an cognitive decline.

**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 via novel methods.

**Prior Research Support in last 3 years**

**New York Columbia Collaborative SPOTRIAS (Specialized Program on Translational Research in Acute Stroke)**

Role: PI; Agency: NIH/NINDS; Type: P50 (NS 049060); Period: 09.30.04-05.31.09

Aims: The major goals of this program project are to perform three innovative acute stroke projects: (1) a dose escalation safety trial of high-dose statins in acute stroke; (2) determine the functional significance of contralateral fMRI activity in acute stroke; and (3) develop and test the efficacy of an innovative behavioral modification intervention to train people how to react if they are having stroke warning symptoms.

**A Primary Hyperparathyroidism - non-classical Manifestations**

Role: Co-I; PI: Silverberg; Agency: NIH/NIDK; Type: R01 (DK 066329); Period: 4.15.05-03.31.11

Aims: This is a prospective study to evaluate the effects of hyperparathyroidism on carotid disease and other cardiovascular outcomes.

**Inflammatory and Infectious Burden and Risk of Stroke**

Role: Co-I; PI: Elkind; Agency: NIH/NINDS; Type: R01 (NS 048134); Period: 03.01.04-02.28.09

Aims: This is a prospective analysis of inflammatory markers and infectious markers as risk factors for vascular outcomes within the Northern Manhattan Study cohort

**Genetic Determinants of Subclinical Carotid Disease**

Role: Co-I; PI: Tanja Rundek; Agency: NIH/NINDS; Type: R01 (NS 047655); Period: 01.01.04-12.31.10

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

**Aortic, Cardiovascular Disease and Silent Brain Infarcts**

Role: Co-I; PI: Di Tullio; Agency: NIH/NINDS; Type: 1R01 (NS 36286); Period: 06.01.97-05.31.10

Aims: To determine whether aortic arch plaques and cardiovascular exposures are risk factors for silent infarcts and vascular outcomes within a prospective cohort study.



### BIOGRAPHICAL SKETCH

Provide the following information for the Senior/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 Clinton B. Wright		POSITION TITLE Scientific Director, Evelyn F. McKnight Center for Age Related Memory Loss Associate Professor of Neurology	
eRA COMMONS USER NAME (credential, e.g., agency login) WRIGHTCL			
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
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: N/A**

**B. Positions and Honors**

**Positions and Employment**

- 1997-1998 Intern, Internal Medicine.
- 1998-2001 Resident, Neurology, New York Presbyterian Hospital; New York, NY
- 2001-2003 Fellowship in Cerebrovascular Disease, Columbia University College of Physicians and Surgeons, New York, NY
- 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 Professor of Neurology, Columbia University, New York, NY (pending)
- 2008-present Associate Professor of Neurology, University of Miami, Miami, FL

**C. Selected Peer-reviewed Publications**

1. **Wright CB**, Rundek T, Paik MC, Elkind MSV, Sacco RL. Alcohol intake, carotid plaque, and cognition. *Stroke* 2006; 37:1160-1164. **PMCID: PMC1447604**
2. **Wright CB**, Sacco RL, Rundek TR, Delman JB, Rabbani LE, Elkind MSV. Interleukin-6 is associated with cognitive function: the Northern Manhattan Study. *J Stroke Cerebrovasc Dis* 2006; 15:34-38. **PMCID: PMC1382058**
3. Prabhakaran S, **Wright CB**, Yoshita M, Delapaz R, Brown T, DeCarli C, Sacco RL. Prevalence and determinants of subclinical brain infarction: the Northern Manhattan Study. *Neurology* 2007; 70:425-30. **PMCID: PMC2714050**
4. Khatri M, **Wright CB**, Nickolas TL, Paik MC, Sacco RL, DeCarli C. Chronic Kidney Disease is associated with White Matter Hyperintensity Volume: The Northern Manhattan Study (NOMAS). *Stroke* 2007; 38: 3121. **PMCID: PMC2948438**
5. **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. **PMCID: PMC2267752**

6. Noble JM, Borrell LN, Papapanou PN, Elkind MSV, Scarmeas N, **Wright, CB**. Periodontitis is associated with cognitive impairment among older adults: analysis of NHANES-III. *Journal of Neurology, Neurosurgery and Psychiatry J. Neurol. Neurosurg. Psychiatry* 2009; 11:1206-11. **PMCID: PMC3073380**
7. Siedlecki KL, Stern Y, Reuben A, Sacco RL, Elkind MSV, **Wright CB**. Construct validity of cognitive reserve in a multiethnic cohort: The Northern Manhattan Study. *The Journal of the International Neuropsychological Society* 2009; 15:558-69. **PMCID: PMC2803322**
8. 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 Nov; 20:2427-32. **PMCID: PMC2799177**
9. Willey JZ, Moon YP, Paik MC, Yoshita M, Decarli C, Sacco RL, Elkind MS, **Wright CB**. Lower prevalence of silent brain infarcts in the physically active: the Northern Manhattan Study. *Neurology*. 2011;76:2112-8. **PMCID: PMC3111237**
10. 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 Sep;42:2639-41. **PMCID: PMC3189513**
11. Vieira JR, Elkind MS, 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. **PMCID: PMC3214939**
12. Siedlecki KL, Rundek T, Elkind MS, 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*. 2011:1-11. **PMCID: PMC3370823**
13. Gardener H, Scarmeas N, Gu Y, Boden-Albala B, Elkind M.S.V, Sacco RL, DeCarli C, **Wright CB**. Mediterranean Diet and White Matter Hyperintensity Volume in the Northern Manhattan Study. *Archives of Neurology* 2012; 69:251-256. **PMCID: PMC3281550**
14. Ramos AR, Dong C, Elkind MS, Boden-Albala B, Sacco RL, Rundek T, **Wright CB**. Association between sleep duration and the mini-mental score: the Northern Manhattan study. *J Clin Sleep Med*. 2013 Jul 15;9(7):669-73. doi: 10.5664/jcsm.2834. PMID:23853560 [PubMed - in process] <http://www.ncbi.nlm.nih.gov/pubmed/23853560>
15. 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 Dec 3;42(2):100-106. <http://www.ncbi.nlm.nih.gov/pubmed/24335048> [Epub ahead of print] PMID: 24335048 [PubMed - as supplied by publisher]

#### D. Research Support

##### Ongoing Research Support

###### **R01HL108623 (PI: Wright)**

03/1/12- 02/28/16

NIH/ NHLBI

FGF-23 and Phosphorus in stroke, subclinical vascular damage, and cognition

Elevated fibroblast growth factor 23 and serum phosphate are novel risk factors for cardiovascular disease and mortality, but their association with cerebrovascular damage is not clear. This study takes advantage of an ongoing population-based cohort study that includes Hispanic, black, and white people living in the same community, to examine elevated serum FGF23 and phosphate and the risk for stroke, subclinical small and large vessel injury, and cognitive decline. Elevated serum phosphate is modifiable and the results of this study have therapeutic potential that can be tested in randomized clinical trials.

###### **R37 NS029993 (PI: Sacco)**

01/07/93 - 03/31/15

NIH/NINDS: Subcontract to Columbia University

*Stroke Incidence and Risk Factors in a Tri-Ethnic Region*

This prospective cohort study (Northern Manhattan Study, NOMAS) investigates risk factors for stroke and other vascular outcomes in a multi-ethnic, urban population. In addition, the study seeks to understand the relationships between these risks factors and cognition and MRI-defined cerebrovascular disease.

Role: Co-investigator

**268200900048C-6-0-1 (Contract) (PI: Dr. David Goff)**

09/24/10-08/02/18

**NIH/NIA: Subcontract with Wake Forest University**

*The Systolic Blood Pressure Intervention Trial (SPRINT)*

The Systolic Blood Pressure Intervention Trial (SPRINT) is a 2-arm, multicenter, randomized clinical trial designed to test whether a treatment program aimed at reducing systolic blood pressure (SBP) to a lower goal than currently recommended will reduce cardiovascular disease (CVD) risk.

Role: Co-investigator

Completed Research Support (last 4 years)

**K02 NS059729 (PI: Wright)**

09/01/2008 – 11/30/13

**NIH/NINDS**

*Vascular Risk and Cognition in a Multi-ethnic Cohort*

The purpose of this grant is to examine vascular risk factors for cognitive dysfunction in a stroke-free multi-ethnic sample.

Aims will focus on identification of traditional and novel vascular risk factors for cognitive dysfunction as well as the role of brain imaging markers of vascular damage.

**XZ003 (PI: Wright/ Crocco)**

07/01/12- 06/30/13

**State of Florida, Division of Elder Affairs**

*University of Miami Memory Disorder Clinic*

The University of Miami Memory Disorder Clinic (UM-MDC) provides comprehensive evaluations to adults presenting with memory loss and/or other cognitive dysfunction.

The UM-MDC also is responsible for caregiver education and support as well as public education and outreach programs.

Status of Candidate on Grant: Principal Investigator

**AHA 0735387N (PI: Wright)**

07/01/08- 06/30/11

**American Heart Association**

*Vascular Risk and Cognition in a Tri- Ethnic Community*

The purpose of this grant is to examine vascular risk factors as correlates of cognitive dysfunction in a stroke-free multi-ethnic sample. Aims will focus on the role of both traditional and novel vascular risk factors.

## **Collaborators**

Antonio Barrientos, Ph.D.

Elizabeth Crocco, M. D.

Sara Czaja, Ph.D.

Hannah Gardener, Ph.D.

Carlos Moraes, Ph.D.

Miguel Perez-Pinzon, Ph.D.

Ami P. Raval, Ph.D.

Juan I. Young, Ph.D.

**BIOGRAPHICAL SKETCH**

Provide the following information for the Senior/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 Antoni Barrientos		POSITION TITLE Associate Professor	
eRA COMMONS USER NAME (credential, e.g., agency login) abarrientos			
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
Univ of Barcelona Teachers School, Spain	BS	1981-1984	Science Education
Univ of Barcelona School of Biology, Spain	BS	1986-1992	Fundamental Biology
Univ of Barcelona School of Medicine, Spain	PhD	1993-1997	Mitochondrial Genetics and Biochemistry
Univ of Miami Miller School of Medicine, Miami	Post-Doc	1997-1999	Mitochondrial Genetics and Biochemistry
Columbia University, New York	Post-Doc	1999-2000	Yeast Mitochondrial Genetics and Biochemistry

**A. Personal Statement. N/A****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. The John Macdonald Foundation. Center for Medical Genetics. University of Miami (Miami, FL)  
**2005-2007. Tenure-earning track Assistant Professor.** Department of Biochemistry and 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 until present. Tenured Associate Professor.** Department of Neurology and Department of Biochemistry & Molecular Biology. University of Miami (Miami, FL)  
**June 2009 until present. 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 candidate to represent the University of Miami for the Ellison Foundation award in Aging Research.  
**2011.** Organizer of the FASEB Summer Research Conference on "Mitochondrial Assembly and Dynamics in Health, Disease and Aging"

**Editorial Responsibilities:**

Ad hoc reviewer for: Cell Metabolism, Nature Genetics, Journal of Biological Chemistry, Journal of Cell Science, 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) in 2012, the Membrane Biology and Protein Processing (MBPP) Study Section in 2011 and 2013, and the Macromolecular Structure and Function A (MSFA) study section in 2013.
- Reviewer in several special emphasis panels (2012-2013)
- Ad hoc reviewer for R13 Scientific Conference Grant (NIH) (2011).
- Stage 1 reviewer for The Fellowships ZRG1 F05-Cell Biology and Development study section (NIH) (in 2010).
- Stage 1 reviewer for Recovery Act RC1 (2009) and RC4 (2010) applications (NIH)

#### 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. Selected peer-reviewed Publications (Selected from a total of 76 papers and 11 book chapters)

- 1- Ocampo A, Liu J and Barrientos A. NAD<sup>+</sup> salvage pathway proteins suppress proteotoxicity in yeast models of neurodegeneration by promoting the clearance of misfolded/oligomerized proteins. *Hum. Mol. Genet.* 22(9):1699-708 (2013) doi: 10.1093/hmg/ddt016
- 2- De Silva D, Fontanesi F and Barrientos A. (2013) The DEAD-Box Protein Mrh4 Functions in the Assembly of the Mitochondrial Large Ribosomal Subunit. *Cell Metab.* 12: 718-25 (2013) PMID in progress
- 3- Barrientos A and Ugalde C. I function, therefore I am: overcoming doubt about mitochondrial supercomplexes. *Cell Metab.* July 18(2):147-9 (2013) PMID in progress
- 4- Ocampo A., Liu J.J., Schroeder E.A., Shadel G.S. and Barrientos A. Mitochondrial respiratory thresholds regulate yeast chronological life span and its extension by caloric restriction. *Cell Metab* 16(1):55-67 (2012)
- 5- Liu J. and Barrientos A. Transcriptional regulation of yeast OXPHOS hypoxic genes by oxidative stress. *Antiox Redox Signal* [Epub ahead of print] (2012)
- 6- Soto IC, Fontanesi F, Myers RS, Hamel P and Barrientos A. A Heme-sensing mechanism in the translational regulation of mitochondrial cytochrome c oxidase biogenesis. *Cell Metab.* 16 (6): 801-813
- 7- Soto I.C., Fontanesi F., Liu J., Barrientos A. Biogenesis and assembly of eukaryotic cytochrome c oxidase catalytic core. *Biochim Biophys Acta.* 1817:883-97 (2012)
- 8- Bourens M., Dabir D.V., Tienson H.L., Sorokina, I., Koehler C.M. and Barrientos A Role of twin-CysX9Cys motif cysteines in mitochondrial import of the cytochrome c oxidase biogenesis factor Cmc1. *J. Biol. Chem.* 287(37):31258-69 (2012)
- 9- Bourens M, Fontanesi F, Soto IC, Liu J, and Barrientos A. (2012) Reactive Oxygen Species and Redox Regulation of Mitochondrial Cytochrome c Oxidase Biogenesis. *Antioxid. Redox Signal.* (2012 Sep 3) [Epub ahead of print]
- 10- Moreno-Lastres D., Fontanesi F., García-Consuegra I., Martín M.A., Arenas J., Barrientos A., Ugalde C. Mitochondrial Complex I plays an Essential Role in Human Respirasome Assembly (2012) *Cell Metab* 15(3):324-35 (2012)
- 11- Yong Pan Y., Schroeder E.A., Ocampo A., Barrientos A. and Shadel G.S. Regulation of yeast chronological life span by TORC1 via adaptive mitochondrial ROS signaling. *Cell Metab.* 13(6): 668-678 (2011)
- 12- Ocampo A. and Barrientos A. Quick and reliable assessment of chronological life span in yeast cell populations by flow cytometry. *Mech. Ageing. Dev.* (2011) Jun 28. [Epub ahead of print]

- 13- Fontanesi F., Clemente P., Barrientos A. Cox25 teams up with Mss51, Ssc1 and Cox14 to regulate mitochondrial cytochrome C oxidase subunit 1 expression and assembly in *Saccharomyces cerevisiae*. *J. Biol. Chem.* 286(1):255-266 (2011)
- 14- Horn D., Zhou W, Trevisson E., Al-Ali H., Harris T.K., Salviati L., and Barrientos A. (2010) The conserved mitochondrial twin CX<sub>9</sub>C protein Cmc2 is a Cmc1 homologue essential for cytochrome c oxidase biogenesis. *J. Biol. Chem.* 285:15088-99.  
<http://www.jbc.org/content/early/2010/03/10/jbc.M110.104786.long>
- 15- Fontanesi F., Soto I.C., Horn D. and Barrientos A. (2009) Mss51 and Ssc1 facilitate translational regulation of cytochrome c oxidase biogenesis. *Mol Cell Biol.* 30: 245-259. PMID2798308
- 16- Soto I.C., Fontanesi F., Valledor M., Horn D., Singh R. and Barrientos A. (2009) Synthesis of cytochrome c oxidase subunit 1 is translationally downregulated in the absence of functional F<sub>1</sub>F<sub>0</sub>-ATP synthase. *Biochim. Biophys. Acta (Mol. Cell. Res.)* 1793:1776-86. PMID2764804
- 17- Ocampo A., Zambrano A. and Barrientos A. (2009) Suppression of polyglutamine-induced cytotoxicity in *Saccharomyces cerevisiae* by enhancement of mitochondrial biogenesis. *FASEB J.* 24(5):1431-41 PMID in progress.
- 18- Soto I.C., Fontanesi F., Valledor M., Horn D., Singh R. and Barrientos A. (2009) Synthesis of cytochrome c oxidase subunit 1 is translationally down-regulated in the absence of functional F<sub>1</sub>F<sub>0</sub>-ATP synthase. *Biochim. Biophys. Acta (Mol. Cell. Res.)* 1793:1776-86
- 19- Barrientos A., Gouget K., Horn D., Soto I.C. and Fontanesi F. (2009) Suppression mechanisms of COX assembly defects in yeast and human: Insights into the COX assembly process. *Biochim. Biophys. Acta. Biochim. Biophys. Acta. (Mol. Cell. Res.)* 1793:97-107. PMID2644423
- 20- Fontanesi F., Jin C., Tzagoloff A., and Barrientos A. (2008) Transcriptional Activators HAP/NF-Y Rescue a Cytochrome c Oxidase Defect in Yeast and Human Cells. *Hum Mol Genet.* 17: 775-788.  
<http://hmg.oxfordjournals.org/cgi/content/full/17/6/775>
- 21- Ocampo A. and Barrientos A. (2008) From the bakery to the brain business: developing inducible yeast models of human neurodegenerative disorders. *Biotechniques* 45(4):Pvii-xiv
- 22- Horn D. and Barrientos A. (2008) Mitochondrial copper metabolism and delivery to cytochrome c oxidase. *IUBMB Life.* 60:421-9 PMID2864105
- 23- Horn D., Al-Ali H., and Barrientos A. (2008) Cmc1p is a conserved mitochondrial twin Cx<sub>9</sub>C protein involved in cytochrome c oxidase biogenesis. *Mol. Cell. Biol.* 28:4354-64. PMID2447134
- 24- Fontanesi F., Soto I.C. and Barrientos A. (2008) Cytochrome c oxidase biogenesis: new levels of regulation. *IUBMB Life.* 60:557-68
- 25- Dave K.R., DeFazio R.A., Raval A.P., Torraco A., Saul I., Barrientos A. and Perez-Pinzon M.A. (2008) Ischemic preconditioning targets the respiration of synaptic mitochondria *via* protein kinase c Epsilon. *J. Neurosc.* 28: 4172-4182
- 26- Wiley D.J., Catanuto P., Fontanesi F., Rios C., Sanchez N., Barrientos A., and Verde F (2008) Bot1p is required for mitochondrial translation, respiratory function and normal cell morphology in the fission yeast *Schizosaccharomyces pombe*. *Eukaryotic Cell*, 7: 619-29
- 27- Zambrano A, Fontanesi F, Solans A, de Oliveira RL, Fox TD, Tzagoloff A, Barrientos A (2007) Aberrant translation of cytochrome c oxidase subunit 1 mRNA species in the absence of Mss51p in the yeast *Saccharomyces cerevisiae*. *Mol Biol Cell.* 18: 523-535. PMID1783774
- 28- Fontanesi F., Soto I.C., Horn D., and Barrientos A. (2006) Assembly of mitochondrial cytochrome c oxidase, a complicated and highly regulated cellular process. *Am. J. Physiol. – Cell Physiol.*, 291(6):C1129-47. <http://ajpcell.physiology.org/cgi/content/full/291/6/C1129>
- 29- Fontanesi F., Soto I.C., Horn D., and Barrientos A. Assembly of mitochondrial cytochrome c oxidase, a complicated and highly regulated cellular process. *Am. J. Physiol. – Cell Physiol.*, 291(6):C1129-47. (2006)
- 30- Solans A., Zambrano A., Rodriguez M., and Barrientos A. (2006) Cytotoxicity of a mutant huntingtin fragment in yeast involves early alterations in mitochondrial OXPHOS complex II and III. *Hum. Mol. Genet.*, 15(20):3063-81. <http://hmg.oxfordjournals.org/content/15/20/3063.long>
- 31- Barrientos A., Zambrano A., and Tzagoloff A. (2004) Mss51p and Cox14p jointly regulate mitochondrial Cox1p expression in *Saccharomyces cerevisiae*. *EMBO J.* 23: 3472-3482. PMID: PMC516630
- 32- Barrientos A. (2003) Yeast models of human mitochondrial diseases. *IUBMB Life.* 55:83-95.

- 33- Barrientos A., Korr D., Barwell K.J., Christian Sjulsen C., Gajewski C.D., Manfredi G., Sharon Ackerman S, and Tzagoloff A (2003) *MTG1* codes for a conserved protein required for mitochondrial translation. *Mol Biol Cell* 14: 2292-2302. PMID: PMC194879
- 34- Barrientos A., Korr D., and Tzagoloff A. (2002) Mitochondrial cytochrome c oxidase assembly: Shy1p is necessary for full expression of subunit 1 in the yeast model of Leigh's syndrome. *EMBO J.* 21: 43-52. PMID: PMC125806

#### Book chapters:

- 1- Fontanesi F and Barrientos A. Mitochondrial Cytochrome c Oxidase Assembly Defects and Human Disease. In "Mitochondrial disorders caused by nuclear genes". Part 3. Wong, LJ Ed. Springer Science. (2013)
- 2- Horn D., Fontanesi F., and Barrientos, A. (2009) Cofactor insertion into mitochondrial cytochrome c oxidase and human disease: Insight from yeast models. In *Yeast as a Model for Human Disease*. Chapter 3. Pg: 41-61. Witt S.N. ed. Transworld Research Network. Trivandrum. India
- 3- Barrientos, A., Fontanesi, F. and Díaz, F. (2009) Evaluation of the Mitochondrial Respiratory Chain and Oxidative Phosphorylation System using Polarography and Spectrophotometric Enzyme Assays. *Curr Protoc Hum Genet*. Chapter 19: Unit 19.3
- 4- Fontanesi, F., Diaz, F. and Barrientos, A. (2009) Evaluation of the Mitochondrial Respiratory Chain and Oxidative Phosphorylation System Using Yeast Models of OXPHOS Deficiencies. *Curr Protoc Hum Genet*. Chapter 19: Unit 19.5
- 5- Horn D., Fontanesi F., and Barrientos A. (2008) Exploring protein-protein interactions involving newly synthesized mitochondrial DNA encoded proteins. *Methods in Molecular Biology: Membrane Trafficking*. Vol. 457. Chapter 9. Pg. 125-139. Ales Vancura, ed. Humana Press
- 6- Gouget K., Verde F. and Barrientos, A. (2008) *In Vivo* Labeling and Analysis of Mitochondrial Translation Products in Budding and in Fission yeasts. *Methods in Molecular Biology: Membrane Trafficking*. Vol. 457. Chapter 8. Pg. 113-124. Ales Vancura, ed. Humana Press

#### 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 COX assembly in wild-type strains and others carrying mutations in evolutionary conserved COX assembly factors, relevant for human mitochondrial diseases. PI: Antoni Barrientos. DC: \$190,000 per year

**1-1-2011 / 12-31-2013.** Research Grant from the Muscular Dystrophy Association. Research project: "Characterization of novel conserved cytochrome c oxidase chaperones". We will characterize the roles of human COX assembly chaperones involved in the expression of mtDNA encoded subunit Cox2 (Cox20, Fam36A) using human cell cultures. PI: Antoni Barrientos. DC: \$95,000 per year

**1-1-2013 / 12-31-2015.** Supplement to RO1 grant from NIH (NIH # 2 R01 GM071775-06A1). "Macromolecular assemblies in cells". We use the human cell culture models to study cytochrome c oxidase assembly and how it is regulated at the translational level through dynamic protein-protein interactions. PI: Antoni Barrientos. DC: \$80,000 per year



**BIOGRAPHICAL SKETCH**

Provide the following information for the Senior/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 Elizabeth A. Crocco, MD		POSITION TITLE Clinical Assistant Professor	
eRA COMMONS USER NAME (credential, e.g., agency login)			
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
Douglas College, Rutgers University, NJ	BS	1989	Biology
UMDNJ – Robert Wood Johnson Medical School, Piscataway, NJ	MD	1993	Medicine

**A. Personal Statement. N/A****B. Positions and Honors.****Positions and Employment**

1993-1997	Residency in Psychiatry, Mount. Sinai Medical Center, New York, N.Y
1996-1997	Administrative Chief Resident, Mount Sinai Medical Center, New York, N.Y.
1997-1998	Chief Fellow, Geriatric Psychiatry, Jackson Memorial Hospital, Miami, FL.
1998-2006	Clinical Director of Psychiatry, Wien Center for Memory Disorder, Mt. Sinai Medical Center, Miami Beach, FL.
1998-present	Clinical Assistant Professor, Department of Psychiatry and Behavioral Sciences, University of Miami Miller School of Medicine, Miami, FL.
2001-present	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-present	Medical Director, Geriatric Medical/Psychiatry Inpatient Unit, Jackson Memorial Hospital, Miami, FL.
4/2010-present	Director, Memory Disorder Center, Department of Psychiatry and Behavioral Sciences, Miller School of Medicine at University of Miami, FL
12/2009-present	Division Chief, Geriatric Psychiatry, Department of Psychiatry and Behavioral Sciences, Miller School of Medicine at University of Miami, Miami, FL

**Professional Memberships**

Florida Psychiatric Society  
Fellow, American Psychiatric Association  
American Association of Geriatric Psychiatry

## **Honors**

Geriatric Fellowship Excellence in Teaching Award, JMH, 2012.

Irma Bland Certificate of Excellence in Teaching Residents, American Psychiatric Association, 2011.

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, 2010.

Geriatric Psychiatry Training Program Teacher of the Year Award, JMH – 2007, 2008

## **C. Selected peer-reviewed publications (in chronological order)**

1. **Crocco, EA**, Eisdorfer, C. Research in Mental Health and Caregiving, The Challenges of Mental Health and Caregiving, Springer, NY, 2014.
2. Curiel, R., **Crocco, E.**, Duara, R, Acevedo, A and Loewenstein, DA . A new scale for the evaluation of proactive and retroactive Interference in mild cognitive Impairment and early Alzheimer's disease. *Journal of Aging Science*. 2013: <http://dx.doi.org/10.4172/jasc.1000102>.
3. **Crocco E**, Curiel RE, Acevedo A, Czaja SJ, Loewenstein DA. An evaluation of deficits in semantic
4. cuing, proactive and retroactive interference as early features of Alzheimer's disease. *The American Journal of Geriatric Psychiatry*, June, 2013: doi:pii: S1064-7481(13)00083-3.10.1016/j.jagp.2013.01.066. [Epub ahead of print].
5. Kohli MA, John-Williams K, Rajbhandary R, Naj A, Whitehead P, Hamilton C, Carney RM, Wright C, **Crocco E**, Gwirtzman HE, Lang R, Beecham G, Martin ER, Gilbert J, Benatar M, Small G, Mash D, Byrd G, Hanes J, Pericak-Vance MA, Zuchner S. Repeat expansion in the C9ORF72 gene contribute to Alzheimer's disease in Caucasians. *Neurobiology of Aging*. 2013;34(5): 1519.e5-1519.e12.
6. **Crocco EA**, Castro, K, Loewenstein D. How late-life depression affects cognition: neural mechanisms. *Current Psychiatric Reports*. 2010;12(1): 34-38.
7. Ownby RL, Hertzog C, **Crocco E**, Duara R. Factors related to medication adherence in memory disorder clinic patients. *Aging and Mental Health*. 2006;10(4): 378-385.
8. Ownby RL, **Crocco E**, Acevedo A, John V, Loewenstein D. Depression and risk for Alzheimer's disease: systematic review, meta-analysis and meta-regression analysis. *The Archives of General Psychiatry*, 2006;63: 530-538.
9. Loewenstein DA, Acevedo A, Agron J, Isaacson R, Strauman S, **Crocco E**, Barker W, Duara R. Cognitive profiles in Alzheimer's disease and in mild cognitive impairment of different etiologies. *Dementia and Geriatric Cognitive Disorder*. 2006; 21: 309-315.
10. **Crocco, E**, Loewenstein DA. Psychiatric aspects of mild cognitive impairment. *Current Psychiatric Reports*. 2005; 7: 32-36.
11. Ownby RL, Rodríguez L, **Crocco E**, Duara R. Patient and caregiver reports of medication adherence. *International Psychogeriatrics*. 2003;15(Supp 2):310.
12. Ownby RL, **Crocco E**, Duara R. Memory disorder clinic patients' reports of medication adherence. *Journal of Clinical Psychiatry*. 2002;63:1076.

**D. Research Support**  
**Ongoing Research Support**

The State of Florida Department of Elder Affairs Alzheimer's Disease Initiative,  
University of Miami Memory Disorder Clinic 5/2010-present

**Principle Investigator: Elizabeth Crocco, MD.**

The University of Miami Memory Disorders Clinic (MDC) is funded by a state of Florida Department of Elder Affairs contract. The purpose of the clinic is to provide clinical and diagnostic services, research and training for individuals with Alzheimer's disease or related disorder, as well as to their caregivers.

Total Agency Funds: \$222,801.

**Completed Research Support**

1 RO1 AG020094-01A1 National Institute on Aging 6/1/03 – 4/30/08 Semantic Interference and Early Detection of Dementia,

Principal Investigator: David A. Loewenstein, Ph.D, Co-Investigator: Elizabeth Crocco, M.D.,

The major goal of this project is to examine the utility of a new semantic interference test and measures of prospective memory in combination with other neuropsychological and genetic predictors (e.g. ApoE) in predicting cognitive decline in patients with mild cognitive impairment without dementia (MCI) and normal community dwelling elderly.

Total Direct Costs \$1,530,000.

**BIOGRAPHICAL SKETCH**

NAME Sara J. Czaja, Ph.D.		POSITION TITLE Professor	
eRA COMMONS USER NAME (credential, e.g., agency login)			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as</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**

**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**

- 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 2013
- Chair, Fellows Selection Committee, Human Factors and Ergonomics Society (HFES) October 2013 -
- 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.
- Member, Technical Expert Panel, Evidence Based Practice Center, Johns Hopkins University, March 2008-present
- Member, Subcommittee, Ely Award, Human Factors and Ergonomics Society, 2007 - present
- Faculty Affiliate, Department of Biomedical Informatics, Columbia University, April 2008 – present

**Honors**

- 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. Selected peer-reviewed publications (in chronological order).

1. **Czaja, S.J.**, Charness N, Fisk AD, Hertzog C, Nair S, Rogers W, Sharit J. Factors predicting the use of technology: findings from the Center on Research and Aging and Technology Enhancement (CREATE). *Psychol Aging* 2006; 21(2): 333-352.
2. **Czaja, S.J.** (contributing author). 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. *Ann Intern Med.* 2006; 145: 727-738.
3. Nichols LO, Chang C, Lummus A, Burns R, Martindale-Adams J, Graney MJ, Coon DW, **Czaja, S.J.** The cost effectiveness of a behavior intervention with caregivers of Alzheimer's patients. *J Am Geriatr Soc.* 2008; 56(3): 389-592.
4. Schulz R, McGinnis KA, Zhang S, Martire LM, Hebert RS, Beach SR, Zdaniuk B., **Czaja, S.J.**, Belle SH Dementia patient suffering and caregiver depression. *Alzheimer Dis Assoc Disord.* 2008; 22(2): 170-186.
5. **Czaja, S.J.** Gitlin LN, Schulz R, Zhang S, Burgio D, Stevens AB., Nichols LO, Gallagher-Thompson D. Development of the risk appraisal measure (RAM): A brief screen to identify risk areas and guide interventions for dementia caregivers. *J Am Geriatr Soc.* 2009; 57:1064-1072.
6. Sharit, J., **Czaja, S.J.**, Hernandez AM, Nair SN. The employability of older workers as teleworkers: An appraisal of issues and an empirical study. *Human Factors and Ergonomics in Manufacturing Engineering* 2009; 19(5): 457-477.
7. Schulz, R., Zdaniuk, B., Belle, S., **Czaja, S.J.**, Arrighi, M., Zbrozek, S. (2010) Baseline Differences and Trajectories of change for Deceased, Placed, and Community residing Alzheimer's Disease Patients". *Alzheimer Disease & Associated Disorders, Vol 24., No. 2, pg. 143-150.*
8. **Czaja, S.J.**, Sharit, J., Lee, C.C., Nair, S.N., Hernandez, M., Arana, N., Fu, S.H. (2012) Factors Influencing Use of an E-health Website in a Community Sample of Older Adults. *J Am Med Inform Assoc.* doi:10.1136/amiajnl-2012-000876
9. Ownby, Raymond L., Hertzog, Christopher, **Czaja, S.J.** (2012) "Tailored Information and Automated Reminding to Improve Medication Adherence in Spanish and English Speaking Elders Treated for Memory Impairment". *Clinical Gerontologist, 35:3 221-238.*
10. Ownby, Raymond L., Hertzog, Christopher, **Czaja, S.J.** (2012) "Relations Between Cognitive Status and Medication Adherence in Patients Treated for Memory Disorders." *Ageing Research, 2012; Vol. 4:e2.*
11. 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.
12. Taha, J., Sharit, J., **Czaja, S.J.** (2013) The Impact of Numeracy Ability and Technology Skills on Older Adults' Performance of Health Management Tasks using a Patient Portal. *Journal of Applied Gerontology.* DOI:10.1177/0733464812447283.
13. Schulz, R., Cook, T.B., Beach, S.R., Lingler, J.H., Martire, L.M., Monin, J.K., & **Czaja, S.J.** (2013) Magnitude and Causes of Bias among Family Caregivers rating Alzheimer's Disease Patients. *American Journal of Geriatric Psychiatry.* 2013 Jan; 21(1):14-25.

## D. Research Support

### Ongoing research

Czaja, S.J. (Co-PI)

4/1/14-3/31/19

NIH/NIA/NINR

Title: “Adherence and Biomarkers Innovative Interventions in Older Transplant Patients”

Northwestern University

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.

1UL1TR000460-01A1 (Szapocznik, J)

7/27/12 – 5/31/17

NCATS

Title: “ **Miami Clinical and Translational Science Institute”**

To propel scientific discovery and its translation into evidence-based practice and community health, the Miami Clinical and Translational Science Institute advances cultural zed health sciences that embrace our majority racial/ethnic community. Fundamental to accomplishing our mission is the orchestration of new and existing research, services and resources that foster excellence in translational research, promote Interdisciplinary, elevate research ethics, build research partnerships in community, and establish strong multidisciplinary graduate research programs.

1P30DA027828-01A1 (Brown, CH)

07/01/11-06/30/16

NIDA/NIH

**Center for Prevention Implementation Methods for Drug Abuse & Sex Risk Behavior**

The proposed Center for Prevention Implementation Methodology (Ce-PIM) for Drug Abuse and Sexual Risk Behavior is designed to accelerate research through the application and integration of system science methods. These system science methods directly model the complex interactions that occur across multiple levels and organizations as prevention programs are implemented.

1 R01 NS0072599-01

Antoni, Michael (PI)

08/16/10-05/31/15

**Patient-Partner Stress Management Effects on CFS Symptoms and Neuroimmune Process**

This is a 5-year study to evaluate the effect of a 10-week patient-partner telephone-based cognitive behavioral stress management (CBSM) intervention on chronic fatigue syndrome (CFS) symptoms in 150 patients diagnosed with CFS.

1R21AG041740-01

04/01/12 – 03/31/14

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.

2 PO1 AG017211-11

Czaja (PI)

08/1/09 – 07/31/14

National Institute on Aging/National Institutes of Health

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

The Center on Research and Education for Aging and Technology Enhancement (CREATE) conducts multidisciplinary research aimed at understanding how age-related changes in function impact on older person's ability to interact successfully with technical systems. The Center also disseminates research findings in a wide variety of settings such as design guidelines for the design of technical systems.

1R01HL096578-01A1 (Ownby, Raymond PI)

08/10/10 – 04/30/14

Nova Southeastern University/NHLBI

**Literacy Measure Development and Validation of a Computer-Administered Health**

To help with the development of new health literacy measure product. Provide guidance with respect to usability issues and protocols, pilot testing, data analysis activities and the development of publications and presentations relevant to the outcomes of this project.

1 R21 HS018831-01A1

Czaja (PI)

04/01/11-09/30/13

Agency for Healthcare Research and Quality (AHRQ)

**Improving Meaningful Access to Internet Health Information for Older Adults**

The primary aims of this project proposal are to refine, through a user-centered iterative design process, a set of relatively new software aiding tools so that they can be used by health consumers, particularly older adults, in the performance of Internet-based health management task.

### BIOGRAPHICAL SKETCH

Provide the following information for the Senior/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 Hannah Gardner, ScD	POSITION TITLE Assistant Scientist		
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 <i>(if applicable)</i>	MM/YY	FIELD OF STUDY
Dartmouth College, New Hampshire	AB	1996-2000	Psychological and Brain Studies
Harvard School of Public Health, Massachusetts	ScD	2003-2007	Epidemiology

**A. Personal Statement. N/A**

**B. Positions and Honors.** List in chronological order previous positions, concluding with your present position. List any honors. Include present membership on any Federal Government public advisory committee.

December 2009- present	Assistant Scientist, Department of Neurology, University of Miami Miller School of Medicine, Miami, FL
April – September 2009	Research Assistant Professor, Department of Pediatrics, University of Miami Miller School of Medicine, Miami, FL
September 2007- April 2009	Post-doctoral Associate, Department of Neurology, University of Miami Miller School of Medicine, Miami, FL
July 2002 - September 2004	Senior Research Assistant, Department of Society, Development and Health, Harvard School of Public Health, Boston, MA

**C. Selected peer-reviewed publications (in chronological order).** Do not include publications submitted or in preparation.

1. **Gardener H**, Rundek T, Wright CB, Elkind MS, Sacco RL. Coffee and tea consumption are inversely associated with mortality in a multiethnic urban population. *J Nutr.* 2013;143(8):1299-308.
2. Gutierrez J, Bagci A, **Gardener H**, Rundek T, Elkind MS, Alperin N, Sacco RL, Wright CB. Dolichoectasia Diagnostic Methods in a Multi-Ethnic, Stroke-Free Cohort: Results from the Northern Manhattan Study. *J Neuroimaging.* In Press.
3. Alsulaimani S, **Gardener H**, Elkind MS, Cheung K, Sacco RL, Rundek T. Elevated homocysteine and carotid plaque area and densitometry in the Northern Manhattan Study. *Stroke.* 2013; 44(2):457-61.
4. **Gardener H**, Goldberg R, Mendez AJ, Wright CB, Rundek T, Elkind MS, Sacco RL. Adiponectin and risk of vascular events in the Northern Manhattan Study. *Atherosclerosis.* 2013; 226(2):483-9.



5. **Gardener H**, Crisby M, Sjoberg C, Hudson B, Goldberg R, Mendez AJ, Wright CB, Rundek T, Elkind MSV, Sacco RL. Serum adiponectin in relation to race-ethnicity and vascular risk factors in the Northern Manhattan Study. *Metabolic Syndrome and Related Disorders*. 2013;11(1):46-55.
6. 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. *US Neurology*. In press.
7. 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):93-8.
8. 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.
9. **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.
10. **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.
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. **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.
13. 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.
14. Ramos A, Wohlgemuth W, Dong C, **Gardener H**, Boden-Albala B, Elkind MSV, Sacco RL, Rundek T. Race-ethnic differences of sleep symptoms in an urban multi-ethnic cohort: The Northern Manhattan Study. *Neuroepidemiology*. 2011;37(3-4):210-215.
15. 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.
16. **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.
17. Wallace DM, Shafazand S, Ramos AR, **Gardener H**, Lorenzo D, Carvalho DZ, Wohlgemuth WK. 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 Medicine*. 2011;12(9):850-859.

18. 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.
19. **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.
20. 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.
21. 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.
22. **Gardener H**, Gao X, Chen H, Schwarzschild MA, Spiegelman D, Alberto A. Prenatal and early life factors and risk of Parkinson's disease. *Movement Disorders*. 2010;25(11):1560-1567.
23. 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.
24. 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.
25. **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.
26. 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.
27. 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.
28. **Gardener H**, Munger KL, Chitnis T, Spiegelman D, Alberto A. The relationship between handedness and risk of multiple sclerosis. *Multiple Sclerosis*. 2009;15(5):587-592.
29. **Gardener H**, Munger KL, Chitnis T, Michels KB, Spiegelman D, Alberto A. Prenatal and perinatal factors and risk of multiple sclerosis. *Epidemiology*. 2009;20(4):611-618.
30. O'Reilly EJ, Chen H, **Gardener H**, Gao X, Schwarzschild MA, Ascherio A. Smoking and Parkinson's disease: using parental smoking as a proxy to explore causality. *American Journal of Epidemiology*. 2009;169(6):678-682.

### 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 <b>Carlos T. Moraes</b>		POSITION TITLE <b>Professor</b>	
eRA COMMONS USER NAME <b>cmoraes</b>			
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
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. N/A**

**B. Positions and Honors.**

**PROFESSIONAL APPOINTMENTS**

- 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. Selected peer-reviewed publications (in chronological order). . (\*co-corresponding authors)**

**MOST RELEVANT PUBLICATIONS**

1. Runu Dey, Antoni Barrientos, and **Carlos T. Moraes.** Functional Constraints of Nuclear - Mitochondrial DNA Interactions in Xenomitochondrial Rodent Cell Lines *J Biol Chem*, 275: 31520-31527 (2000).
2. Barrientos, A., Kenyon, L. and Moraes, C. T.\* Human xenomitochondrial cybrids. Cellular models of mitochondrial complex I deficiency. *J Biol Chem*, 273:14210-7 (1998)
3. Hirokazu Fukui, Francisca Diaz, Sofia Garcia, **Carlos T. Moraes.** Cytochrome c Oxidase Deficiency in Neurons Decreases both Oxidative Stress and Amyloid Formation in a Mouse Model of Alzheimer's Disease. *Proc Natl. Acad. Sci. USA* 104:14163-14168 (2007)

4. T. Wenz, F. Diaz, B. M. Spiegelman and **C. T. Moraes\*** Activation of the PPAR/PGC-1 $\alpha$  pathway prevents a bioenergetic deficit and effectively improves a mitochondrial myopathy phenotype. *Cell Metabolism* 8:249-56. (2008)
5. Tina Wenz, Susana G. Rossi, Richard L. Rotundo, Bruce Spiegelman and **Carlos T. Moraes\*** Increased muscle PGC-1 $\alpha$  expression protects from sarcopenia and metabolic disease during aging. *Proc. Natl. Acad. Sci. USA* 106:20405-20410 (2009)
6. Siôn L. Williams, Jia Huang, Yvonne JK Edwards, Richard Ulla, Lloye Dillon, Tomas Prolla, Jeffery Vance, **Carlos T. Moraes\*** and Stephan Züchner.\* The mtDNA mutation spectrum of the progeroid Polg mutator mouse includes abundant control region multimers. *Cell Metabolism*, 12:675-82 (2010)
7. Milena Pinto, Alicia M. Pickrell, Hirokazu Fukui and **Carlos T. Moraes.\*** Mitochondrial DNA damage in a mouse model of Alzheimer's disease decreases A $\beta$  plaque formation. *Neurobiology of Aging*, 34:2399-407 (2013).
8. Bacman, S, Williams S, Pinto M, **Moraes CT.** Altering mtDNA heteroplasmy with mitoTALEN. *Nat. Med.* 19:1111-3. (2013).

#### ADDITIONAL RELEVANT PUBLICATIONS

1. **Moraes, C.T.,** DiMauro, S., Zeviani, M., Lombes, A., Shanske. S., Miranda, A. F et al. Mitochondrial DNA deletions in progressive external ophthalmoplegia and Kearns-Sayre syndrome. *New England Journal of Medicine*, 320: 1 293- 1299 (1989).
2. **Moraes, C.T.,** Shanske, S., Trishler H-J., Aprille, J.R., Andreetta, F., Bonilla, E., Schon, E.A. and DiMauro, S., Mitochondrial DNA depletion with variable tissue expression: A novel genetic abnormality in mitochondrial diseases. *American Journal of Human Genetics*, 48: 492-501 (1991).
3. **Moraes, C.T.,** Ciacci, F., Bonilla, E., Ionascescu, V., Schon, E.A., and DiMauro, S. A mitochondrial tRNA anticodon swap associated with a muscle disease. *Nature Genetics*, 4:284-287 (1993).
4. Maria Pilar Bayona-Bafaluy, Bas Blits, Brendan Battersby, Eric A. Shoubridge, and **Carlos T. Moraes.** Rapid Directional Shift of Mitochondrial DNA Heteroplasmy in Animal Tissues by a Mitochondrially-Targeted Restriction Endonuclease. *Proc. Natl. Acad. Sci. USA* 102: 14392–14397 (2005)
5. Tina Wenz, Corneliu Luca, Alessandra Torraco and **Carlos T. Moraes\*** MTERF2 regulates oxidative phosphorylation by modulating mtDNA transcription. *Cell Metabolism* 9:499-511 (2009)
6. Sarika Srivastava, Francisca Diaz, Luisa Iommarini, Karine Aure, Anne Lombes and **Carlos T. Moraes.\*** PGC-1 $\alpha/\beta$  induced expression partially compensates for respiratory chain defects in cells from patients with mitochondrial disorders. *Human Molecular Genetics* 18:1805-12. (2009)
7. Bacman SR, Williams SL, Garcia S, **Moraes CT.** Organ-specific shifts in mtDNA heteroplasmy following systemic delivery of a mitochondria-targeted restriction endonuclease. *Gene Ther.* 17:713-20. (2010)
8. Hirokazu Fukui and **Carlos T. Moraes\***. Mechanisms of formation and accumulation of mitochondrial DNA deletions in aging neurons. *Human Molecular Genetics* 18:1028-36 (2009)
9. Tina Wenz, Susana G. Rossi, Richard L. Rotundo, Bruce Spiegelman and **Carlos T. Moraes.\*** Increased muscle PGC-1 $\alpha$  expression protects from sarcopenia and metabolic disease during aging. *Proc. Natl. Acad. Sci. USA* 106:20405-20410 (2009)
10. Pickrell AM, Pinto M, Hida A, **Moraes CT.** Striatal dysfunctions associated with mitochondrial DNA damage in dopaminergic neurons in a mouse model of Parkinson's disease. *J Neurosci.* 31:17649-58. (2011)
11. Xiao Wang, Alicia M. Pickrell, Susana G. Rossi, Milena Pinto, Lloye M. Dillon, Aline Hida, Richard L. Rotundo, and **Carlos T. Moraes.** Transient systemic mtDNA damage leads to muscle wasting by reducing the satellite cells pool. *Hum. Mol. Genet.*, 21:2288-97 (2012)
12. Susana Peralta, Alessandra Torraco, Tina Wenz, Sofia Garcia, Francisca Diaz and **Carlos T. Moraes.** Partial Complex I deficiency due to the CNS conditional ablation of Ndufa5 results in a mild encephalopathy and no increase in oxidative damage. *Hum. Mol. Genet.*, 2013 Nov 11. [Epub ahead of print]

### **C. Research Support.**

#### **Active**

5R01EY010804-11 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

1R01AG036871-02 Moraes 06/01/2010 – 05/31/2015

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

MDA172638 Moraes 7/1/2010 – 6/30/2013

Muscular Dystrophy Association (MDA)

*"Increased Mitochondrial Biogenesis as Therapy to Mitochondrial Disorders"*

The objective of this project is to investigate whether a mitochondrial myopathy in mice can be treated by drugs that induce mitochondrial biogenesis. Role: PI

**BIOGRAPHICAL SKETCH**

Provide the following information for the Senior/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 <b>Miguel A. Perez-Pinzon, PhD, FAHA</b>		POSITION TITLE <b>Professor</b>	
eRA COMMONS USER NAME (credential, e.g., agency login) <b>mperezpinzon</b>			
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
University of Panama	B.Sc.	1983	Biology
University of Miami	M.Sc.	1987	Marine Biology (MB)
University of Miami	Ph.D.	1991	Neuroscience (MB)
New York University	Postdoc	1992	Neurophysiology
Stanford University	Postdoc	1993	Neuroscience

**A. Personal Statement – N/A**

**B. Position and Honors**

**Positions and Employment**

- 1994 – 1995      Research Associate, Department of Neurology, University of Miami School of Medicine. Dr. Thomas J. Sick (Supervisor)
- 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, FI (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
- 2006 – 2010      NIH-NINDS BINP Study Section
- 2006 – present    Director of Cerebral Vascular Disease Center, University of Miami, Miller School of Medicine, Miami, FI
- 2006 – present    Professor, Department of Neurology, University of Miami Miller School of Medicine, Miami, FI
- 2007 – 2008      International Stroke Conference Program Committee: Co-Chair–Experimental Mechanisms and Models.
- 2008 – 2010      International Stroke Conference Program Committee: Chair–Experimental Mechanisms and Models.
- 2007 – present    Associate Chair for Basic Science, Department of Neurology, University of Miami Miller School of Medicine, Miami, FL
- 2010 – present    Vice-Chair for Basic Science, Department of Neurology, University of Miami Miller School of Medicine, Miami, FI

**Honors, Awards, and Professional Societies**

- 1982, 1983      Fellowships (2), Smithsonian Tropical Research Institute (STRI).
- 1986              Fellowship, Fishing and Conservation Trust. Miami, FI
- 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, (Student of the year) for excellence in graduate research and education, Rosenstiel School of Marine and Atmospheric Science, University of Miami, Miami, FI

Program Director/Principal Investigator (Last, First, Middle): Perez-Pinzon, Miguel A.

- 1991 Invited speaker at the Society for Experimental Biology in Birmingham, U.K.
- 1996 James A. Shannon Director's Award from the National Institute of Neurological Disorders and Stroke, NIH.
- 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)
- 2012-13 Co-Chair of the Program Committee for the International Society of Cerebral Blood Flow and Metabolism (Brain 13), Shanghai, China

### C. Publications (out of 114)

1. Thompson JW, Dave KR, Saul I, Narayanan SV, & Perez-Pinzon MA (2013) Epsilon PKC Increases Brain Mitochondrial SIRT1 Protein Levels via Heat Shock Protein 90 following Ischemic Preconditioning in Rats. *PLoS One* 8(9):e75753.
2. Thompson JW, Dave K, Young J, & Perez-Pinzon MA (2013) Ischemic preconditioning alters the epigenetic profile of the brain from ischemic intolerance to ischemic tolerance. *Neurotherapeutics* In Press.
3. Raval AP, Borges-Garcia R, Javier Moreno W, Perez-Pinzon MA, & Bramlett H (2013) Periodic 17beta-estradiol pretreatment protects rat brain from cerebral ischemic damage via estrogen receptor-beta. *PLoS One* 8(4):e60716.
4. Neumann JT, Cohan CH, Dave KR, Wright CB, & Perez-Pinzon MA (2013) Global cerebral ischemia: synaptic and cognitive dysfunction. *Curr Drug Targets* 14(1):20-35.
5. Narayanan SV, Dave KR, & Perez-Pinzon MA (2013) Ischemic preconditioning and clinical scenarios. *Curr Opin Neurol* 26(1):1-7.
6. Lin HW, Saul I, Gresia VL, Neumann JT, Dave KR, & Perez-Pinzon M (2013) Fatty Acid Methyl Esters and Solutol HS 15 Confer Neuroprotection after Focal and Global Cerebral Ischemia. *Transl Stroke Res* In Press.
7. Lin HW & Perez-Pinzon M (2013) The role of Fatty acids in the regulation of cerebral vascular function and neuroprotection in ischemia. *CNS Neurol Disord Drug Targets* 12(3):316-324.
8. Koch S & Perez-Pinzon M (2013) Proceedings of the 2nd Translational Preconditioning Meeting Miami. *Transl Stroke Res* 4:1-2.
9. Daviaud N, Garbayo E, Schiller PC, Perez-Pinzon M, & Montero-Menei CN (2013) Organotypic cultures as tools for optimizing central nervous system cell therapies. *Exp Neurol* 248:429-440.
10. Dave KR, Della-Morte D, Saul I, Prado R, & Perez-Pinzon MA (2013) Ventricular fibrillation-induced cardiac arrest in the rat as a model of global cerebral ischemia. *Transl Stroke Res* In Press.
11. Thompson JW, Narayanan SV, & Perez-Pinzon MA (2012) Redox signaling pathways involved in neuronal ischemic preconditioning. *Curr Neuropharmacol* 10(4):354-369.
12. Perez-Pinzon MA, Stetler RA, & Fiskum G (2012) Novel mitochondrial targets for neuroprotection. *J Cereb Blood Flow Metab* 32(7):1362-1376.
13. Lin HW, Della-Morte D, Thompson JW, Gresia VL, Narayanan SV, Defazio RA, Raval AP, Saul I, Dave KR, Morris KC, Si ML, & Perez-Pinzon MA (2012) Differential effects of delta and epsilon protein kinase C in modulation of postischemic cerebral blood flow. *Adv Exp Med Biol* 737:63-69.
14. Koch S, Sacco RL, & Perez-Pinzon MA (2012) Preconditioning the brain: moving on to the next frontier of neurotherapeutics. *Stroke* 43(6):1455-1457.
15. Ding D, Enriquez-Algeciras M, Dave KR, Perez-Pinzon M, & Bhattacharya SK (2012) The role of deimination in ATP5b mRNA transport in a transgenic mouse model of multiple sclerosis. *EMBO Rep* 13(3):230-236.
16. Dezfulian C, Alekseyenko A, Dave KR, Raval AP, Do R, Kim F, & Perez-Pinzon MA (2012) Nitrite therapy is neuroprotective and safe in cardiac arrest survivors. *Nitric Oxide* 26(4):241-250.
17. Della-Morte D, Guadagni F, Palmirotta R, Ferroni P, Testa G, Cacciatore F, Abete P, Rengo F, Perez-Pinzon MA, Sacco RL, & Rundek T (2012) Genetics and genomics of ischemic tolerance: focus on cardiac and cerebral ischemic preconditioning. *Pharmacogenomics* 13(15):1741-1757.

18. Dave KR, Christian SL, Perez-Pinzon MA, & Drew KL (2012) Neuroprotection: lessons from hibernators. *Comp Biochem Physiol B Biochem Mol Biol* 162(1-3):1-9.
19. Morris KC, Lin HW, Thompson JW, & Perez-Pinzon MA (2011) Pathways for ischemic cytoprotection: role of sirtuins in caloric restriction, resveratrol, and ischemic preconditioning. *J Cereb Blood Flow Metab* 31(4):1003-1019.
20. Lin HW, Thompson JW, Morris KC, & Perez-Pinzon MA (2011) Signal transducers and activators of transcription: STATs-mediated mitochondrial neuroprotection. *Antioxid Redox Signal* 14(10):1853-1861.
21. Koch S, Katsnelson M, Dong C, & Perez-Pinzon M (2011) Remote ischemic limb preconditioning after subarachnoid hemorrhage: a phase Ib study of safety and feasibility. *Stroke* 42(5):1387-1391.
22. Garbayo E, Raval AP, Curtis KM, Della-Morte D, Gomez LA, D'Ippolito G, Reiner T, Perez-Stable C, Howard GA, Perez-Pinzon MA, Montero-Menei CN, & Schiller PC (2011) Neuroprotective properties of marrow-isolated adult multilineage-inducible cells in rat hippocampus following global cerebral ischemia are enhanced when complexed to biomimetic microcarriers. *J Neurochem* 119(5):972-988.
23. Della-Morte D, Raval AP, Dave KR, Lin HW, & Perez-Pinzon MA (2011) Post-ischemic activation of protein kinase C epsilon protects the hippocampus from cerebral ischemic injury via alterations in cerebral blood flow. *Neurosci Lett* 487(2):158-162.
24. Defazio RA, Levy S, Morales CL, Levy RV, Dave KR, Lin HW, Abaffy T, Watson BD, Perez-Pinzon MA, & Ohanna V (2011) A protocol for characterizing the impact of collateral flow after distal middle cerebral artery occlusion. *Transl Stroke Res* 2(1):112-127.
25. Dave KR, Bhattacharya SK, Saul I, DeFazio RA, Dezfulian C, Lin HW, Raval AP, & Perez-Pinzon MA (2011) Activation of protein kinase C delta following cerebral ischemia leads to release of cytochrome C from the mitochondria via bad pathway. *PLoS One* 6(7):e22057.
26. Lin HW, Defazio RA, Della-Morte D, Thompson JW, Narayanan SV, Raval AP, Saul I, Dave KR, & Perez-Pinzon MA (2010) Derangements of post-ischemic cerebral blood flow by protein kinase C delta. *Neuroscience* 171(2):566-576.
27. Lin B, Levy S, Raval AP, Perez-Pinzon MA, & Defazio RA (2010) Forebrain ischemia triggers GABAergic system degeneration in substantia nigra at chronic stages in rats. *Cardiovasc Psychiatry Neurol* 2010:506952.
28. Kim EJ, Raval AP, Hirsch N, & Perez-Pinzon MA (2010) Ischemic Preconditioning Mediates Cyclooxygenase-2 Expression Via Nuclear Factor-Kappa B Activation in Mixed Cortical Neuronal Cultures. *Transl Stroke Res* 1(1):40-47.
29. Curtis KM, Gomez LA, Rios C, Garbayo E, Raval AP, Perez-Pinzon MA, & Schiller PC (2010) EF1alpha and RPL13a represent normalization genes suitable for RT-qPCR analysis of bone marrow derived mesenchymal stem cells. *BMC Mol Biol* 11:61.
30. Schaller BJ, Sandu N, Cornelius JF, Filis A, & Perez-Pinzon MA (2009) Oxygen-conserving implications of the trigemino-cardiac reflex in the brain: the molecular basis of neuroprotection? *Mol Med* 15(5-6):125-126.
31. Schaller B, Cornelius JF, Sandu N, Ottaviani G, & Perez-Pinzon MA (2009) Oxygen-conserving reflexes of the brain: the current molecular knowledge. *J Cell Mol Med* 13(4):644-647.
32. Sandu N, Cornelius J, Filis A, Arasho B, Perez-Pinzon M, & Schaller B (2009) Ischemic tolerance in stroke treatment. *Expert Rev Cardiovasc Ther* 7(10):1255-1261.
33. Raval AP, Saul I, Dave KR, DeFazio RA, Perez-Pinzon MA, & Bramlett H (2009) Pretreatment with a single estradiol-17beta bolus activates cyclic-AMP response element binding protein and protects CA1 neurons against global cerebral ischemia. *Neuroscience* 160(2):307-318.
34. Della-Morte D, Dave KR, DeFazio RA, Bao YC, Raval AP, & Perez-Pinzon MA (2009) Resveratrol pretreatment protects rat brain from cerebral ischemic damage via a sirtuin 1-uncoupling protein 2 pathway. *Neuroscience* 159(3):993-1002.
35. DeFazio RA, Raval AP, Lin HW, Dave KR, Della-Morte D, & Perez-Pinzon MA (2009) GABA synapses mediate neuroprotection after ischemic and epsilonPKC preconditioning in rat hippocampal slice cultures. *J Cereb Blood Flow Metab* 29(2):375-384.
36. Dave KR, Anthony Defazio R, Raval AP, Dashkin O, Saul I, Iceman KE, Perez-Pinzon MA, & Drew KL (2009) Protein kinase C epsilon activation delays neuronal depolarization during cardiac arrest in the euthermic arctic ground squirrel. *J Neurochem* 110(4):1170-1179.



37. Cornelius JF, Sandu N, Perez-Pinzon MA, & Schaller B (2009) Treatment of acute ischemic stroke: role of ischemic tolerance in intravenous and endovascular therapies. *Expert Rev Cardiovasc Ther* 7(4):331-332.
38. Yenari M, Kitagawa K, Lyden P, & Perez-Pinzon M (2008) Metabolic downregulation: a key to successful neuroprotection? *Stroke* 39(10):2910-2917.
39. Raval AP, Lin HW, Dave KR, Defazio RA, Della Morte D, Kim EJ, & Perez-Pinzon MA (2008) Resveratrol and ischemic preconditioning in the brain. *Curr Med Chem* 15(15):1545-1551.
40. Kim EJ, Raval AP, & Perez-Pinzon MA (2008) Preconditioning mediated by sublethal oxygen-glucose deprivation-induced cyclooxygenase-2 expression via the signal transducers and activators of transcription 3 phosphorylation. *J Cereb Blood Flow Metab* 28(7):1329-1340.
41. Della Morte D, Abete P, Gallucci F, Scaglione A, D'Ambrosio D, Gargiulo G, De Rosa G, Dave KR, Lin HW, Cacciatore F, Mazzella F, Uomo G, Rundek T, Perez-Pinzon MA, & Rengo F (2008) Transient ischemic attack before nonlacunar ischemic stroke in the elderly. *J Stroke Cerebrovasc Dis* 17(5):257-262.
42. Dave KR, DeFazio RA, Raval AP, Torraco A, Saul I, Barrientos A, & Perez-Pinzon MA (2008) Ischemic preconditioning targets the respiration of synaptic mitochondria via protein kinase C epsilon. *J Neurosci* 28(16):4172-4182.
43. Raval AP, Dave KR, DeFazio RA, & Perez-Pinzon MA (2007) epsilonPKC phosphorylates the mitochondrial K(+) (ATP) channel during induction of ischemic preconditioning in the rat hippocampus. *Brain Res* 1184:345-353.
44. Perez-Pinzon MA (2007) Mechanisms of neuroprotection during ischemic preconditioning: lessons from anoxic tolerance. *Comp Biochem Physiol A Mol Integr Physiol* 147(2):291-299.
45. Kim E, Raval AP, Defazio RA, & Perez-Pinzon MA (2007) Ischemic preconditioning via epsilon protein kinase C activation requires cyclooxygenase-2 activation in vitro. *Neuroscience* 145(3):931-941.
46. Rodenas-Ruano A, Perez-Pinzon MA, Green EJ, Henkemeyer M, & Liebl DJ (2006) Distinct roles for ephrinB3 in the formation and function of hippocampal synapses. *Dev Biol* 292(1):34-45.
47. Raval AP, Dave KR, & Perez-Pinzon MA (2006) Resveratrol mimics ischemic preconditioning in the brain. *J Cereb Blood Flow Metab* 26(9):1141-1147.

#### **D. Research Support**

R01 NS45676-05 **Pérez-Pinzón (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.

R01 NS34773-11 **Pérez-Pinzón (PI)** 6/1/09-4/30/14

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

**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 (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
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: N/A****B. Positions and Honors:****Professional Experience:**

Research Assistant Professor: University of Miami, U.S.A. 2/1/2006 - Present  
Assistant scientist: University of Miami, U.S.A. 9/1/2003 – 12/31/2006.  
Lecturer: Zoology, M. S. University of Baroda, Gujarat, India. 07/1994 to 11/2000.

**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. Publications (out of 56) Note: \* represents equal contribution; Underline represents corresponding author**

1. Raval AP, Dave KR, Saul I, Gonzalez GJ, Diaz F. (2012) Synergistic inhibitory effect of nicotine plus oral contraceptive on mitochondrial complex-IV is mediated by estrogen receptor- $\beta$  in female rats. J Neurochemistry 121(1):157-67. (PMID:22248091)
2. Raval AP, Hirsch N, Dave KR, Yavagal DR, Bramlett H, Saul I. (2011) Nicotine and estrogen synergistically exacerbate cerebral ischemic injury. Neuroscience 181:216-25. (PMID: 21334425)
3. Raval AP, Borges-Garcia R, Moreno WJ, Perez-Pinzon MA and Bramlett H. (2013) Periodic 17 $\beta$ -estradiol pretreatment protects rat brain from cerebral ischemic damage via estrogen receptor- $\beta$ . Plos One; ;8(4):e60716. (PMID:23593292)
4. Raval AP, Borges-Garcia R, Diaz F, Sick TJ and Bramlett H. (2013) Oral contraceptives and nicotine synergistically exacerbate cerebral ischemic injury in the female brain. Translational Stroke Research (In press)
5. Raval AP. (2011) Nicotine addiction causes unique detrimental effects on female brain. Journal of Addictive Diseases. Review 30(2):149-58. (PMID: 21491296)

Principal Investigator/Program Director (Last, First, Middle): Raval Ami P.

6. **Raval AP**, Sick JT, Gonzalez GJ, Defazio RA, Dong C and Sick TJ. (2012) Chronic nicotine exposure inhibits estrogen-mediated synaptic functions in hippocampus of female rats. *Neuroscience letters*; 517(1):41-6
7. **Raval AP**, Saul I, Dave KR, DeFazio RA, Perez-Pinzon MA, Bramlett H. (2009) Pretreatment with a single estradiol-17 $\beta$  bolus activates CREB and protects CA1 neurons against global cerebral ischemia. *Neuroscience*. 160; 307–318. (PMID: 19272413; PMCID: 2711690)
8. **Raval AP**, Bhatt A, Saul I. (2009) Chronic nicotine exposure inhibits 17 $\beta$ -estradiol-mediated protection of the hippocampal CA1 region against cerebral ischemia in female rats. *Neuroscience letters*. 458(2):65-69. (PMID: 19442878)
9. **Raval AP**, Bramlett H and Perez-Pinzon MA. (2006) Estrogen preconditioning protects the hippocampal CA1 against ischemia. *Neuroscience*. 141(4):1721-1730. (PMID: 16777351)
10. **Raval AP**, Dave KR, DeFazio RA, Perez-Pinzon MA. (2007). Epsilon PKC phosphorylates the mitochondrial K<sup>+</sup>ATP channel during induction of ischemic preconditioning in the rat hippocampus. *Brain Res*. 1184:345-353. (PMID: 17988655; PMCID: 2577914)
11. **Raval AP\***, Dave KR\*, Prado R, Katz LK, Busto R, Sick TJ, Ginsberg MD, Mochly-Rosen D, Pérez-Pinzón MA. (2005). Protein kinase c delta cleavage initiates an aberrant signal transduction pathway after cardiac arrest and oxygen glucose deprivation. *J Cereb Blood Flow Metab*. 25(6):730-741. (PMID: 15716854)
12. **Raval AP\***, Dave KR\*, Perez-Pinzon MA. (2005). Resveratrol mimics ischemic preconditioning in the brain. *J Cereb Blood Flow Metab*. 26(9):1141-1147. (PMID: 16395277)
13. **Raval AP\***, Dave KR\*, Prado R, Katz LK, Busto R, Sick TJ, Ginsberg MD, Mochly-Rosen D, Pérez-Pinzón MA. Protein kinase c delta cleavage initiates an aberrant signal transduction pathway after cardiac arrest and oxygen-glucose deprivation. *J Cereb Blood Flow Metab*. 2005; 25(6):730-41. (PMID:15716854)
14. Lange-Asschenfeldt C\*, **Raval AP\***, Dave KR, Mochly-Rosen D, Sick TJ, Pérez-Pinzón MA. (2004)  $\epsilon$ PKC mediated ischemic tolerance requires activation of the ERK pathway in the organotypic hippocampal slice. *J Cereb Blood Flow Metab*. 24(6):636-645. (PMID: 15181371)
15. **Raval AP**, Dave KR, Mochly-Rosen D, Sick TJ, Perez-Pinzon MA. (2003)  $\epsilon$ PKC is required for the induction of tolerance by ischemic and NMDA-mediated preconditioning in the organotypic hippocampal slice. *J Neuroscience*. 23(2): 384-391. (PMID: 12533598)

#### D. Active Support

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, 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

Principal Investigator/Program Director (Last, First, Middle): Raval Ami P.

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).

University of Miami Specialized Center Of Research on Addiction & Health in Women, Children & Adolescents (UM-SCOR) 10/1/2011-3/31/2013  
Nicotine inhibits estrogen-mediated synaptic plasticity after cerebral ischemia in female rat  
Role: PI, no % efforts

***Completed Research Support (past 3 years):***

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  
R01 NS45676 Dr. Pérez-Pinzón, P.I. 6/1/04- 5/30/08  
Mechanisms of Neuroprotection against Cardiac Arrest  
The major goal of this project was to study the mechanisms of synaptic dysfunction and putative neuroprotective agents following cardiac arrest.  
Role: Dr. Raval, Co-investigator % efforts 5%

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  $\epsilon$ PKC protect neuronal mitochondria whereas  $\delta$ PKC promotes cell death after cerebral ischemia.  
Role: Dr. Raval, Co-investigator % efforts 6%

Developmental Center for AIDS Research  
University of Miami, Dr. Michelin McCarthy, P.I. 5/1/08-5/30/09  
Organotypic slice cultures to model neurogenesis and neuronal survival in HIV-1 infection.  
Role: Dr. Raval, Co-investigator

**BIOGRAPHICAL SKETCH**

Provide the following information for the Senior/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 Juan I. Young		POSITION TITLE Assistant Professor	
eRA COMMONS USER NAME (credential, e.g., agency login) JIYOUNG1			
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
School of Exact and Natural Sciences, University of Buenos Aires, Argentina	MSc	1992	Biological Sciences
University of Buenos Aires, Argentina	PhD	1998	Molecular Genetics

**A. Personal Statement. N/A**

**B. Positions and Honors**

**Positions and Employment**

- 1993-1995 Junior Research Fellowship, National Council of Scientific and Technological Research (CONICET-Argentina)
- 1995-1997 Senior Research fellowship, National Council of Scientific and Technological Research (CONICET-Argentina)
- 1997 Visiting Student, Oregon Health Science University, Vollum Institute for Advanced Biomedical Research (OHSU-VIABR).
- 1998-2001 Postdoctoral Associate, Baylor College of Medicine, Houston, Texas.
- 2001-2004 Postdoctoral Associate, Baylor College of Medicine, Houston, Texas.
- 2005-2009 Assistant Professor, Centro de Estudios Científicos-CECS, Valdivia, Chile.
- 2009 Assistant Professor, Dr. John T. Macdonald Foundation Department of Human Genetics, Leonard M. Miller School of Medicine, University of Miami, Miami, Florida
- 2010 Director, Division for Epigenetics, John P. Hussman Institute for Human Genomics. University of Miami Miller School of Medicine
- 2013 Co-Director , Center for Human Molecular Genetics, John P. Hussman Institute for Human Genomics. University of Miami Miller School of Medicine

**Other Experience and Professional Memberships**

- 2009 American Society of Human Genetics, Member

**Honors**

- 1991 Research Grant for Advanced Students- University of Buenos Aires
- 1997 Bernardo A. Houssay Award-Argentina
- 2002 RSRF Research Award-USA
- 2002 Alan P. Wolfe Memorial Fellowship (RSRF)-USA
- 2004 Extension of the RSRF Research Award-USA
- 2005 Proyecto Fondecyt Regular-Chile # 1051079
- 2006 RSRF Research Award-USA

**C. Selected Peer-reviewed Publications** (Selected more than 31 peer-reviewed publications)

1. Shahbazian M, **Young JI**, Yuva-Paylor L, Spencer C, Antalffy B, Noebels J, Armstrong D, Paylor R, Zoghbi H. Mice with truncated MeCP2 recapitulate many Rett syndrome features and display hyperacetylation of histone H3. *Neuron* July 18; **35**:243-54, 2002.
2. **Young JI** and Zoghbi H.Y. X-chromosome inactivation patterns are unbalanced and affect the phenotypic outcome in a mouse model of Rett syndrome. *Am. J. Hum. Genet.* Mar; **74**:511-20, 2004. PMID: PMC1182264
3. **Young JI**, Hong E.P., Castle J.C., Crespo-Barreto J., Bowman A.B., Rose M.F., Kang D., Richman R., Johnson J.M., Berget S. and Zoghbi H.Y. Regulation of RNA splicing by the methylation-dependent transcriptional repressor methyl-CpG binding protein 2. *Proc Natl Acad Sci U S A.* Dec 6; **102**:17551-8, 2005. PMID: PMC1266160
4. Alvarez-Saavedra M, Sáez MA, Kang D, Zoghbi HY and **Young JI**. Cell-specific expression of wild-type MeCP2 in mouse models of Rett syndrome yields insight about pathogenesis. *Human Molecular genetics*, Oct 1; **16** :2315-25, 2007.
5. Kerr B, Alvarez-Saavedra M, Sáez MA, Saona A and **Young JI**. Defective body weight regulation and motor control in *Mecp2* hypomorphic mice. *Human Molecular Genetics*, Jun 15; **17**:1707-17, 2008.
6. Alvarez-Saavedra M, Carrasco L, Sura-Trueba S, Demarchi Aiello V, Walz K, Xavier Neto J, **Young JI**. Elevated expression of MeCP2 in cardiac and skeletal tissues is detrimental for normal development. *Hum Mol Genet.* Jun 1; **19**(11):2177-90, 2010.
7. Kerr B, Silva PA, Walz K, **Young JI**. Unconventional transcriptional response to environmental enrichment in a mouse model of Rett syndrome. *PloS One.* Jul 12; **5**:e11534, 2010. PMID: PMC2902516
8. Carmona-Mora P, Encina CA, Canales CP, Cao L, Molina J, Kairath P, **Young JI**, Walz K. Functional and cellular characterization of human Retinoic Acid Induced 1 (RAI1) mutations associated with Smith-Magenis Syndrome. *BMC Mol Biol.* 2010 Aug 25; **11**(1):63. PMID: PMC2939504
9. Ricard G, Molina J, Chrast J, Gu W, Gheldof N, Pradervand S, Schütz F, **Young JI**, Lupski JR, Raymond A, Walz K. Phenotypic consequences of copy number variation: insights from Smith-Magenis and Potocki-Lupski syndrome mouse models. *PloS Biol.* 2010 Nov 23; **8**(11):e1000543. PMID: PMC2990707
10. Tekin M, Chioza BA, Matsumoto Y, Diaz-Horta O, Cross HE, Duman D, Kokotas H, Moore-Barton HL, Sakoori K, Ota M, Odaka YS, Foster J 2nd, Cengiz FB, Tokgoz-Yilmaz S, Tekeli O, Grigoriadou M, Petersen MB, Sreekantan-Nair A, Gurtz K, Xia XJ, Pandya A, Patton MA, **Young JI**, Aruga J, Crosby AH. SLITRK6 mutations cause myopia and deafness in humans and mice. *J Clin Invest.* 2013 May 1; **123**(5):2094-102. PMID: 23543054
11. Kerr B, Soto J, Saez M, Abrams A, Walz K, **Young JI**. Transgenic complementation of MeCP2 deficiency: phenotypic rescue of *Mecp2*-null mice by isoform-specific transgenes. *Eur J Hum Genet.* 2012 Jan; **20**(1):69-76. PMID: PMC3234513
12. Carmona-Mora P, Canales CP, Cao L, Perez IC, Srivastava AK, **Young JI**, Walz K. RAI1 Transcription Factor Activity is Impaired in Mutants Associated with Smith-Magenis Syndrome. *PloS ONE* 2012, **7**(9): e45155. PMID: PMC3445574

13. Cukier HN, Lee JM, Ma D, **Young JI**, Mayo V, Butler BL, Ramsok SS, Rantus JA, Abrams AJ, Wright HH, Abramson RK, Haines JL, Cuccaro ML, Gilbert JR, Pericak-Vance MA. The Expanding Role of MBD Genes in Autism: Identification of a MECP2 Duplication and Novel Alterations in MBD5, MBD6 and SETDB1. Autism Research, 2012 Dec;5(6):385-97. PMCID: PMC3528798
14. Minor EA, Court BL, **Young JI**, Wang G. Ascorbate induces Ten-eleven translocation (Tet) methylcytosine dioxygenase-mediated generation of 5-hydroxymethylcytosine. J Biol Chem. 2013 May 10;288(19):13669-74. PMCID: PMC3650403
15. Cao L, Molina J, Abad C, Carmona-Mora P, Oyarzo AC, Young JI, Walz K. Correct developmental expression levels of Rai1 in forebrain neurons is required for control of body weight, activity levels and learning and memory. Hum Mol Genet. 2013 Nov 11. PMID: 24218365

#### **D. Research Support**

##### **Ongoing Research Support**

**2P50NS071674-02**

(Vance JM)

09/01/11 -08/31/16

NIH/NINDS

“Genetics of Parkinsonism” – Morris K. Udall Parkinson’s Disease Research Center of Excellence”

Project 2 “Long ncRNAs as Epigenomic Modulators and CSF Biomarkers in Parkinson’s Disease”

The overall goal of the center is to identify genes that cause or contribute to an individual’s susceptibility to Parkinson Disease (PD). The discovery of PD risk genes will provide insight into the biological and environmental mechanisms that cause PD.

Role: Co-PI Project 2

**1R01NS081208-01A1**

(Faghihi, M).

04/01/13-03/30/18

NIH/NINDS

“Antisense RNA Mediated Epigenetic Regulation of Brain Derived Neurotrophic Factor”

The major goal of this research is to investigate epigenetic regulation of BDNF, both in vitro and in vivo and to study potential beneficial effect of BDNF upregulation on Rett Syndrome mouse model.

Role: Co-I

**5 R21MH093876-02**

(Young, JI)

04/01/12-03/31/14

NIH

“Modulation of Rett-Like Phenotypes in Mouse Models of Rett Syndrome”

We will use mouse and cellular models of Rett syndrome to test whether the effect of mutations that affect MeCP2’s functionality (but do not eliminate the protein) could be reversed by transgenic restoration of MeCP2.

Role: PI

**1R21AI103547-01**

(Adkins, R)

4/10/13-3/31/15

NIH

“Genetic and Epigenetic Contributions to the Neonatal Th2 Bias”

This proposal will examine the contribution of selective components of the genome to the poor immunity in newborn animals. This information will provide an important foundation for developing novel approaches to meet the health challenges of pediatric life, such as (a) enhancing vaccine responsiveness, (b) mitigating pediatric-onset asthma, and (c) increasing resistance to pathogenic microorganisms.

Role: Co-I

**Jérôme Lejeune Foundation** (Young, JI) 07/01/11-09/06/14

“Modulation of Rett-like phenotypes in mouse models of Rett syndrome”

We will use mouse models of Rett syndrome to test whether the effect of a truncating mutation that affects MeCP2's functionality could be reversed by transgenic restoration of MeCP2.

Role: PI

**Jérôme Lejeune Foundation** (Walz, K) 07/01/11-09/06/14

“Exploring the reversibility of neuron functional deficiency”

The presence of microdeletions or microduplications in our genome is often related to various diseases. Our studies will uncover if restoring the appropriate amount of key proteins can prevent or ameliorate the phenotypic consequences related to abnormal gene dosage.

Role: Co-I

### **Completed Research Support**

**NIH/NIAID 2R56AI044923-11** (Adkins, RD) 07/01/11-07/01/12

“Developmentally regulated epigenetic programs in fetal/neonatal T lineage cells”

The purpose of this proposal is to investigate genetic and epigenetic contributions to gene expression in T lineage cells during the newborn phase of life.

Role: Co-investigator

**UM SCOR - University of Miami** (Itzhak, Y / Young, JI) 06/01/11-05/30/12

“Epigenetic mechanisms in sex- and age-dependent differences in response to cocaine”

We hypothesize that sex- and age-dependent differences in the behavioral responses to cocaine are due to distinct effects of cocaine on epigenetic modifications, such as DNA methylation, in the NAC of males and females and adolescent and adult subjects.

Role: Co-PI

**Proyecto Regular/1051079** (Young JI) 2005-2009

Fondecyt –Chile

Es posible revertir el síndrome de rett? Restitucion condicional de mecp2 en modelos murinos para esta enfermedad.

Role: PI

**Proyecto Regular/1061067** (Walz K) 2006-2009

Fondecyt –Chile

Estudio de la participacion de la proteina inducida por acido retinoico 1 (rai1) en el fenotipo observado en el síndrome dup (17) (p11.2p11.2) utilizando modelos murinos.

Role: Co-PI

**RSRF Research Award** (Young JI) 2006-2008

Rett Syndrome Research Foundation

MeCP2's function in post-translational regulation of gene expression.

Role: PI