

MILLER SCHOOL of MEDICINE

#### EVELYN F. McKNIGHT BRAIN INSTITUTE

January 14, 2013

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Dear Trustees,

Enclosed please find a copy of the Evelyn F. McKnight Brain Institute Progress Report for 2012. 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 2013. 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

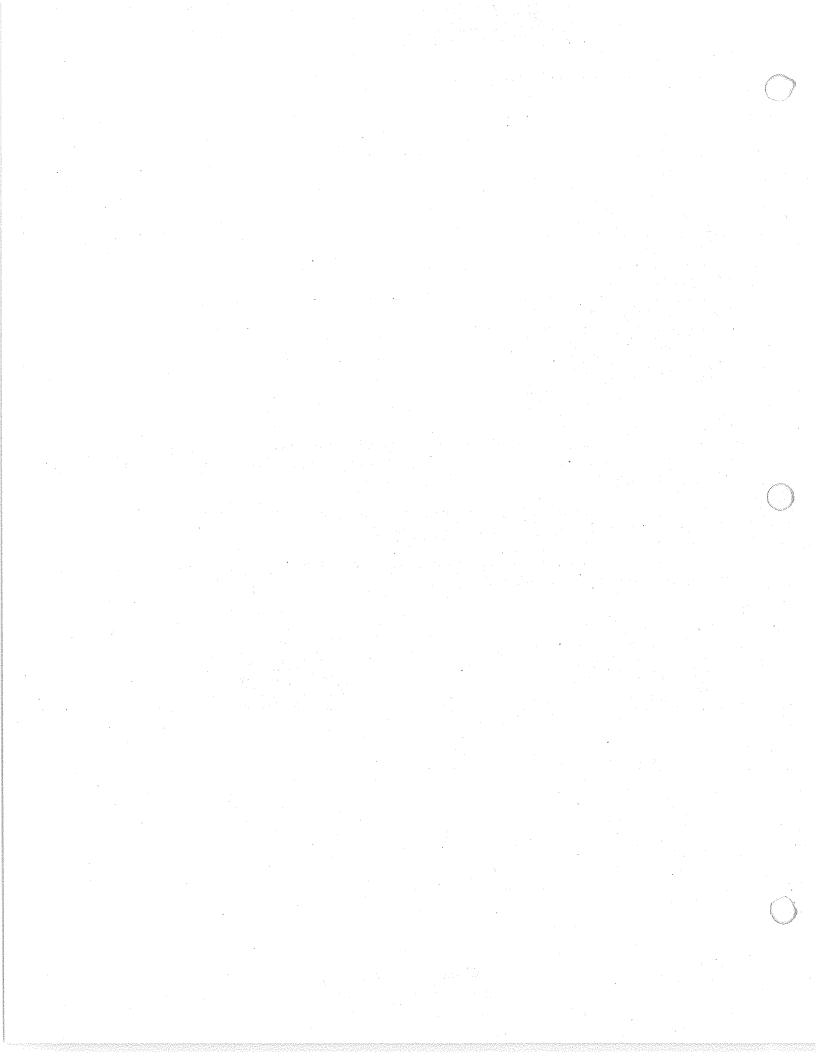
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Scientific Director

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## 1. Summary of Scientific Achievements since Last Report

In 2012 the University of Miami Evelyn F. McKnight Brain Institute (UM-MBI) had an energetic year, with the introduction of new programs, the development of existing programs, the beginning of fresh collaborations across McKnight Institutes, and new extramural funding. Our programs now extend fully across the spectrum from laboratory experiments, the clinic, large-scale epidemiologic studies, and multi-site genetic consortia. Our focus continues to be studies of cognitive aging, with an emphasis on the effect of novel modifiable vascular risk factors, underlying genetics, and the interaction of these factors with the aging process.

The cognitive component of the Northern Manhattan Study entered its 11th year of federal funding in 2012. Drs. Wright, Sacco, Rundek and others have continued to use this rich dataset to answer questions about brain aging and cognition and publications related to this are detailed below. Dr. Wright was awarded an R01 to study vitamin D and phosphorus metabolism, and other novel risk factors in this pathway, in relation to subclinical cerebrovascular disease and cognitive decline as well as stroke. Our collaborative genetics studies with the large Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) Consortium, a group of population-based cohort studies with multiple aging phenotypes in common, also continued in 2012.

The Cornfeld Family Neuroimaging Center opened its doors with the completion of construction and the start of scanning using the new 3T MRI machine. This dedicated neuroimaging facility will provide imaging infrastructure for many UM-MBI research studies that depend on structural and functional imaging.

Our UM-MBI Clinical and Biorepository Registry entered its second year and continued to enroll. We now have 214 participants in the multi-disciplinary study. Our source is the comprehensive memory clinic for people with cognitive complaints. The State of Florida Department of Elder Affairs funds the medical program and the UM-MBI supports the biomarker and imaging research. We have continued to collect data using the National Alzheimer Coordinating Center (NACC) Uniform Data Set (UDS) used by all federally funded centers nationwide to collect standardized epidemiologic data, and we also collect high quality neuroimaging data, and data for our Aging and Memory Brain Hemodynamic (AMBH) study that we initiated in 2011. We have also continued to enroll patients in dementia genetics studies in collaboration with Dr. Margaret Pericak-Vance, and the Hussman Institute for Human Genomics, and into the Brain Endowment Bank. Dr. Levin began a study with the help of graduate student Agustina Rosetti on inflammation and cognition using this sample. We have also begun examining the imaging data with a project on the importance of white matter disease location to cognitive function.

Our translational program has advanced with work in the Animal Behavior Core under the leadership of Dr. Perez-Pinzon. We have continued to collaborate with Dr. Carol Barnes from the Arizona MBI to develop our behavioral model of the effects of experimental brain ischemia on learning and memory, and Dr. Barnes visited our lab in July to answer questions and provide advice on behavioral testing. This work is also part of our educational program with experiments being carried out by post-doctoral fellow Jacob Neumann and graduate student Charles Cohan.

We completed enrollment into the MRI substudy of 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. We will continue to follow these participants and will acquire a second MRI to measure longitudinal changes in brain morphology beginning in 2014.

We have continued to educate members of the UM scientific community with our McKnight Research Seminars. In addition, we have educated the community through the highly successful Brain Fair at the Miami Science Museum in March and by giving educational lectures at senior centers as part of our memory screenings.

We have also participated in three collaborative groups with other McKnight Brain Institutes. Dr. Wright co-chairs the MRI Standardization Working Group with Dr. Gene Alexander from Arizona's MBI and Drs. Nahab, Alperin and others from UM joined this effort (see Section 13 for further details). The Epigenetics working group has met twice and several researchers from UM participated, including Drs. Susan Blanton, Juan Young, and Chuanhui Dong. We have also continued to participate in the Cognitive Assessment Battery Working Group, in which Dr. Levin participates.

In addition to the above, we participated in the MBRF Poster Session at the Society for Neuroscience. Representatives from our McKnight Brain Institute also presented data at important national and international meetings, including the American Academy of Neurology, the International Stroke Conference of the American Heart Association, the Society for Neuroscience, the International Society for Hydrocephalus, the International Society for Magnetic Resonance in Medicine, Summer Research Conference in Mitochondrial Assembly and Dynamics in Health, Disease and Aging, the American Society of Human Genetics Annual Meeting, the International Conference on Quantification of Brain Function with PET, and the Eastern Atlantic Student Research Forum among others (see Section 4 for further details).

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

Alperin N, Lam BL, Tain RW, Ranganathan S, Letzing M, Bloom M, Alexander B, Aroucha PR, Sklar E. Evidence for altered spinal canal compliance and cerebral venous drainage in untreated idiopathic intracranial hypertension. *Acta Neurochir*. Suppl. 2012;114:201-5. doi: 10.1007/978-3-7091-0956-4\_39.

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. *Am J Neuroradiol.* 2012; [Epub ahead of print].

Barrientos A. Complementary roles of mitochondrial respiration and ROS signaling on cellular aging and longevity. *Aging*. 2012; 4:578-9.

Bacman SR, Williams SL, Duan D, Moraes CT. Manipulation of mtDNA heteroplasmy in all striated muscles of newborn mice by AAV9-mediated delivery of a mitochondria-targeted restriction endonuclease. *Gene Ther.* 2012; 19:1101-6.

Boden-Albala B, Roberts ET, Bazil C, Moon Y, Elkind MS, Rundek T, Paik MC, Sacco RL. Daytime sleepiness and risk of stroke and vascular disease: findings from the Northern Manhattan Study (NOMAS). Circ Cardiovasc Qual Outcomes. 2012; 5:500-7.

Böhm M, Cotton D, Foster L, Custodis F, Laufs U, Sacco R, Bath PM, Yusuf S, Diener HC. Impact of resting heart rate on mortality, disability and cognitive decline in patients after ischaemic stroke. *Eur Heart J.* 2012; 33:2804-12.

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; 7e45155.

Cukier HN, Lee JM, Ma D, Young JI, Mayo V, Butler BL, Ramsook SS, Rantus JA, Abrams AJ, Whitehead PL, Wright HH, Abramson RK, Haines JL, Cuccaro ML, Pericak-Vance MA, Gilbert JR. The Expanding Role of MBD Genes in Autism: Identification of a MECP2 Duplication and Novel Alterations in MBD5, MBD6, and SETDB1. *Autism Res.* 2012; 5:385-97.

Czaja SJ, Lee CC, Branham J, Remis P. OASIS Connections: Results from an Evaluation Study. *The Gerontologist.* 2012; 52.

Czaja, SJ, Sharit J, Lee CC, Nair SN, Hernandez M, Arana N, Fu SH. Factors Influencing Use of an E-health Website in a Community Sample of Older Adults. *J Am Med Inform Assoc.* 2012 doi: 10.1136/amiajnl-2012-000876.

DeCarli C, Kawas C, Morrison JH, Reuter-Lorenz PA, Sperling RA, Wright CB. Session II: Mechanisms of Age-Related Cognitive Change and Targets for Intervention: Neural Circuits, Networks, and Plasticity. *J Gerontol A Biol Sci Med Sci.* 2012; 67:747-53. doi: 10.1093/gerona/gls111.

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; 323:93-8. doi: 10.1016/j.jns.2012.08.020.

Della-Morte D, Dong C, Bartelsa S, Cabral D, Blanton SH, Sacco RL, Rundek T. Association of the sirtuin and mitochondrial uncoupling protein genes with carotid intima-media thickness. *Transl Res.* 2012; 160:389-90. doi: 10.1016/j.trsl.2012.05.010.

Dhamoon MS, Moon YP, Paik MC, Sacco RL, Elkind MS. Trajectory of functional decline before and after ischemic stroke: the Northern Manhattan study. Stroke. 2012; 43:2180-4.

Diaz F, Enriquez JA, Moraes CT. Cells lacking Rieske Iron Sulfur Protein have a ROS-associated decrease in respiratory complexes I and IV. Mol Cell Biol. 2012; 32:415-29.

Diaz F, Garcia S, Padgett KR, **Moraes CT**. A defect in the mitochondrial Complex III, but not Complex IV, triggers early ROS dependent damage in defined brain regions. *Human Molecular Genetics*. 2012; 21:5066-77.

Dillon LM, Hida A, Garcia S, Prolla TA, Moraes CT. Long-term bezafibrate treatment improves skin and spleen phenotypes of the mtDNA mutator mouse. PLoS One. 2012; 7:e44335.

Dillon LM, Rebelo AP, Moraes CT. The role of PGC-1 coactivators in aging skeletal muscle and heart. *IUBMB Life*. 2012; 64:231-41.

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Dong C, Beecham A, Wang L., Blanton SH, Rundek T, Sacco RL. Follow-up association study of linkage regions reveals multiple candidate genes for carotid plaque in Dominicans. *Atherosclerosis.* 2012; 223:177-83.

Dong C, Rundek T, Wright CB, Anwar Z, Elkind MS, Sacco RL. Ideal Cardiovascular Health Predicts Lower Risks of Myocardial Infarction, Stroke, and Vascular Death across Whites, Blacks and Hispanics: the Northern Manhattan Study. *Circulation*. 2012; 125:2975-84.

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Ertl-Wagner B, Korte I, **Alperin N**, et al. Non-specific alterations of craniocervical venous drainage in multiple sclerosis revealed by cardiac-gated phase-contrast MR imaging (in press) *Multiple Sclerosis Journal*. 2012;18:1000-7. doi: 10.1177/1352458511432742.

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Gardener H, Scarmeas N, Gu Y, Boden- Albala B, Elkind MSV, Sacco RL, DeCarli C, Wright CB. A Mediterranean- Style Diet and White Matter Hyperintensity Volume: the Northern Manhattan Study. *Arch Neurol.* 2012; 69:251-6.

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; 43:1123-5.

Geldmacher DS, Levin BE, Wright CB. Characterizing healthy samples for studies of human cognitive aging. Front. Ag. Neurosci. 2012; 4:23.

Haubenberger D, McCrossin G, Considine E, Toro C, Nahab FB, Aug S, Buchwald P, Grimes GJ, Starling J, Potti G, Scheider L, Kalowitz D, Bowen D, Carnie A, Hallett M. Safety and efficacy of octanoic acid in essential tremor. A randomized controlled study. *Neurology*. (in press).

Iwata S, Jin Z, Schwartz JE, Homma S, Elkind MS, Rundek T, Sacco RL, Di Tullio MR. Relationship between ambulatory blood pressure and aortic arch atherosclerosis. *Atherosclerosis*. 2012; 221:427-31.

Jiang H, Ye Y, Debuc DC, Lam BL, Rundek T, Tao A, Shao Y, Wang J. Human conjunctival microvasculature assessed with a retinal function imager (RFI). *Microvasc Res.* 2012; doi:pii: S0026-2862(12)00166-5.

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Kerr B, Soto C 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; 20:69-76.

Koch S, Sacco RL, Perez-Pinzon MA. Preconditioning the Brain: Moving on to the Next Frontier of Neurotherapeutics. Stroke. 2012; 43:1455-7. doi: 10.1161/STROKEAHA.

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Raval AP, Dave KR, Saul I, Gonzalez GJ, Diaz F. Synergistic inhibitory effect of nicotine plus oral contraceptive on mitochondrial complex-IV is mediated by estrogen receptor-β in female rats. J Neurochemistry. 2012; 121:157-67.

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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. *Frontiers Aging Neuroscience*. 2012; 4:6.

Romano JG, Arauz A, Koch S, **Dong C**, Marquez JM, Artigas C, Merlos M, Hernandez B, Roa LF, **Rundek T**, **Sacco RL**. Disparities in stroke type and vascular risk factors between two Hispanics populations in Miami and México city. *Journal of Stroke and Cerebrovascular Diseases*. 2012; [Epub ahead of print].

Russo C, Jin Z, Palmieri V, Homma S, Rundek T, Elkind MS, Sacco RL, Di Tullio MR. Arterial stiffness and wave reflection: sex differences and relationship with left ventricular diastolic function. *Hypertension*. 2012; 60:362-8.

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Shafazand S; Wallace DM; Vargas SS; Del Toro Y; Dib S; Abreu AR; Ramos A; Nolan B; Baldwin CM; Fleming L. Sleep disordered breathing, insomniasymptoms, and sleep quality in a clinical cohort of US Hispanics in South Florida. *J Clin Sleep Med.* 2012; 8:507-514.

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Whitcomb DC, Larusch J, Krasinskas AM, Crocco E, Wright CB et al. Common genetic variants in the CLDN2 and PRSS1-PRSS2 loci alter risk for alcohol-related and sporadic pancreatitis. *Nat Genet.* 2012; 44:1349-54.

White MG, Saleh O, Nonner D, Barrett EF, Moraes CT, Barrett JN. Mitochondrial dysfunction induced by heat stress in cultured rat CNS neurons. *J Neurophysiol.* 2012; 108:2203-14.

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# 3. Publications (Other)

Alter KA, Nahab FB. Lower limb dystonia. In: Alter KA, ed. Ultrasound guided chemodenervation procedures: Text and Atlas. DemosMedical, 2012.

Alter KA, Nahab FB. Upper motor neuron syndrome. In: Alter KA, ed. Ultrasound guided chemodenervation procedures: *Text and Atlas. DemosMedical*, 2012.

Assuras S, Levin B. Special Considerations for the Neuropsychological Interview with Older Adults. In . Ravdin L and Katzen H. (eds) Handbook on the Neuropsychology of Aging and Dementia, Springer Science + Business Media: New York; pgs. 3-9, 2012.

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. [Epub ahead of print].

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Liu J. and Barrientos A. Transcriptional regulation of yeast OXPHOS hypoxic genes by oxidative stress. Antiox Redox Signal [Epub ahead of print] (2012).

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 15:324-35.

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Soto IC, Fontanesi F, Liu J, Barrientos A. Biogenesis and assembly of eukaryotic cytochrome c oxidase catalytic core. *Biochim Biophys Acta* 2012. 1817:883-97.

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## 4. Presentations at Scientific Meetings

Alperin N, Bagci AM, Schmidtman J, Pomschar A, Ertl-Wagner B, Wright C. Assessment of Regional Rates of Change in CBF in Response to Changes in PaCO2: A Combined ASL and Phase Contrast Study. The International Society for Magnetic Resonance in Medicine Annual Meeting; Melbourne, Australia. 2012.

Alperin N, Ranganathan S, Aroucha P, Joshua Pasol J, Lam L. Evidence for Larger Extra Ventricular Cranial CSF Volume in Idiopathic Intracranial Hypertension.

Alperin N, Muehlmann M, Koerte I, Lehner M, Peraud A, Ertl-Wagner B. Comparing MR Estimate of Intracranial Pressure with Valve Opening Pressure in Shunted Patients.

Arauz A, Romano JG, Ruiz A, Shang T, **Dong C, Rundek T**, Koch S, Hernández B, Pacheco G, Katsnelson M, **Sacco RL**. Lipid differences in two Hispanic ischemic stroke populations. Poster presentation (#515) at the 21st European Stroke Conference, Lisbon, Portugal. May 22-25, 2012.

Bagci AM, Ranganathan S, Gomez JS, Lam BL, Alperin N. Automated Quantitation of CSF Volumes in Central Nervous System by MRI. The International Society for Magnetic Resonance in Medicine Annual Meeting; Melbourne, Australia. 2012.

Bagci AM, Alperin N. Automated Quantitation of CSF Volumes in the Central Nervous System by MRI.

Barrientos A. Mitochondrial respiration, ROS and aging. Mitochondrial Club at the Max Planck Institute and University of Cologne, Cologne (Germany) June, 2012.

Blanton, SH, Beecham AH, Wang L, Dong C, Cabral D, Hudson BI, Kiryiya M, Jasmine F, Pierce B, Demmer R, Habibul A, Desvarieux M, Sacco RL, Rundek T. A genome wide association study of carotid intima-medial thickness, a preclinical marker of atherosclerosis. Poster (#1638T). The 62nd American Society of Human Genetics Annual Meeting, San Francisco, CA. November 6-10, 2012.

Borges-Garcia R, Behairy M, Bramlett H, Perez-Pinzon MA, Raval AP. Chronic nicotine hinders hippocampus-dependent learning and memory in female rats. Program#/Poster#:

845.03/B68, 2012 Neuroscience Meeting Planner. New Orleans: Society for Neuroscience, 2012.

Borges-Garcia R, Behairy M, Bramlett H, **Perez-Pinzon MA**, **Raval AP**. Chronic nicotine hinders hippocampus-dependent learning and memory in female rats. McKnight Brain Research Foundation, New Orleans: Society for Neuroscience, 2012.

Czaja SJ. Assessing the Usefulness of Software Tools for Aiding Meaningful Access of Internet Health Information by Older Users. The Human Factors and Ergonomics Society Annual Meeting. Boston, MA. October 2012.

Dong C, Cabral D, Marquez C, Elkind MSV, Sacco RL, Rundek T. Segment-specific association of body mass index with carotid plaque and intima-media thickness: the Northern Manhattan Study. Oral presentation (#86) at Arteriosclerosis, Thrombosis, Vascular Biology. Chicago, Illinois. April 18-20, 2012

Dong C, Wang L, Cabral D, Beecham A, Blanton SH, Zhao H, Rundek T, Sacco RL. RCBTB1 genotypes modulate smoking effect on carotid intima-media thickness: A finding from a genome-wide interaction analysis. Poster (#78) presentation at Arteriosclerosis, Thrombosis, Vascular Biology 2012 Scientific Sessions, Chicago, Illinois. April 18-20, 2012.

Dong, C, Wang L, Beecham A, Cabral D, Wright CB, Blanton SH, Rundek T, Zhao H, Sacco RL. Loci on chromosomes 2q12, 6p21 and 13q14 modulate the effect of smoking on carotid intima-media thickness in whites, blacks and Hispanics. Abstract (#1635). The 62nd American Society of Human Genetics Annual Meeting, San Francisco, CA. November 6-10, 2012.

Galvin J, Isaacson RS, Callegari F, Strohmaier C, Somogyi M. Evaluating the efficacy and safety of high-dose (13.3 mg/24 h) rivastigmine patch: focus on a unique study design. Presented at the American Academy of Nurse Practitioners meeting, Toronto, ON, Canada, October, 2012.

Galvin J, Isaacson RS, Callegari F, Strohmaier C, Somogyi M. Evaluating the efficacy and safety of high-dose (13.3 mg/24 h) rivastigmine patch: focus on a unique study design. Presented at the American Academy of Geriatric Psychiatry meeting, Washington DC, May 2012.

Gutierrez J, Gardener H, Bagci A, Marquez C, Rundek T, DeCarli C, Elkind SE, Alperin N, Sacco R, Wright C. A Population-based Study Of Arterial Diameters In Dolichoectasia: The Northern Manhattan Study. International Stroke Conference, New Orleans. February, 2012.

Gutierrez J, Gardener H, Bagci A, Marquez C, Rundek T, DeCarli C, Elkind SE, Alperin N, Sacco R, Wright C. Dolichoectasia and intracranial arterial characteristics in a race-ethnically diverse community-based sample: The Northern Manhattan study. International Stroke Conference, New Orleans. February, 2012.

Hudson BI, Liu-Mares W, Dong C, Gardener H, Elkind MSV. Wright CB, Sacco RL, Rundek T. Association of soluble RAGE levels with carotid atherosclerotic plaque characteristics by high-resolution ultrasound. Abstract (# 61). Journal of Neuroimaging

22(1):106, 2012. Poster presentation at the 35th Annual Meeting of the American Society of Neuroimaging in Miami, FL. January 26-29, 2012.

Isaacson, Richard. Opportunities for the Clinician Educator in Neurology. American Academy of Neurology Annual Meeting, Clerkship and Program Directors Meeting and Consortium of Neurology Program Directors Meeting. April, 2012.

Isaacson, Richard. Quantitative Methods in Education Research. American Academy of Neurology Annual Meeting, Education Research Colloquium. April 2012.

Ivkovic M, Katzen H, Kovanlikaya I, Bagci AM, Heier L, Alperin N, et al. MRI biomarkers capable of detecting effects of an experimental pharmacologic therapy for idiopathic Normal Pressure Hydrocephalus. The International Society for Magnetic Resonance in Medicine Annual Meeting; Melbourne, Australia. 2012.

Katsnelson M, Rundek T, Sacco R, Gardener H, Malik S, Southerland AM, Gamble D, Barrett KM, Ossi R, Arsava E, Rexrode K, Biffi A, Helenius J, Huq M, Labovitz D, Weissman D, Sheikh H, Rhodes D, Saraf N, Brenner D, Peddareddygari L, McArdle P, Rosand J, Woo D, Smoller S, Arnett D, Grewal R, Worrall B, Meschia J, Brown RD, Ay H, Kittner S. Stroke subtypes in Hispanic patients in the NINDS Stroke Genetics Network (SiGN): A comparison of two classification systems. International Stroke Conference, New Orleans, LA, February, 2012.

Kuo F, Gardener H, Dong C, Cabral D, Della-Morte D, Blanton SH. Santiago, M., Elkind, M.S.V., Sacco, R.L., Rundek, T., Traditional cardiovascular risk factors explain only small proportion of the variability in carotid plaque. Poster (#2346) presentation at the 2012 International Stroke Conference, New Orleans, Louisiana. February 1-3, 2012.

Nahab F. Co-chair and Lecturer, 6th Annual Johns Hopkins Dystonia & Spasticity Practicum - Title: Chemodenervation, Miami, FL. December, 2012.

Nahab F. Faculty, International Neurotoxin Association Symposium - Title: Managing Patient Satisfaction, Safety and Therapeutic Efficacy in Cervical Dystonia, Miami, FL. December, 2012.

Nahab F. Faculty, Neurology Update and Stroke Intensive - Title: Brain Mapping for Epilepsy Pre-surgical Evaluation. Miami, FL. January, 2012.

Nahab F. Faculty, Neurology Update and Stroke Intensive - Title: Gait Disorders, Miami, FL. January, 2012.

Nahab F. Invited Lecturer - Title: Essential Tremor - Capital Medical University - Beijing, China. June, 2012.

Nahab, F. Faculty, International Neurotoxin Association Annual Meeting - Chemodenervation Demonstration, Miami, FL. December, 2012.

Raval AP, Borges-Garcia R, Moreno W, Bramlett H, Perez-Pinzon MA. Intermittent 17β-estradiol treatment protects the hippocampal CA1 region against cerebral ischemia via estrogen receptor-β. Neuroscience Meeting Planner. New Orleans: Society for Neuroscience. 2012.

- Raval AP, Borges-Garcia R, Moreno W, Bramlett H, Perez-Pinzon MA. Intermittent 17β-estradiol treatment protects the hippocampal CA1 region against cerebral ischemia via estrogen receptor-β. McKnight Brain Research Foundation, New Orleans: Society for Neuroscience. 2012.
- Raval AP, Borges-Garcia R, Moreno WJ, Saul I, Bramlett H. Cyclic 17b-estradiol injection improves spatial memory performance and cerebral ischemia outcome in female rats. Endocrinology meeting, Houston. 2012.
- Relkin N, Ivkovic M, Katzen H, Kovanlikaya I, Bagci AM, Heier L, et al. Feasibility of MRI-Guided Pharmacologic Therapy for Idiopathic Normal Pressure Hydrocephalus (iNPH) American Academy of Neurology, 64th Annual meeting; New Orleans, Louisiana. February, 2012.
- Sacco, RL. Stroke Prevention: An Unfinished Story with New Perspectives, Wartenberg Lecture 2012. American Academy of Neurology Annual Meeting, New Orleans, LA. April, 2012.
- Wang L, Beecham A, Dong C, Gardener H, Blanton SH, Rundek T, Sacco RL. Fine mapping study revealed novel candidate genes for carotid intima-media thickness in Dominicans. Oral presentation (#14) at the International Stroke Conference, New Orleans, Louisiana. February 1-3, 2012.
- Wright C, Dong C, Yoshita M, Disla N, Elkind MS, DeCarli C, Sacco RL, Rundek T. Asymptomatic Internal Carotid Artery Stenosis is Associated with More Cortical Subclinical Brain Infarcts: the Northern Manhattan Study (NOMAS) International Stroke Conference, New Orleans. February, 2012.
- Wright CB, Dong C, Yoshita M, Disla N, Elkind MSV, DeCarli C, Sacco RL. Rundek T. Asymptomatic Internal Carotid Artery Stenosis is associated with more cortical subclinical brain infarcts: the Northern Manhattan Study (NOMAS). Poster (#3166) presentation at The International Stroke Conference, New Orleans, Louisiana. February 1-3, 2012.
- Wright CB. Biomarkers in the Diagnosis of Alzheimer's Disease, XXII Jornadas Neurologicas: Images of Neurology: Early Identification for Targeted Intervention, San Juan, PR. August, 2012.
- Wright CB. Blood Pressure, Cognition and White Matter", Concurrent Symposium-Blood Pressure & the Brain: White Matter, Infarcts, Microbleeds and Consequences for Cognitive Impairment International Stroke Conference, New Orleans. February, 2012.
- Wright CB. Hypertension, subclinical brain infarction, and white Matter Lesions, XXII Jornadas Neurologicas: Images of Neurology: Early Identification for Targeted Intervention, San Juan, PR. August, 2012.
- Wright CB. Hypertension, subclinical brain infarction, and white Matter Lesions, XXI Congreso Internacional de Neurología y Neurocirugía, Santo Domingo, DR. August, 2012.

Wright CB. Modern Acute Stroke Management, Neurology Update and Stroke Intensive. The Mayfair Hotel and Spa, Coconut Grove, Miami FL. January, 2012.

Wright CB. Use of Biomarkers in the Diagnosis of Alzheimer's Disease, XXI Congreso Internacional de Neurología y Neurocirugía, Santo Domingo, DR. September, 2012.

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

Crocco, Elizabeth. Lecture to 1st year medical students, "Geriatric Psychiatry & Mental Status Examination. March, 2012.

Crocco, Elizabeth. Lecture to 1st year medical students, "Depression & Anxiety." March, 2012.

Crocco, Elizabeth. Lecture entitled, "Antipsychotic Use in Dementia to Geriatric Medicine faculty & fellows. March, 2012.

Crocco, Elizabeth. Lecture entitled "Agitation in Dementia". 1st year Psychiatry Residents. March, 2012.

**Crocco, Elizabeth.** Bedside training of clinical evaluation and management of geriatric patients with psychiatric disorders and/or memory impairment. Geriatric Psychiatry Fellows. January – March, 2012.

**Crocco, Elizabeth.** MDC staff- Caregiver/patient education during MDC Family Conference. January – March, 2012.

**Isaacson, Richard.** How to Find Fellowship Training in the United States and Canada. American Academy of Neurology Annual Meeting. April, 2012.

Isaacson, Richard. Neurology Board Review. New York University, Department of Internal Medicine. Internal Medicine Resident Lecture Series. April, 2012.

**Isaacson, Richard.** Neurology Board Review. American College of Physicians Internal Medicine Board Review Course. February, 2012.

Ramos, Alberto. Introduction to Sleep Disorders. Miami Brain Fair, Miami Museum of Science, Miami, FL. March 17, 2012.

Ramos, Alberto. Sleep Disorders and Neurocognitive function. Neuropsychology Graduate Students. Course Director: Dr. Bonnie Levin. Department of Neurology, University of Miami-Miller School of Medicine, Miami, FL. November 28, 2012.

Ramos, Alberto. Vascular Cognitive Impairment. Eight Annual Brain Injury Conference. Baptist Hospital-Rehabilitation Center. JW Marriot Hotel, Miami, FL. October 14, 2012. (CME Event)

Ramos, Alberto. Neurology Grand Rounds. Sleep Health and Vascular Disease. Department of Neurology, University of Miami, Miller School of Medicine, Miami, FL. October, 2012.

Sacco, Ralph. Plenary IV: Stroke of Unknown Cause and the Heart, International Conference on Heart & Brain, Paris, France, March 1-3, 2012

Sacco, Ralph. Primary Stroke Prevention in 2012 and Beyond. David Sherman Endowed Lecture, University of Texas, San Antonio. March 30, 2012.

Sacco, Ralph. Reducing Stroke Risk in Women, 97th Annual Meeting of American Medical Women's Association: Achieving Success as Women in Medicine, Miami, Florida, April 13-15, 2012

Wright, Clinton. Modern Acute Stroke Management, Neurology Update and Stroke Intensive 2012. The Mayfair Hotel and Spa, Coconut Grove, Miami FL. January, 2012.

Wright, Clinton. Introductory Lecture Series-Vascular Dementia. Residents and Fellows of the Department of Neurology, University of Miami, Miller School of Medicine, Miami, FL. July, 2012.

Wright, Clinton. The Neurological Examination. Neuropsychology Graduate Students. Course Director: Dr. Bonnie Levin. Department of Neurology, University of Miami-Miller School of Medicine, Miami, FL. September, 2012.

## 6. Awards (other)

**Dr. Sacco** received the American Academy of Neurology, Wartenberg Lecture Award at the AAN Meeting 2012 at New Orleans, Louisiana.

**Dr. Wright** was selected by the Neurology housestaff for the Chairman's Award for Teaching Excellence.

Thomas Hughes was selected as one of 8 recipients of 2013 American Brain Foundation Minority Scholars Program for outstanding achievements as a medical student. First ever UM medical student to be chosen.

**Dr. Ahmet Bagci**, Post-doctoral research fellow of Dr. Alperin Noam was awarded the Chiari & Syringomyelia Foundation research trainee grant award. The purpose of this grant is to develop and validate an automated tool for segmentation of the volumes of the posterior cranial fossa and its contents, utilizing a tailored atlas-based approach.

Dr. Heather Katzen is a Co-Principal Investigator for an award received from the MS Society/Fast Forward Program. The goal of this study is to examine the safety, tolerability and efficacy of Caprylic Triglyceride for the treatment of executive dysfunction and memory impairment in Multiple Sclerosis.

Dr. Clinton Wright was awarded a R01 from NIH/ NHLBI. To examine elevated serum FGF23 and phosphate and the risk for stroke, subclinical small and large vessel injury, and cognitive decline.

**Dr. Kunjan Dave** was awarded his first R01 from NIH/ NINDS. To determine the mechanism by which repeated hypoglycemic episodes increase cerebral ischemic injury in diabetes mellitus.

Dr. Fatta Nahab was awarded the R01 from NIH/ NINDS. The major goals of this project are to define the brain networks responsible for tremor generation, identify imaging correlates of various tremor phenotypes and elucidate the mechanisms of treatment response.

**Dr. Antonio Barrientos** was awarded the R01 from NIH for the use of 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.

**Dr. Hung Wen "Kevin" Lin** was awarded a National Scientist Development Grant from American Heart Association.

**Dr. Juan Young** was awarded the R21 from NIH to study the use of 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.

## 7. Faculty

Faculty is divided between those receiving direct support from the Institute (Members) and those with whom the Institute is collaborating within the University of Miami (Collaborators)

| Name                         | Center Role            | Area of Expertise                  |  |  |
|------------------------------|------------------------|------------------------------------|--|--|
| 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        |  |  |
| Richard S. Isaacson, M.D.    | Education Director     | Education, neurology, cognition    |  |  |
| Heather L. Katzen, Ph.D.     | Member Neuropsychology |                                    |  |  |
| Bonnie E. Levin, Ph.D.       | Schoninger Professor   | Neuropsychology                    |  |  |
| Fatta B. Nahab, M.D.         | Member                 | Neurology (Movement), fMRI         |  |  |
| 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 |  |  |

| NT   | Canalan Dala | AuganCTT-wasting  |
|------|--------------|-------------------|
| Name | Lenter Kole  | Area of Expertise |
|      |              |                   |

| Antonio Barrientos, Ph.D.  | Collaborator | Neuroscience, genetics         |
|----------------------------|--------------|--------------------------------|
| Elizabeth Crocco, M.D.     | Collaborator | Psychiatry                     |
| Sara Czaja, Ph.D.          | Collaborator | Aging, psychology, engineering |
| Hannah Gardener, Ph.D.     | Collaborator | Epidemiology                   |
| Carlos Moraes, Ph.D.       | Collaborator | Neuroscience                   |
| Miguel Perez-Pinzon, Ph.D. | Collaborator | Neuroscience                   |
| Ami P. Raval, Ph.D.        | Collaborator | Neuroscience                   |

#### 8. Trainees

| Name                       | Center Role          | Area of Expertise         |
|----------------------------|----------------------|---------------------------|
| Ahmet Murat Bagci, Ph.D.   | Postdoctoral trainee | Bio-engineering           |
| Madiley Broz, Ph.D.        | Postdoctoral trainee | Neuropsychology           |
| Charles Cohan, B.S.        | Graduate Student     | Neuroscience              |
| Hung Wen "Kevin" Lin       | Postdoctoral trainee | Neuroscience              |
| Thomas Hughes, B.S.        | Medical Student      | Education Research        |
| Morgan Mandigo, M.S.       | Medical Student      | Miller School of Medicine |
| Teshame Monteith, M.D.     | Neurology            | Headache                  |
| Nooshin Nabizadeh, M.S.    | Graduate student     | Electrical Engineering    |
| Jacob Neumann, Ph.D.       | Postdoctoral Fellow  | Neuroscience              |
| Agustina Rosetti, M.S.     | Graduate Student     | Psychology                |
| Qian Shen, Ph.D.           | Postdoctoral trainee | Neuroscience              |
| Jessica Warsch, M.D. Ph.D. | Resident             | Epidemiology              |

# 9. Clinical/Translational Programs

# **New Programs**

Dr. Wright received the R01 entitled, "Fibroblast Growth Factor 23 and the Risk of Stroke and Cognitive Decline". This National Heart Lung and Blood Institute funded four year study will examine a group of biomarkers related to phosphorus metabolism, including vitamin D, to examine their importance as novel risk factors for changes in brain morphology and cognitive decline as well as stroke.

Drs. Levin and mentee graduate 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. Nahab began enrollment in September 2012 for his Neuroimaging of Gait Disorders study. This study is focused on understanding the links between cognitive impairment, the development of walking impairment in an aged population, and the impacts on brain structure and function seen by MRI. This is a collaborative project between Dr. Nahab's Functional Imaging of Neurodegenerative Disorders (FIND) lab, Dr. Luca who performs objective gait studies on the participants, Dr. Pattany in Radiology, and Dr. Levin assisting with cognitive testing. To date, a total of 8 participants have completed all aspects of data collection. A preliminary analysis is planned when we reach 20 subjects. The goal for this project is to use this preliminary data collection as the basis for an NIH R01 grant.

# Update on Existing Clinical Studies

As noted above, Dr. Wright completed enrollment into SPRINT with a total of 73 participants. This will provide baseline data for this multicenter federally funded clinical trial on the effect of intensive blood pressure lowering on brain volume, white matter lesions, and cognitive decline.

Under the direction of Dr. Tatjana Rundek, we continued the **Aging and Memory Brain Hemodynamic (AMBH)** study as part of our UM Memory Disorder Clinic. This is a
prospective neuroimaging study of cerebral blood flow assessments using Transcranial Doppler
(TCD), a non-invasive procedure that uses high-frequency ultrasound waves through the skull to
evaluate blood flow in the basal cerebral arteries. TCD will allow us to test the hypothesis that
age-related memory loss is in part associated with brain hemodynamic changes, either reduced
flow or increased brain hemodynamics with resulting reductions in cerebrovascular reserve.
These findings may be relevant to the diagnosis, treatment and prevention of age-related
memory loss. Since the study began in November of 2011, we have enrolled 70 participants and
39 were enrolled in 2012. Our preliminary data show evidence of lower blood flow velocities
beyond age and sex specific normative values in this memory clinic sample.

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 postmitotic 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.

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 have continued our analysis of brain MRI scans from the Northern Manhattan Study (NOMAS). Dr. Wright and trainee Nooshin Nabizadeh in collaboration with Drs. Alperin and post-doctoral fellow Ahmet Bagci have continued to quantitate regional brain volumes and white matter lesions among 800 participants. The focus of this work is age-related cognitive problems.

We have done further genome-wide association studies in the NOMAS imaging sample. We have three projects in this area that are continuing, including analyses of genes for white matter lesions, and specific polymorphisms related to cognitive dysfunction. An important ongoing study as part of the CHARGE consortium will focus on genes related to ventricular atrophy, a measure of neurodegenerative and vascular damage.

In 2012 we performed 189 neuropsychological assessments among the NOMAS cohort, in collaboration with our team at Columbia University. The cognitive assessment done by telephone annually has been collected since 2001 and continues to provide a measure of cognitive decline for longitudinal studies of the trajectory of cognitive aging.

Drs. Noam Alperin and trainee Ahmet Bagci in the Physiologic Imaging and Advanced Image Processing Laboratory developed a novel method of localizing white matter lesions to provide a basis for studying the effects of their location on cognition. Dr. Alperin's work on cerebral blood flow and cerebrospinal fluid dynamics is another area of research in our UM-MBI registry.

During 2012 Dr. Barrientos has continued studies on the role of mitochondrial dysfunction and aging using yeast models in collaboration with Yale University. He has shown that mitochondrial respiratory thresholds and adaptive free radical (ROS) signaling regulate the yeast lifespan in a complimentary manner. His lab has also shown that these two mitochondrial parameters control the development of cellular protection mechanisms and contribute to the extended yeast life span induced by caloric restriction or by mutations in the target of rapamycin (TOR) signaling pathway.

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 Alperin are working together on a project to assess declines in cognition related to the combination of stroke and neurodegeneration, and are working toward the goal of a federally funded project.

# 10. Technology Transfer

Patent applications
 No Patents have been applied for or received

 Revenue generated from technology Not applicable

#### 11. Budget update

- 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 2012 budget: \$435,142
  - Memory Disorder Clinic
     Source: Florida Department of Elder Affairs
     Principal Investigators: Elizabeth Crocco, Clinton Wright
     2012 budget: \$ 250,000
  - Systolic Pressure Intervention Trial
     Source: Wake Forest University (sub-contract)
     Principal Investigator: Clinton Wright
     2012 budget: \$65,433
  - Independent Scientist Award Source NINDS (K02 NS059729)
     Principal Investigator: Clinton Wright, MD MS 2012 budget: \$126,198
  - Stroke Incidence and Risk Factors in a Tri-ethnic Region Source: NIH, NINDS (R37 NS 029993-18) Principal Investigator: Ralph Sacco MD MS 2012 budget: \$ 1,787,011
  - Functional imaging of tremor circuits and mechanisms of treatment response
     Source: NIH, NINDS (R01 NS073683-02)
     Principal Investigator: Fatta Nahab, MD
     2012 budget: \$333,296

Genetic Determinants of Extreme Phenotypes of Subclinical Atherosclerosis

Source: NIH, NINDS (K24 NS 062737) Principal Investigator: Tatjana Rundek

2012 budget: \$ 203,429

Development and Early Clinical Evaluation of Noninvasive MRI Measurement of ICP

Measurement of ICP

Source: NIH, NINDS (R01 NS052122) Principal Investigator: Noam Alperin

2012 budget: \$ 380,000

Mechanisms of Neuroprotection Against Cardiac Arrest

Source: NIH, NINDS (R01 NS045676)

Principal Investigator: Miguel Perez-Pinzon

2012 budget: \$ 327,994

Ischemic Preconditioning: Mechanisms of Neuroprotection

Source: NIH, NINDS (R01NS034773)

Principal Investigator: Miguel Perez-Pinzon

2012 Budget: \$327,994

Cytochrome c oxidase assembly in health and disease

Source: NIH (RO1 GM071775-06)

Principal Investigator: Antoni Barrientos

2012 budget: \$255,105

• Increased cerebral ischemic injury by repeated hypoglycemic episodes

in diabetes

Source: NIH/NINDS (RO1 NS073779)

Principal Investigator: Kunjan Dave

2012 budget: \$271,098

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

Source: NIH (R21)

Principal Investigator: Juan I Young

2012 budget: \$229,500

A Randomized Double-Blind Placebo-Controlled Study of Caprylic

Triglyceride for Cognitive Impairment in Multiple Sclerosis

Source: MS Society/Fast Forward Program

Principal Investigator: Heather Katzen

2012 budget: \$167,607

Role of Fatty Acid Methyl Esters on Cerebral Blood Flow Source: American Heart Association Principal Investigator: Hungwen "Kevin" Lin 2012 budget: \$75,000

# 12. Educational programs focusing on age related memory loss

#### Scientific

The Schoninger Neuropsychology Program is actively engaged in teaching and training 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. Three students will also be joining the Schoninger Neuropsychology Program to pursue their dissertation topic. Other educational activities include lectures for medical students and residents covering neuropsychology for neurologists.

Our Memory Disorder Clinic trains students at all levels through exposure to patients and caregivers. 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. A multidisciplinary team from neurology, psychiatry, and neuropsychology provide teaching.

A multi-center education research pilot study, fully supported by our McKnight Brain Institute, addresses the question "Can we enhance Health Information Technology via the Electronic Medical Record (EMR) to improve education about age-related memory loss and other Neurologic disorders?" Dr. Isaacson worked with computer specialists to develop software that delivers patient-specific clinical and educational resources (e.g., peer-reviewed publications, practice guidelines, multimedia lectures, patient educational materials) based on real-time EMR data. Neurology and Internal Medicine residents and faculty at the Universities of Miami, Pennsylvania, Rochester, Cornell University, and Harvard University were invited to complete EMR software simulations based on four neurology patient encounters, including a case of cognitive decline and one of age-related memory loss. We tracked click rates of resources identified by the software and collected user preferences. Of the nearly 200 participants, 82% felt access software could improve education, 84% felt it could improve clinical decision making, and remarkably 96% identified ≥1 educational resource that could change their practice. A reprint of the study will be requested after publication and will be included in the 2013 annual report.

Another project during 2012 is currently in progress, entitled "Age-Related Memory Loss and Alzheimer's Disease: A Web-based Educational Intervention in Patient Waiting Rooms". This

project is entirely funded and supported by the UM\_MBI. Dr. Isaacson has recruited two 2<sup>nd</sup> year medical students to help on the project (Thomas Hughes and Kevin Fu), to replace the recently graduated medical student Marytery Fajardo (who was accepted for Pediatric Neurology training at Northwestern University). This project was submitted to the 2013 AAN Annual Meeting and was selected as a Platform Presentation in the Neurologic Education category, marking the second year in a row that a McKnight education research study was selected (top 5 of nearly 100 abstracts submitted). An IRB amendment was approved to invite subject participation via social networking sites, including Facebook, and collection of participants continues, with the next data analysis planned in February 2013. To view the web-module, visit: http://neurology.med.miami.edu/interactive/Learning\_aboutMem/player.html

Our 2012 UM-MBI Seminar Series continued to bring scientists together:

| Speaker                                     | Area of Expertise              | Title  |
|---|--------------------------------|--|
| Kunjan Dave, PhD.                           | Neuroscience                   | "A model of cerebral ischemia in aged rats"  |
| Heather Katzen, Ph.D. & Noam Alperin, Ph.D. | Neuropsychology &<br>Radiology | Update in Adult Hydrocephalus: Neuropsychological profile and post-shunt outcomes and MRI- based Morphologic and physiologic measures of response to treatment |
| Sara J. Czaja Ph.D.                         | Engineering                    | Aging and Cognition: An Update of the Research Activities at the Center on Aging   |
| David Loewenstein, Ph.D.                    | Neuropsychology                | Neuropsychology, Everyday Functioning and the Development of New Measures  |
| J. Paul Taylor, MD, PhD                     | Neurobiology                   | Mutations in prion-like domains in<br>two RNA-binding proteins cause<br>multisystem proteinopathy  |
| Fatta B. Nahab, M.D.                        | Neurology                      | Impairment of Gait and Cognition   |

#### **Public**

#### Brain Fair: Saturday March 17, 2012, The Miami Science Museum

The third annual Miami Brain Fair was a highly successful community educational event. This free event for the local community was held during Brain Awareness Week on March 17, 2012. The event had four aims: to educate the public about neuroscience, to promote brain/spinal

cord injury prevention, to provide teaching opportunities for neuroscientists at all career stages, and to develop a network within the neuroscience community for the Miami Society for Neuroscience (SFN) Chapter. The event was attended by 2,158 people, and they received education on neuroscience ranging from neuroanatomy to adaptive learning techniques. The 256 volunteers at the event ensured high quality one-on-one interactions with the attendees. Dr. Isaacson led an exhibit on learning and memory. This event was free to the public.



Drs. Wright and Crocco organized memory screenings with educational programs about agerelated memory loss and other forms of cognitive decline for local seniors and senior centers and retirement communities.

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

Drs. Wright, Nahab, and Alperin met with members of other McKnight Institutes as part of the MRI Standardization Working Group. We have met once in New Orleans and drafted an outline for two papers on structural and functional MRI in aging research that are to be submitted in 2013 as part of a series. In addition, the group is working on gathering preliminary data to facilitate imaging studies across Institutes.

Drs. Blanton, Young and Dong have been representing the University of Miami at the Epigenetics Strategic Planning meetings. The group, led by Dr. Sweatt at the University of Alabama, first met in August in Gainesville and then met this January in New Orleans. The group is drafting a proposal for submission to the McKnight board for support of epigenetic studies. A related manuscript on the role of epigenetics in cognitive aging and methods of investigation is planned.

Dr. Levin participated in the Cognitive Assessment Working Group and is working with other Institute members to define a library of neuropsychological tests that could be used to study cognitive aging across sites. They have another meeting planned in 2013.

The UM-MBI now has two focused research collaborations with the University of Arizona at Tucson site. We have continued to collaborate with Dr. Gene Alexander, studying the effects of blood pressure on brain anatomy using voxel-based morphometry to examine regional differences in brain volume. Data from this collaboration were presented at the Inter-Institutional Meeting in Miami. We have also continued the collaboration with Dr. Carol Barnes as we have developed our animal behavior core to study the effects of cerebral ischemia on cognitive decline.

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

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.

Drs. Alperin and Katzen continue their collaboration with Cornell University Medical College examining cerebrospinal fluid pressure and normal pressure hydrocephalus.

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

We will continue our work in 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. This study is currently funded with MBI support and will provide pilot data for a possible future grant submission related to cognition in a study with Dr. Wright and Crocco.

Drs. Wright, Czaja, and Alperin are working toward a study assessing technology use among stroke survivors. This is an important study because 80% of stroke survivors do not go to a rehabilitation facility and must go home and live independently. This is relevant to the McKnight Institute because age-related cognitive deficits are critical to people's ability to recover and remain independent and it is this process that is to be studied.

We will continue work on aging and cerebral ischemia using our cardiac arrest model in 18 month 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.

#### 16. Endowment Investment Results

Please see attached report.

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

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

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

We do not request any modifications to the Gift Agreement.

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

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

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?

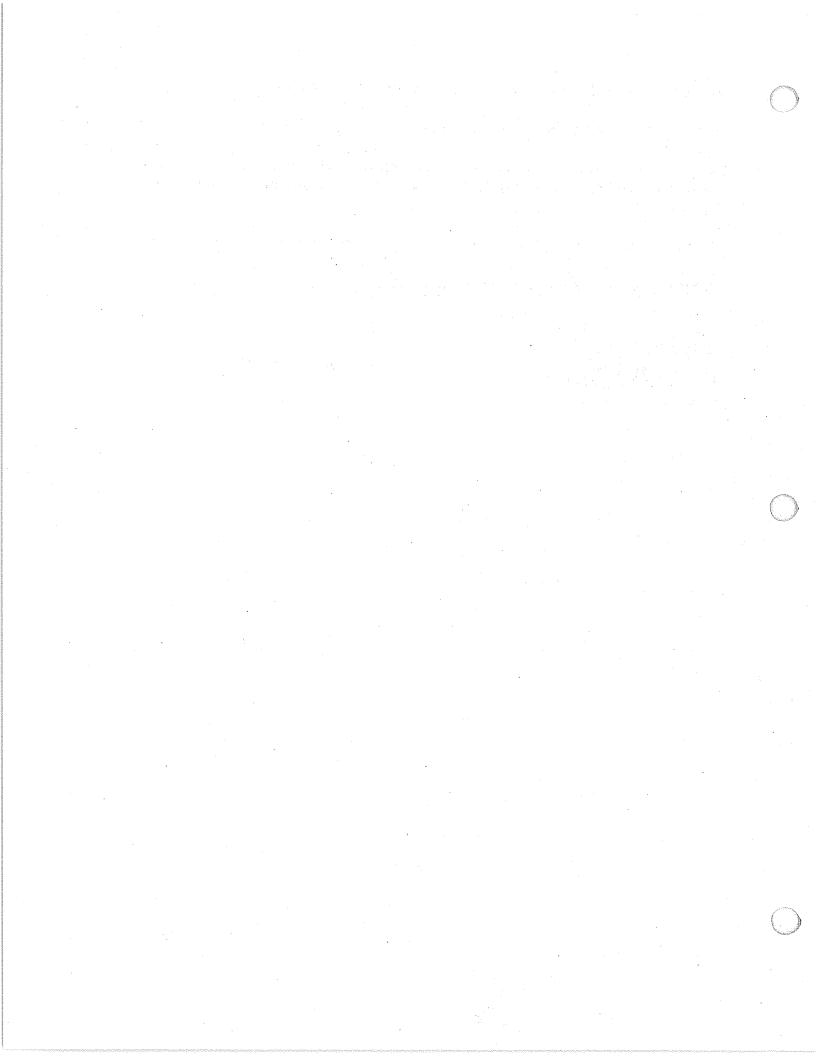
No negative events occurred to impact the ability of the Institute to carry out its Mission.

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

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

Scientific Director

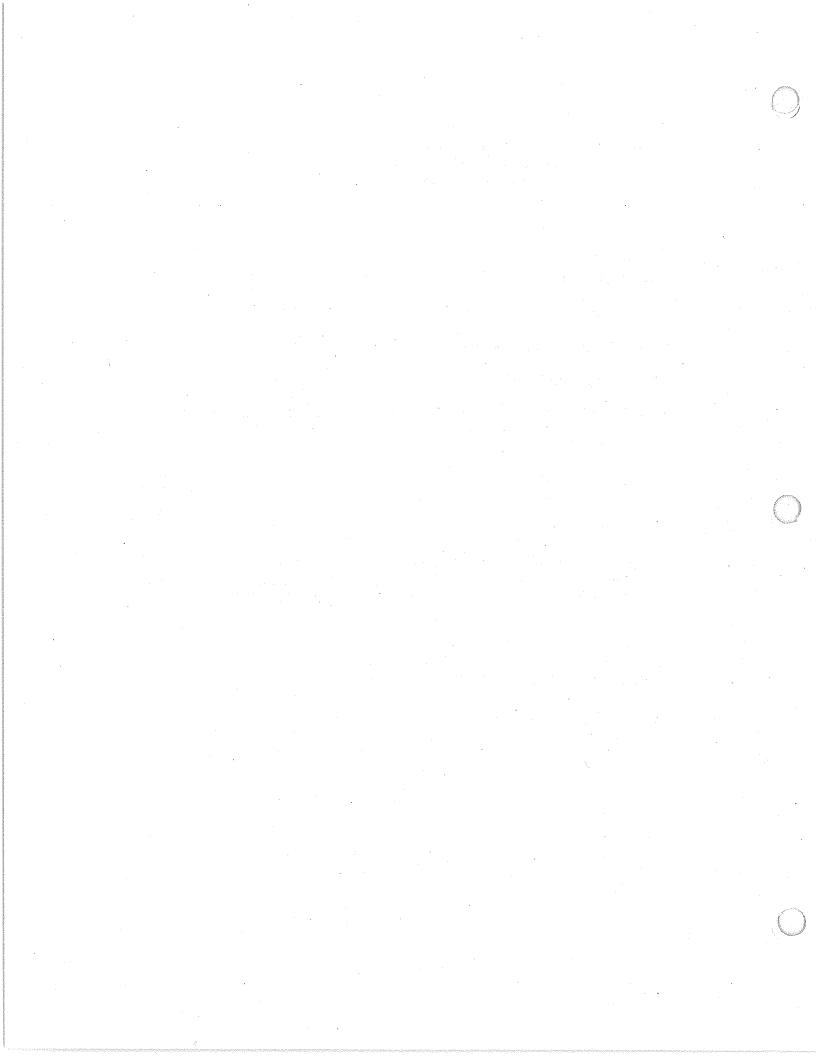
January 14, 2013



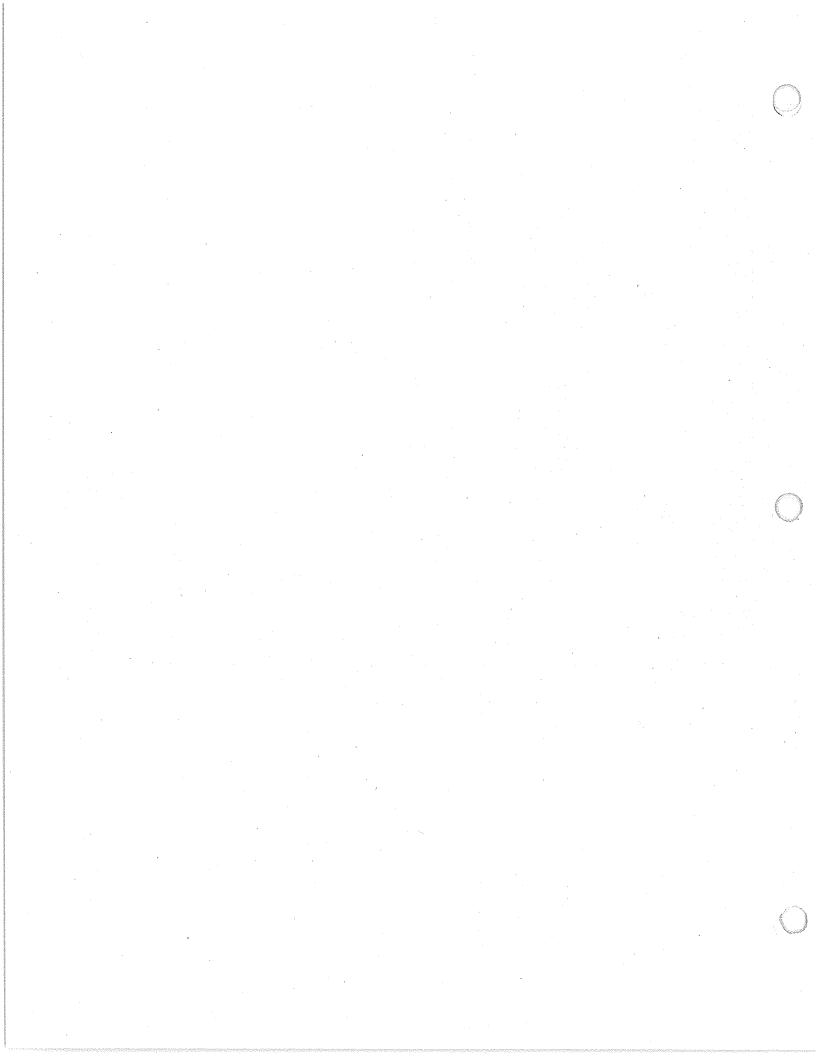
# University of Miami Evelyn F. McKnight Center for Age-Related Memory Loss Summary Analysis at Market Value June 1, 2011 - May 31, 2012

| Beginning Balance at Market, 6/1/11 | \$7,861,449 |
|-------------------------------------|-------------|
| Investment Return                   | (356,734)   |
| Distributions for Spending          | (450,301)   |
| Additional Contributions            | 354,126 *   |
| Ending Balance at Market, 5/31/12   | \$7,408,540 |

<sup>\*</sup> Transfers from other University func \$121,693 For spending Matching gifts 232,433
Total 354,126



|  | ·                           |               |   | Budget          | Actual at 11/30/12 | Projected at Yr End | Variance to Budget |
|--|-----------------------------|---------------|---|-----------------|--------------------|---------------------|--------------------|
| Revenue  | •                           |               |   | 541,907         | 378,111            | 541,907             | -                  |
| McKnight Project                                   |                             |               |   |                 |                    |                     |                    |
| Clinical and Clinical Research Program             |                             |               | ļ                                       |                 |                    |                     |                    |
|  |                             |               |   |                 |                    | -                   |                    |
| Personnel  |                             |               |   |                 |                    |                     |                    |
| Subtotal Faculty Salary/CFB                        |                             |               |   | 196,023         | 98,254             | 194,302             | 1,721              |
| Faculty  | Role in Project             | <b>Effort</b> | CFB Rate                                | -               |                    |                     |                    |
| Clinton Wright, MD                                 | Scientific Director         | 5.00%         | 22.60%                                  |                 |                    | '                   |                    |
| Ralph Sacco, MD                                    | Executive Director          | 8.00%         | 22.60%                                  |                 |                    |                     |                    |
| Fatta Nahab, MD                                    | Imaging                     | 4.00%         | 22.60%                                  |                 |                    |                     |                    |
| Bonnie Levin, MD                                   | Neuropsychology             | 30.00%        | 24.60%                                  |                 |                    |                     |                    |
| Heather Katzen                                     | Neuropsychology             | 10.00%        | 24.60%                                  |                 |                    |                     |                    |
| Susan H. Blanton                                   | Genetics                    | 5.00%         | 24.60%                                  |                 |                    |                     |                    |
| Richard Isaacson                                   | <b>Educational Director</b> | 10.00%        | 22.60%                                  |                 |                    |                     | ` <del>:</del>     |
| Noam Alperin                                       | Radiology                   | 5.00%         | 24.60%                                  |                 | 1                  |                     |                    |
| Kunjan Dave  | Neuroscience                | 25.00%        | 24.60%                                  |                 | _                  |                     |                    |
|  | •                           |               |   |                 |                    |                     |                    |
| Subtotal Staff Salary/CFB                          |                             |               |   | 292,767         | 109,379            | 252,877             | 39,890             |
| <u>Staff</u>                                       | Role in Project             | <u>Effort</u> | CFB Rate                                |                 |                    |                     |                    |
| Ahmet Bagci  | Radiology                   | 40%           | 39.90%                                  |                 |                    |                     |                    |
| Charles Harlan Cohan                               | Grad Student                | 100%          | 0.00%                                   |                 |                    |                     |                    |
| Maria C. Mendoza-Puccini                           | Clinical Coordinator        | 90%           | 39.90%                                  |                 |                    |                     | ·                  |
| Nooshin Nabizadeh Ardakani                         | Grad Student                | 100%          | 0.00%                                   |                 |                    |                     |                    |
| Amina Rivero                                       | Neuropychology              | . 30%         | 39.90%                                  |                 |                    |                     |                    |
| Madiley Broz                                       | Neuropychology              | 30%           | 39.90%                                  |                 |                    |                     | ,                  |
| Isabel Saul  | Neuroscience Res Assoc      | 30%           | 39.90%                                  |                 |                    |                     |                    |
| John Thompson .                                    | Neuroscience Post Doc       | 9%            | 12.67%                                  |                 | • .                |                     |                    |
| Maria Rosetti                                      | Neuropychology              | 50%           | 0.00%                                   |                 |                    |                     |                    |
| Total Personnel                                    |                             |               |   | 488,790         | 207,633            | 447,180             | 41,610             |
| Non Borround Francis                               |                             |               |   | ·               |                    |                     |                    |
| Non Personnel Expenses                             |                             |               |   | 9 474           | 4 070              | 3 000               | 14401              |
| Communications                                     |                             |               |   | 3,474           |                    | 3,920               |                    |
| Consulting and Other Outside Services              |                             |               |   | 6,000           | I                  | 6,000               |                    |
| Dues & Subscriptions Internal UM Services Provided |                             |               |   | 885             | 439                | 1                   | 1                  |
| 1  |                             |               |   | 15,692          | 14,836             | 1                   | , , , , , , ,      |
| Supplies   |                             |               |   | 10,700          | 1                  | 1                   |                    |
| Travel Other                                       |                             |               |   | 12,100          | 1                  | 29,472              | 1                  |
| Total Non Personnel Expenses                       |                             |               |   | 4,266<br>53,117 |                    |                     |                    |
| Total Noil Personnel Expenses                      |                             |               |   | 53,11/          | 20,499             | 34,727              | (41,610)           |
| Grand Total Expenses                               |                             |               |   | 541,907         | 228,133            | 541,907             | 0                  |
| Net Operating Income                               |                             |               |   | (0)             | 149,978            | 0                   | 0                  |
| wer oberating infome                               |                             |               | *************************************** | 10)             | 1 743,370          |                     | 1                  |



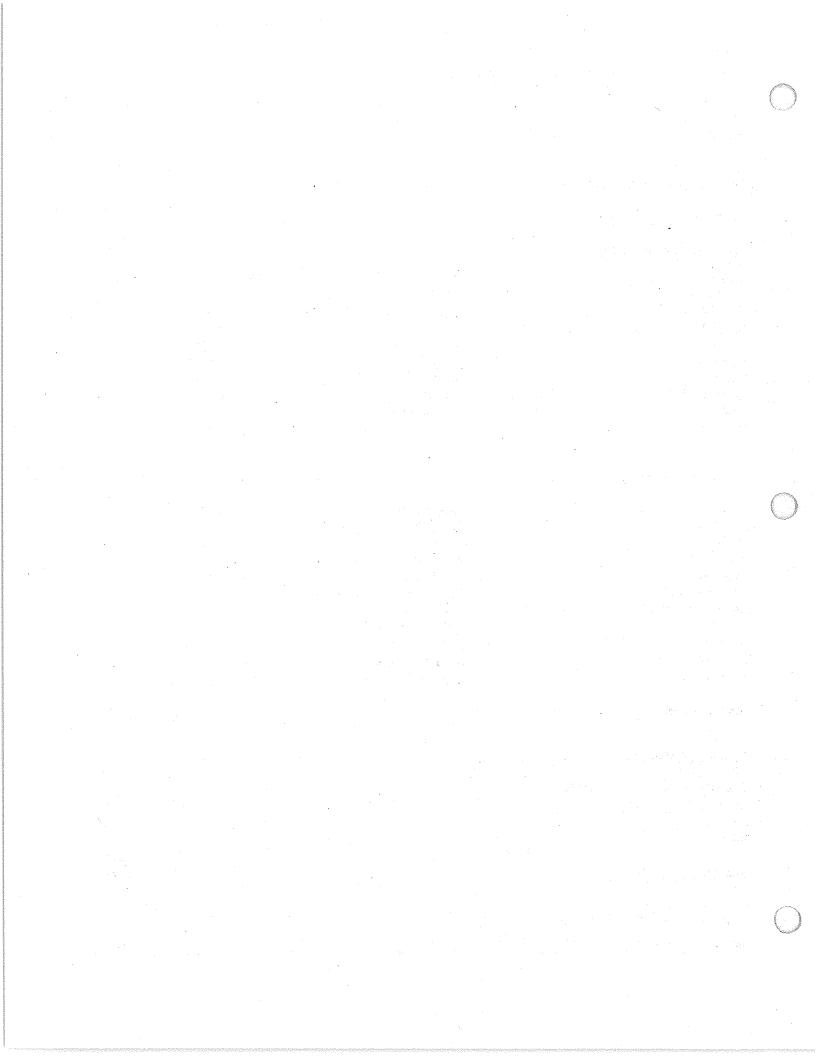
# "McKnight

Net Operating Income

Budget Estimate for the period of June 1, 2013 - May 31, 2014

| •  |                               |               |                 | Budget     |
|--|-------------------------------|---------------|-----------------|------------|
| Revenue  |                               | •             |                 | 570,000.00 |
| Malfwight Duck at  |                               |               |                 |            |
| McKnight Project <u>Clinical and Clinical Research Program</u> |                               |               |                 |            |
| Chincal and Chincal Research Flogram                           |                               |               |                 |            |
| Personnel  |                               |               |                 | •          |
| Subtotal Faculty Salary/CFB                                    | <del></del>                   | •             |                 | 100 oro es |
| Subtotal Faculty Salary/CFB                                    |                               |               |                 | 187,853.68 |
| <u>Faculty</u>   | <u>Role in Project</u>        | <u>Effort</u> | <u>CFB Rate</u> |            |
| .Clinton Wright, MD  | Scientific Director           | 8%            | 23.05%          |            |
| Ralph Sacco, MD  | Executive Director            | 5%            | 23.05%          |            |
| Fatta Nahab  | Imaging                       | 4%            | 23.05%          |            |
| Isaacson, Richard  | Educational Director          | 10%           | 23.05%          |            |
| Noam Alperin   | Radiology                     | 5%            | 25.09%          |            |
| Susan H. Blanton   | Genetics                      | 5%            | 25.09%          |            |
| Bonnie Levin, PHD  | Neuropsychology               | 30%           | 25.09%          |            |
| Heather Katzen   | Neuropsychology               | 5%            | 25.09%          |            |
| Dave Kunjan  | Basic Science                 | 5%            | 25.09%          |            |
|  | ,                             |               |                 |            |
| Subtotal Staff Salary and CFB                                  |                               |               |                 | 293,425.04 |
| <u>Staff</u>   | Role in Project               | <b>Effort</b> | CFB Rate        |            |
| Ahmet Bagci  | Radiology                     | 20%           | 40.70%          |            |
| Madiley Broz   | Neuropsychology               | 30%           | 40.70%          | •          |
| Digna Cabral   | Administrative Support        | 15%           | 40.70%          | •          |
| Charles Cohan  | Med Grad Student              | 100%          | 0.00%           |            |
| Maria Mendoza-Puccini  | Clinical Research Coordinator | 90%           | 40.70%          |            |
| Nooshin Nabizadeh  | Teaching Assistant            | 100%          | 0.00%           |            |
| Isabel Saul  | Research Support Specialist   | 30%           | 40.70%          |            |
| Maria Rosetti  |                               |               |                 |            |
| Ida Babakhanyan  | Neuropsychology               | 50%           | 0.00%           |            |
| TBA Reseach Assist   | Neuropsychology               | 100%          | 40.70%          |            |
| TDA Resedul Assist   | Research Asst/Technician      | 50%           | 40.70%          |            |
| Total Personnel  |                               |               |                 | 481,278.72 |
|  |                               |               |                 |            |
| Non Personnel Expenses   | ennouse.                      |               |                 |            |
| Communcations  |                               |               |                 | 4,038      |
| Consulting and Other Outside Services                          |                               |               |                 | 6,000      |
| Internal UM Services Provided                                  |                               |               |                 | 18,570     |
| Supplies   |                               |               |                 | 2,000      |
| Travel .   |                               |               |                 | 3,000      |
| Other  |                               |               |                 | 55,114     |
| <u>Total Non Personnel Expenses</u>                            |                               |               | •               | 88,721     |
| Grand Total Expenses   |                               |               |                 | E70 000 00 |
| Craria rotal Expenses  |                               |               |                 | 570,000.00 |

(0.00)



# Faculty

Noam Alperin, Ph.D.

Susan Blanton, Ph. D.

Kunjan R. Dave, Ph.D.

Chuanhui Dong, Ph. D.

Richard S. Isaacson, M.D.

Heather L. Katzen, Ph.D.

Bonnie E. Levin, Ph.D.

Fattah B. Nahab, M.D.

Tatjana Rundek, M.D., M.S.

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

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



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<br>Noam Alperin, PhD  | POSITION TITE             | E                    |                                |
|--|---------------------------|----------------------|--------------------------------|
| eRA COMMONS USER NAME (credential, e.g., agency login) nalperin  | Professor o               | of Radiology an      | d Biomedical Engineering       |
| EDUCATION/TRAINING (Begin with baccalaureate or other initial pro-<br>residency training if applicable.) | ofessional education,     | such as nursing, inc | lude postdoctoral training and |
| INSTITUTION AND LOCATION   | DEGREE<br>(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 |
| <i>_</i> 2009- | Professor, Department of Radiology, Uni. of Miami   |
| /% 4 II        |   |

### Other Experience and Professional Memberships

| SCHOL POWN | CHOILOC AIRA I CHOSSICHAI MICHINGI SHIPS                   |
|------------|--|
| 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

- 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)
- 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.

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.
- 10. 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
- 11. 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.
- 12. 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 Alperin (PI)

08/01/07-07/31/13

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.

Completed Research Support

R41 NS46185 Alperin (PI)

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

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         |           |              |                 |          | PO | SITION | TITLE     |     |
|--------------|-----------|--------------|-----------------|----------|----|--------|-----------|-----|
| Blanton, Sus | an Hallor | an.          |                 |          | As | sociat | e Profess | sor |
| eRA COMMONS  | USER NAM  | E (credentia | l, 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<br>(if applicable) | 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

Shblanton

## **B.** Positions and Honors

| Positions and Er | <b>nployment</b> , a satisfact of this continue of a single continue of this continue of this continue for the |
|------------------|--|
| 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, Charolottesville   |
| 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                                       |

| 1990-1995 Member, Tuberous Sclerosis Advisory Board                   | :   |
|---|-----|
| 1995-1998 Research Proposal Reviewer, MD Anderson Cancer Center       | r   |
| 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 Biotechnolog | y   |
| 2008 Reviewer, March of Dimes   |     |
| 2011 NCBDDD, Fragile X/Rare Disorders special emphasis pa             | nel |

| <b>Honors</b> |               |            |         |          |          |
|---------------|---------------|------------|---------|----------|----------|
| 1980          | Phi Kappa Phi | , Virginia | Commonw | ealth Un | iversity |

1980 Biology Award to Oustanding 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 140 peer-reviewed publications)

- 1. Recent publications of importance to the field (in chronological order) **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. PMCID: 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. PMCID: 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. PMCID: 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. PMCID: 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. PMCID: 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. PMCID: PMC3004531.
- 8. Züchner S, Dallman J, Wen R, Beecham G, Naj A, Farooq A, Kohli MA, Whitehead PL, Hulme W, Konidari I, Edwards YJK, Buxbaum JD, Cai G, Peter I, Seo D, Haines JL, **Blanton S,** Young J, Alfonso E, Vance JM, Lam BL, Pericak-Vance MA. Whole-exome sequencing links a variant in DHDDS to retinitis pigmentosa. Am J Hum Genet. 2011 Feb 11;88(2):201-6. PMCID: PMC3035708.
- 9. 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.
- 10. 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. PMCID: PMC3042493.
- 11. 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. PMCID: PMC3116444.
- 12. 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. PMCID: PMC3122911.
- 13. 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. PMCID: PMC3383876 [Available on 2013/7/1].
- 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. PMCID: PMC3199748.

15. 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. PMCID: PMC3483411 [Available on 2013/12/15].

# D. Research Support Ongoing Research Support

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

# 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

# 1R01NS065114-02 (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 Athersoclerosis"

Role: Collaborator

Program Director/Principal Investigator (Last, First, Middle): Blanton, Susan Halloran

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

# Completed Research Support (last three years)

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

04/01/99-03/31/12 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: Pl 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: Pl 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

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             |             |                    |           | <br>POSITION TITLE |            |         |  | - |
|---|------------------|-------------|--------------------|-----------|--------------------|------------|---------|--|---|
|   | Kunjan R. Dave   |             |                    |           | Research Ass       | sistant Pr | ofessor |  |   |
| • | eRA COMMONS USER | NAME (crede | ntial, e.g., agend | cy login) |                    |            |         |  |   |
|   | KRDAVE           |             | a jaja Titatya     |           |                    |            |         |  |   |

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<br>(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                  |
|   |                           |           | kan dibagan dibaga ya dib. |

#### A. Personal Statement: NA.

# B. Positions and Honors

### Professional experience:

- Research Assistant Professor (2006 ) 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 Alzheimerlike 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.
- Narayanan S. V., Dave K. R., Perez-Pinzon M. A. Ischemic preconditioning and clinical scenarios. Curr Opin Neurol. 2012 (In press)

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. 2012 (In press)

3) Dave K.R., Bhattacharya S.K., Saul I., DeFazio R.A., Dezfulian C., Lin H.W., Raval A.P., Perez-Pinzon M.A. Activation of protein kinase C delta following cerebral ischemia leads to release of cytochrome C from the mitochondria via bad pathway. PLoS One. 2011;6(7):e22057.

4) 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.

5) 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.

\* 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.

7) \* 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.

8) 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.

9) \* 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

10) \* 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.

- 11) \* 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
- 12) \* 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
- 13) \* 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
- 14) Raval, A.P., K.R. Dave, D. Mochly-Rosen, T.J. Sick, M.A. Pérez-Pinzón, ε PKC is required for the induction of tolerance by ischemic and NMDA - mediated preconditioning in the organotypic hippocampal slice. Journal of Neuroscience, 23:384-391, 2003
- 15) Dave, K.R., I. Saul, R. Busto, M.D. Ginsberg, T.J. Sick, M.A. Perez-Pinzon, Mitochondrial function following global cerebral ischemia in rat hippocampus. Journal of Cerebral Blood Flow and Metabolism, 21:1401-1410, 2001

# 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

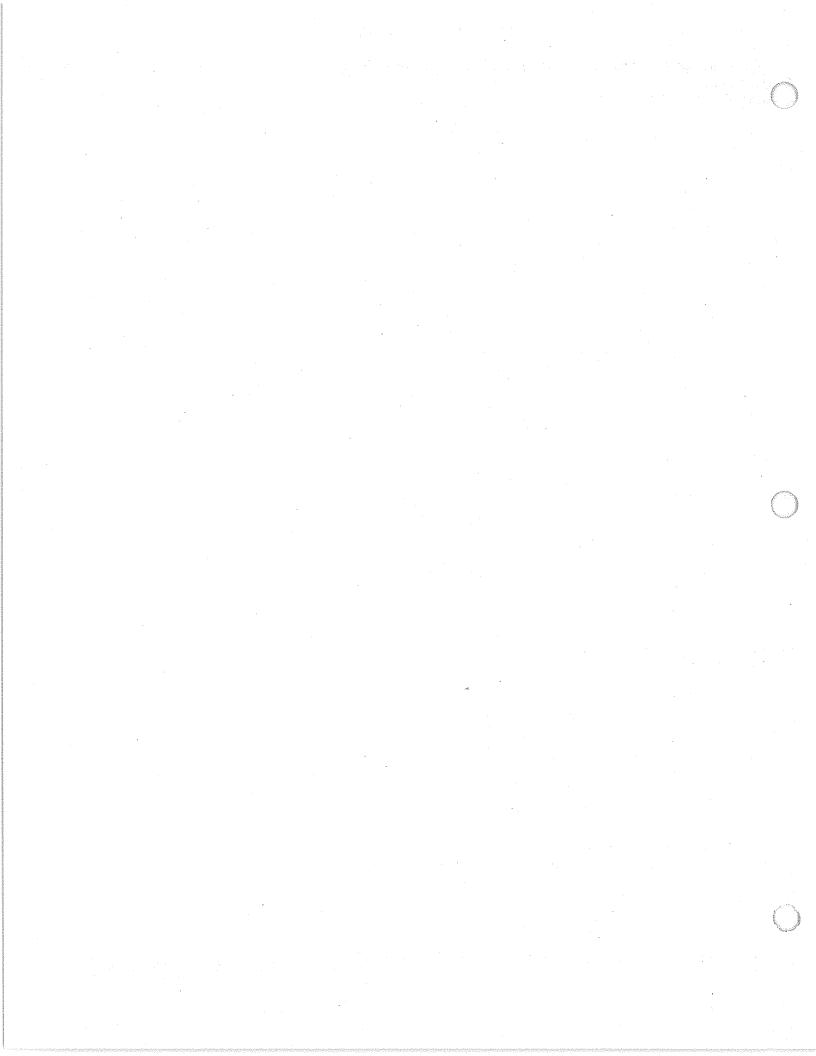
NIH/NINDS

Ischemic preconditioning: mechanisms of neuroprotection

Program Director/Principal Investigator (Last, First, Middle): Dave, Kunjan R.

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

Role: Co-investigator



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   | POSITION TITLE               |
|--|------------------------------|
| Dong, Chuanhui   |                              |
| eRA COMMONS USER NAME (credential, e.g., agency login) | Research Assistant Professor |
| CHDONG07   |                              |

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<br>(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

| <b>Positions</b> | and E | impl | oyment |
|------------------|-------|------|--------|
|                  |       |      |        |

| 1 00 00 10 10 10 00 00 | n n o was somet and give in we general the was   |
|------------------------|--|
| 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 65 peer-reviewed publications in international Journals and 25 in national journals)

- 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. PMCID: PMC2834349
- 2. **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. PMCID: PMC3004531
- 3. **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

- 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. PMCID: PMC3122911
- 5. **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
- 6. Kuo, F., Gardener, H., **Dong, C.,** Cabral, D., Della-Morte, D., Blanton, S.H., Elkind, M.S., Sacco, R.L., Rundek, T. (2012). Traditional cardiovascular risk factors explain the minority of the variability in carotid plaque. Stroke. 43(7):1755-60. PMCID: PMC3383876.
- 7. Fatta B. Nahab, F.B., Handforth, A., Brown, T., Christopher Shin, C., Quesada, A., **Dong, C.,** Haubenberger, D., Hallett, M. (2012) Octanoic acid suppresses harmaline-induced tremor in mouse model of essential tremor. Neurotherapeutics. 9(3):635-8. PMID: 22454323
- 8. **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
- 9. **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
- Katsnelson M., Mackenzie L., Frangos, S., Oddo M., Levine J.M., Pukenas B., Faerber, J., Dong, C., Kofke, W.A., LeRoux, P.D. (2012) Are initial radiographic and clinical scales associated with subsequent intracranial pressure and brain oxygen levels after sever traumatic brain injury? Neurosurgery. 70(5):1095-1105. PMID: 22076531
- 11. Romano, J.G., Arauz, A., Koch, S., **Dong, C.,** Marquez, J.M., Artigas, C., Merlos, M., Hernandez, B., Roa, L.F., Rundek, T., Sacco, R.L. (2012) Disparities in stroke type and vascular risk factors between two Hispanics populations in Miami and México city. Journal of Stroke and Cerebrovascular Diseases. 2012 Jun 29. [Epub ahead of print], PMID: 22749627
- 12. Wong ML, **Dong C,** Andreev V, Arcos-Burgos M, Licinio J., Prediction of susceptibility to major depression by a model of interactions of multiple functional genetic variants and environmental factors. (2012). Mol Psychiatry. 17(6):624-33. PMCID: PMC3359641
- 13. Della-Morte, D., **Dong, C.,** Bartelsa, S., Cabrala, D., Blanton, S.H., Saccoa, R.L., Rundek, T. (2012) Association of the sirtuin and mitochondrial uncoupling protein genes with carotid intima-media thickness. Translational Research. 160(5):389-90. PMID: 22750084
- Waldrop-Valverde, D., Dong, C., Gonzalez, P., Ownby, R.L. (2012). Medication-taking self-efficacy and medication adherence among HIV infected cocaine users. Journal of the Association of Nurses in AIDS Care Nov 1. [Epub ahead of print], PMID: 23122904
- 15. Changli Wei, C., Trachtman, H., Li, J., Dong, C., Friedman, A.L., Gassman, J.J., McMahan, J.L., Radeva, M., Heil, K.M., Trautmann, A., Anarat, A., Emre, S., Ghiggeri, G.M., Fatih Ozaltin, F., Haffner, D., Gipson, D.S., Kaskel, F., Fischer, D.C., Franz Schaefer, F., Jochen Reiser, J. (2012). Characteristics of circulating suPAR in two distinct primary FSGS Cohorts. Journal of the American Society of Nephrology 2012 Nov 8. [Epub ahead of print], PMID: 23138488

# 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.

Dong, Chuanhui Program Director/Principal Investigator (Last, First, Middle):

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: 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: Statistician

2R01NS040807

Ralph Sacco (PI)

09/09-06/17

Family study of stroke risk and carotid atherosclerosis

To investigate genes influencing carotid atherosclerosis through exome sequencing.

Role: Statistician

R37 NS 029993

Ralph Sacco (PI)

02/03-03/13

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

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

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: Statistician

Completed Research Support (within the last three years):

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

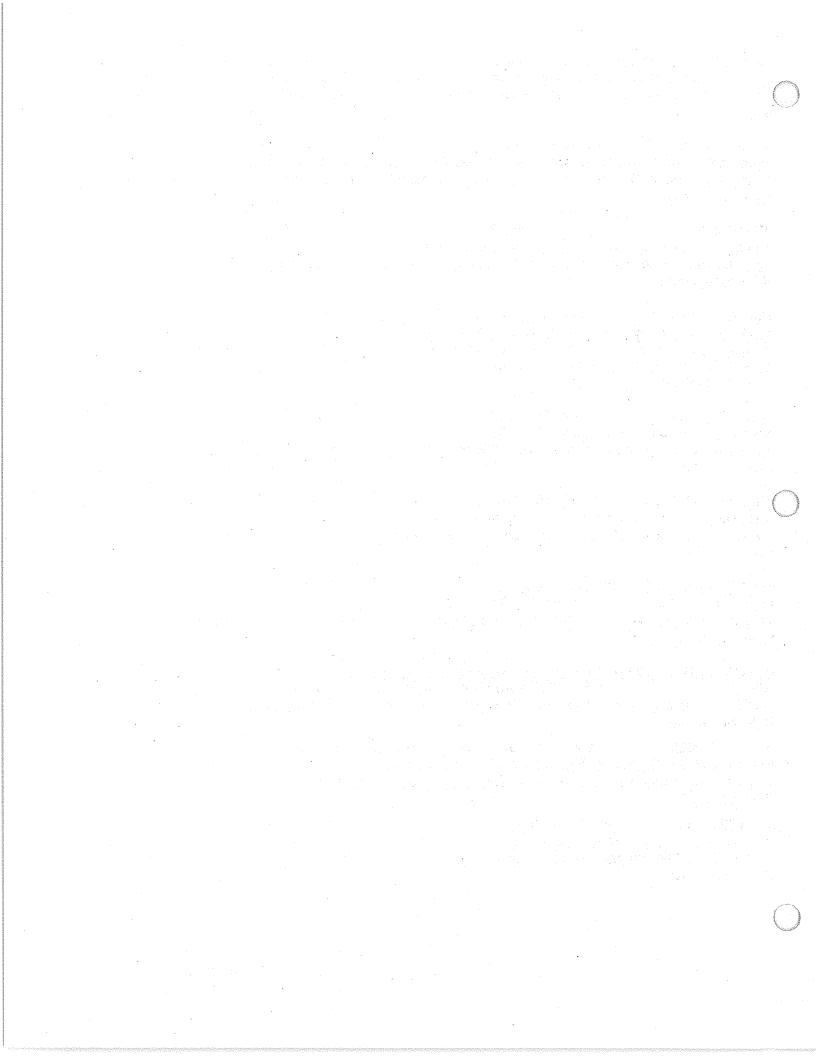
Ma-Li Wong (PI)

07/03-05/10

Pharmacogenetics of Antidepressant Drugs

To identify genetic variants associated with antidepressant response.

Role: Statistician



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| NAME   | POSITION TITLE                                  |
|--|---|
| Isaacson, Richard Scott                                | Associate Professor of Clinical Neurology       |
| eRA COMMONS USER NAME (credential, e.g., agency login) | 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<br>(if applicable) | MM/YY     | FIELD OF STUDY    |  |
|---|---------------------------|-----------|-------------------|--|
| University of Missouri–Kansas City<br>Kansas City, MO                       | B.A.                      | 1995-1997 | Liberal Arts      |  |
| University of Missouri–Kansas City School of<br>Medicine<br>Kansas City, MO | M.D.                      | 1997-2001 | Medicine          |  |
| Mount Sinai Medical Center, University of Miami                             | Internship                | 2001-2002 | Internal Medicine |  |
| Beth Israel Deaconess Med Ctr, Harvard Med<br>School                        | Residency                 | 2002-2005 | Neurology         |  |
|   |                           |           |                   |  |

## A. Personal statement: N/A

# **B.** Positions and Honors

# Positions and Employment

| 2004-2005  | Chief Resident (Neurology), Harvard Medical School, Beth Israel Deaconess Medical Center        |
|------------|---|
| 2002-2005  | Clinical Fellow in Neurology, Harvard Medical School  |
| 2005-2007  | Associate Medical Director, Wien Ctr for Alzheimer's Disease and Memory Disorders, MSMC         |
| 2005-2007  | Director, Research Unit in Medical Education, Mount Sinai Medical Center                        |
| 2005-2007  | Attending Neurologist, Mount Sinai Medical Center   |
| 2005- pres | American Academy of Neurology, Undergraduate Education Subcommittee                             |
| 2005- pres | Assistant Professor of Medicine, University of Miami Miller School of Medicine                  |
| 2007- pres | Assistant Professor of Neurology, University of Miami Miller School of Medicine                 |
| 2007- pres | Director, Neurology Residency Training Program, UM Miller School of Medicine                    |
| 2007- pres | Associate Director, Neurology Medical Student Clerkship, U. Miami Miller School of Medicine     |
| 2008- pres | Co-Director, Neuromodule, Neuroscience and Behavior 1 <sup>st</sup> year medical student course |
| 2008- pres | Consortium of Neurology Clerkship Directors Task Force, ED-2/Core Curriculum for Students       |
| 2008- pres | Vice Chair of Education, Department of Neurology, U. Miami Miller School of Medicine            |
| 2010- pres | Associate Professor of Clinical Neurology, U. Miami Miller School of Medicine                   |
| 1997, 1999 | Laboratory of Central Nervous System Studies, National Institute of Neurological Disorders      |
| (summer)   | and Stroke, National Institutes of Health, Bethesda, MD; Mentor: Dr. Clarence J. Gibbs          |
|            |   |

# Other Experience and Professional Memberships

| 2001- pres | American Academy of Neurology   |
|------------|---|
| 2004       | Harvard Academy Medical Education Symposium, Workshops in Medical Education               |
| 2004       | Laboratory teaching assistant, Harvard Medical School, Human Nervous System and Behavior, |
|            | Second year medical student course  |
| 2004       | Study Group Instructor, Tufts University Medical School, Neuroanatomy and Neurophysiology |
| 2005- 2007 | Graduate Medical Education/Academic Affairs Committee, Mount Sinai Medical Center         |
| 2006- 2007 | Vice-Chair, Continuing Medical Education Committee, Mount Sinai Medical Center            |

| 2007- pres | Association of University Professors of Neurology                                    |
|------------|--|
| 2008- pres | Graduate Medical Education Committee (Voting member), UM/Jackson Memorial Hospital   |
| 2008- pres | Associate Member, Educational Development Office, U. Miami Miller School of Medicine |
| 2008- pres | Board of Directors, Florida Society of Neurology                                     |
|            |  |

# Honors

| 2003 | Congressional Representative for the American Academy of Neurology, Neurology on the Hill    |
|------|--|
| 2005 | Teacher of the Year/Attending of the Year, Internal Medicine Residency Training Program,     |
|      | Mount Sinai Medical Center   |
| 2006 | Invited Course Director/Speaker, ACGME Annual Educational Conference, March 2007,            |
|      | Orlando, FL; Topic: "Practice-Pattern-based Curriculum Development"                          |
| 2006 | Alumni of Distinction Award, Commack High School, Commack, NY                                |
| 2008 | Invited Speaker, American Academy of Neurology 2008 Annual Meeting                           |
|      | Topic: "Measuring Educational Outcomes in Neurology"; Clerkship/Program Directors Conf       |
| 2008 | Invited Speaker, Association of University Professors of Neurology - Clerkship Dir Boot Camp |
|      | Topic: "Education Research Methods in Dementia"  |
| 2008 | American Academy of Neurology Leadership Development Program                                 |
| 2008 | Congressional Representative for the American Academy of Neurology, Neurology on the Hill    |
| 2008 | Chairman's Award for Teaching Excellence, Dept of Neurology, UM Miller School of Medicine    |
| 2009 | Scientific Highlights Session (Top 5% of program)/Platform presentation, American Academy of |
|      | Neurology Annual Meeting, AAN Education Research Grant                                       |
| 2009 | American Academy of Neurology, A.B. Baker Teacher Recognition Award                          |
| 2009 | Visiting Professor of Neurologic Education, University of Rochester                          |
|      | Topic: "Measuring Educational Outcomes in Neurology"   |
| 2010 | Faculty Mentor of the Year   |
|      | University of Miami Miller School of Medicine, Academic Societies                            |
| 2011 | Moderator, Education Research Highlights Session   |
|      | American Academy of Neurology Annual Meeting   |
|      |  |

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

- 1. Seifan A, Mandigo M, Price RS. Galetta S, Jozefowicz RF, Jaffer A, Symes S, Safdieh JE, <u>Isaacson RS</u>. Can My Electronic Health Record Teach Me Something? A Multi-Institutional Pilot Study. *Neurology*, 2013 [Accepted, In press]
- 2. Ochner CN, Barrios D, Lee C, Greer CE, <u>Isaacson RS</u>. Evidence on Diet Modification for Alzheimer's Disease and Mild Cognitive Impairment. J Nutrition Health & Aging. Vol 16:9; 9 Nov 2012.
- 3. Padilla CR, <u>Isaacson RS.</u> Genetics of Dementia. In *Continuum*: Neurogenetics, Publication Date: April 2011. Ed. Jeffrey Vance, MD, PhD
- 4. <u>Isaacson RS</u>, Ochner C, Safdieh J. Evaluating the Effectiveness of Continuum as a Teaching Tool for Medical Students: A Randomized, Multi-Center Trial. *Neurology*. 2011 Jan; 76(2):125-30.
- 5. Wolk DA, Dickerson BC; Alzheimer's Disease Neuroimaging Initiative (Isaacson R). Apolipoprotein E (APOE) genotype has dissociable effects on memory and attentional-executive network function in Alzheimer's disease. *Proc Natl Acad Sci* U S A. 2010 Jun 1;107(22):10256-61.
- 6. Lynne J, Ali I, Newman-Toker D, <u>Isaacson RS</u>. ACE Journal Watch from ACE (Alliance For Clinical Education): Review of Medical Education Articles in Neurology 2007-2008. Teach Learn Med. 2009 Oct;21(4):351-4.
- 7. Holland D, Brewer JB, Hagler DJ, Fenema-Notestine C, Dale AM; Alzheimer's Disease Neuroimaging Initiative (<u>Isaacson R</u>). Subregional neuroanatomical change as a biomarker for Alzheimer's disease. *Proc Natl Acad Sci* U S A. 2009 Dec 8;106(49):20954-20959. [Epub ahead of print]
- 8. Jack CR Jr, Lowe VJ, Weigand SD, Wiste HJ, Senjem ML, Knopman DS, Shiung MM, Gunter JL, Boeve BF, Kemp BJ, Weiner M, Petersen RC; Alzheimer's Disease Neuroimaging Initiative (Isaacson R). Serial

PIB and MRI in normal, mild cognitive impairment and Alzheimer's disease: implications for sequence of pathological events in Alzheimer's disease. *Brain*. 2009 May;132(Pt 5):1355-65.

- 9. Mormino EC, Kluth JT, Madison CM, Rabinovici GD, Baker SL, Miller BL, Koeppe RA, Mathis CA, Weiner MW, Jagust WJ; Alzheimer's Disease Neuroimaging Initiative (<u>Isaacson R</u>). Episodic memory loss is related to hippocampal-mediated beta-amyloid deposition in elderly subjects. *Brain*. 2009 May;132(Pt 5):1310-23.
- 10. <u>Isaacson RS</u>, Utley B, Cheng N, Portnoy K. Advice to Medical Students: Neurology. American Academy of Neurology website, August 2008. Published in print and on-line at

http://www.aan.com/go/education/students/medical/advice, refereed by the Undergraduate Education Subcommittee.

- 11. Chediak A, Esparis B, <u>Isaacson R</u>, De la Cruz L, Ramirez J, Rodriquez JF, Abreu A. How many polysomnograms must sleep fellows score before becoming proficient at scoring sleep? *J Clin Sleep Med*, 2006; 2(4):427-430.
- 12. <u>Isaacson RS</u>. Practice-Pattern Based Curriculum Development. *ACGME Bulletin*, pg. 15-19. April 2006. Published in print and on-line at https://www.acgme.org/acWebsite/bulletin/bulletin/04\_06.pdf.
- 13. Loewenstein DA, Acevedo A, Agron A, <u>Issacson R</u> (sic), Strauman S, Crocco E, Duara R. Cognitive Profiles in Alzheimer's Disease and in Mild Cognitive Impairment of Different Etiologies. *Dement Geriatr Cogn Disord*, 2006; 21:309-315.
- 14. Loewenstein DA, Acevedo A, Ownby R, Agron J, Barker WW, <u>Isaacson R</u>, Strauman S, Duara R. Using Different Memory Cutoffs to Assess Mild Cognitive Impairment. *Am J Geriatr Psychiatry* 2006; 14(11):911-919. 15. Duara R, Loewenstein DA, Barker WW, <u>Isaacson RS</u>, Greig-Custo, M. A Clinical Perspective of Mild Cognitive Impairment: What the Radiologist Should Know. *Neuroimaging Clin N Am*, 2005 Nov; 15(4):779-788.

# B. Research Support

# **Ongoing Research Support:**

Optimizing healthcare delivery via an integrated electronic medical record-outcomes assessment and database tool Principal Investigator: Richard S. Isaacson, MD; Mentor: Ralph L. Sacco, MD, MS, FAAN, FAHA Miami McKnight Center for Cognitive Aging, 08/01/07-06/30/2012

National Institutes of Health - Clinical Research LRP, 07/01/08-06/30/11

Role: Principal Investigator

Network for Excellence in Neuroscience Clinical Trials (NEXT)

Sponsor of Study: National Institutes of Health (NIH)

Status: Funded, July 2011

Institution: University of Miami - Miller School of Medicine

Role: Co-Investigator (Pls: Benatar, Sacco)

# **Completed Research Support:**

Evaluating the Effectiveness of Continuum as a Teaching Tool for Medical Students

Principal Investigator: Richard S. Isaacson, MD

American Academy of Neurology, 01/01/08-06/30/09

Role: Principal Investigator

Cyanobacterial toxin (BMAA) in brain and hair tissue of Alzheimer's disease patients

Principal Investigator: Richard S. Isaacson, MD

Alzheimer's Association, 01/1/09-05/31/10

Role: Principal Investigator

Cognitive-Cardiovascular Screening and Educational Intervention Program for Hispanics and Non-Hispanics Principal Investigators: Richard S. Isaacson, MD (Education), Ranjan Duara, MD (Clinical)

Principal Investigator/Program Director (Last, First, Middle): Isaacson Richard S

Mount Sinai Medical Center Foundation, 07/01/06-6/30/07

Role: Co-Principal Investigator

Alzheimer's Disease Neuroimaging Initiative (ADNI) Principal Investigator (MSMC Site): Ranjan Duara, MD National Institutes of Health, 01/01/06-06/30/07

Role: Co-Investigator/Study Physician (MSMC site)

A Randomized Double-Blind Placebo-Controlled Trial of the Effects of Docosahexaenoic Acid (DHA) in Slowing the Progression of Alzheimer's Disease

Principal Investigator (MSMC Site): Ranjan Duara, MD

National Institute on Aging, Alzheimer's Disease Cooperative Study (ADCS), 01/01/06-06/30/07

Role: Co-Investigator/Study Physician (MSMC site)

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               | es and a second |               |            | <br>POSITION | TITLE    |           |    |  |  |
|--------------------|-----------------|---------------|------------|--------------|----------|-----------|----|--|--|
| Katzen, Heather    |                 |               |            | Research     | Assistan | t Profess | or |  |  |
| eRACOMMONS USER NA | ME (credential  | l, e.g., ager | ncy login) |              |          |           |    |  |  |
| HLKATZEN           |                 |               |            |              | i        |           |    |  |  |

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<br>(if applicable) | MM/YY        | FIELD OF STUDY                |
|--|---------------------------|--------------|-------------------------------|
| Emory University, Atlanta, GA<br>University of Miami, Coral Gables, FL | BS<br>MS                  | 1993<br>1996 | Psychology<br>Neuropsychology |
| University of Miami, Coral Gables, FL                                  | PhD                       | 2000         | Neuropsychology               |

# A. Personal Statement: N/A

# B. Positions and Honors

# Research and Professional Experience

| Positions an | d Employment  |
|--------------|---|
| 1993-1994    | Teaching Assistant, Department of Psychology, University of Miami, Coral Gables, FL           |
| 1993-1997    | Research Assistant, Department of Neurology, Division of Neuropsychology,                     |
|              | University of Miami School of Medicine, Miami, FL   |
| 1996         | Course Instructor, Abnormal Psychology, University of Miami, Coral Gables, FL.                |
| 1996-1997    | Supervisor of Undergraduate Independent Research, Department of Psychology, University of     |
|              | Miami, Coral Gables, FL   |
| 1997-1998    | Neuropsychology Intern, Long Island Jewish Medical Center/Hillside Hospital, Glen Oaks, NY    |
| 1998-2000    | Predoctoral Fellow in Neuropsychology, Department of Neurology, University of Miami School of |
|              | Medicine, Miami, FL   |
| 2000-2002    | Postdoctoral Fellow, Neuropsychology in Neurology, Weill Cornell Medical College-New York     |
|              | Presbyterian Hospital, New York, NY   |
| 2002-2003    | Instructor of Neuropsychology in Neurology, Weill Cornell Medical College                     |
| 2002-2003    | Assistant Attending Neuropsychologist, New York Presbyterian Hospital                         |
| 2003-2006    | Neuroscience Scientific Liaison, Medical Affairs, Ortho-McNeil Janssen, Johnson & Johnson     |
| 2006-        | Assistant Research Professor, Department of Neurology, University of Miami Miller School of   |
|              | Medicine  |
| 2006-        | Adjunct Research Assistant Professor, Neuropsychology in Neurology, Department of Neurology   |
|              | and Neuroscience, Weill Medical College of Cornell University                                 |
|              | 이 사용하는 사람이 일반이 살려서 사용하는 살려고 살아가 살라지 않는데 살았다.  |

| <b>Honors</b> |   |
|---------------|---|
| 1990-1993     | Dean's List, Emory University   |
| 1993-1994     | Graduate School Scholarship and Teaching Assistantship: Department of Psychology        |
| 1994-1996     | Graduate School Scholarship and Research Assistantship: Department of Neurology and the |
|               | National Parkinson Foundation   |
| 1996-1997     | Graduate School Scholarship and Research Assistantship: Department of Neurology and the |
|               | Dade County Juvenile Court System   |
| 1996-1997     | Letters of Commendation, University of Miami, Department of Psychology                  |

Principal Investigator/Program Director (Last, First, Middle): Katzen, Heather

#### **Licensure and Professional Societies**

2001- Licensed Psychologist, State of New York, October 2001; Registration #014973

2006- Licensed Psychologist, State of Florida, June 2006; License #7371

1994- Member, American Psychological Association: Division 40

1998- Member, International Neuropsychological Society

#### **B.** Selected Peer-reviewed Publications

- 1. **Katzen, H.**, Levin, B. &Llabre, M. (1998). Age of disease onset influences cognition in Parkinson's disease. Journal of the International Neuropsychological Society, 4, 285-290. (PMID: 9623003)
- Levin, B.E., Katzen, H.L., Klein, B.K. &Llabre, M.M. (2000). Cognitive decline affects subject attrition in longitudinal research. Journal of Clinical and Experimental Neuropsychology, 22(5): 580-586. (PMID: 11094393)
- 3. Ravdin&Katzen. (2003) Verbal Fluency Performance in Normal Aging: Effect of Mild Depression and Age Stratified Norms, The Clinical Neuropsychologist, 17 (2); 195-202.
- 4. Grossman, A. Levin, B., **Katzen**, **H**., and Lechner (2004). PTSD Symptoms and Onset of Neurologic Disease in Elderly Trauma Survivors, Journal of Clinical and Experimental Neuropsychology, 26 (5); 698-705. (PMID: 15370391)
- 5. **Katzen, H.L.**, Levin, B.E., Weiner, W. (2006). Side and Type of Motor Symptom Influence Cognition in Parkinson's Disease. Movement Disorders, 21 (11); 1947-1953. (PMID: 16991155)
- LaRusse, S., Katzen, H., Brown, T. Barber, M., Whitehouse, P., Green, R., Ravdin, L., Roberts, S. Cupples, L.A. and Relkin, N. (2006). Recall of disclosed apolipoprotein E (APOE) genotype and lifetime risk estimates for Alzheimer's disease: The REVEAL Study. Med. Dec; 8(12); 746-751. (PMID: 17172937)
- 7. Ravdin L.D., &Katzen, H. (2007). Taking Stock of Cognitive Reserve: Factors affecting the brain's vulnerability to disease and trauma. Journal of Clinical and Experimental Neuropychology, 1-2.
- 8. Papapetropoulos, S., **Katzen, H.,**Schrag, A., Singer, C., Scanlon, B. K., Nation, D., Guevara, A., & Levin, B. (2008). A questionnaire-based (UM-PDHQ) study of hallucinations in Parkinson's disease. BMC Neurology, 8(21). (PMID: 18570642)
- 9. Ravdin L.D. & Katzen, H., Relkin, N.R. (2008). Features of Gait Most responsive to Tap Test in Normal Pressure Hydrocephalus. Clinical Neurology and Neurosurgery, 110(5):455-61. (PMID: 18359152)
- Nation, D. A., Katzen, H. L., Scanlon, B. K., Papapetropoulos, S., & Levin, B. E. (2009). Defining Subthreshold Depression in Parkinson's Disease. International Journal of Geriatric Psychiatry, Feb 11.; 24(9): 937-943. [Epub ahead of print]. (PMID: 19212967)
- 11. Tsakanikas, D. **Katzen, H.L.,**Ravdin, L.D., &Relkin, N.R. (2009). Upper extremity motor measures of Tap Test response in Normal Pressure Hydrocephalus. Clinical Neurology and Neurosurgery, Nov: 111 (9): 752-7. (PMID: 19720451)
- 12. 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. (PMID: 20976095)

- 13. **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. (PMID: 20689283)
- 14. **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. (PMID: 21135747)
- 15. Levin, B.E., **Katzen,H**., Maudsley, A., Post, J., Myerson, C., Govin, V., Nahab, F., Scanlon, B., & Mittel, A. (in press). Whole-brain Proton MR Spectroscopic Imaging in Parkinson's Disease. Journal of Neuroimaging. (PMID: 23228009)

# C. Research Support

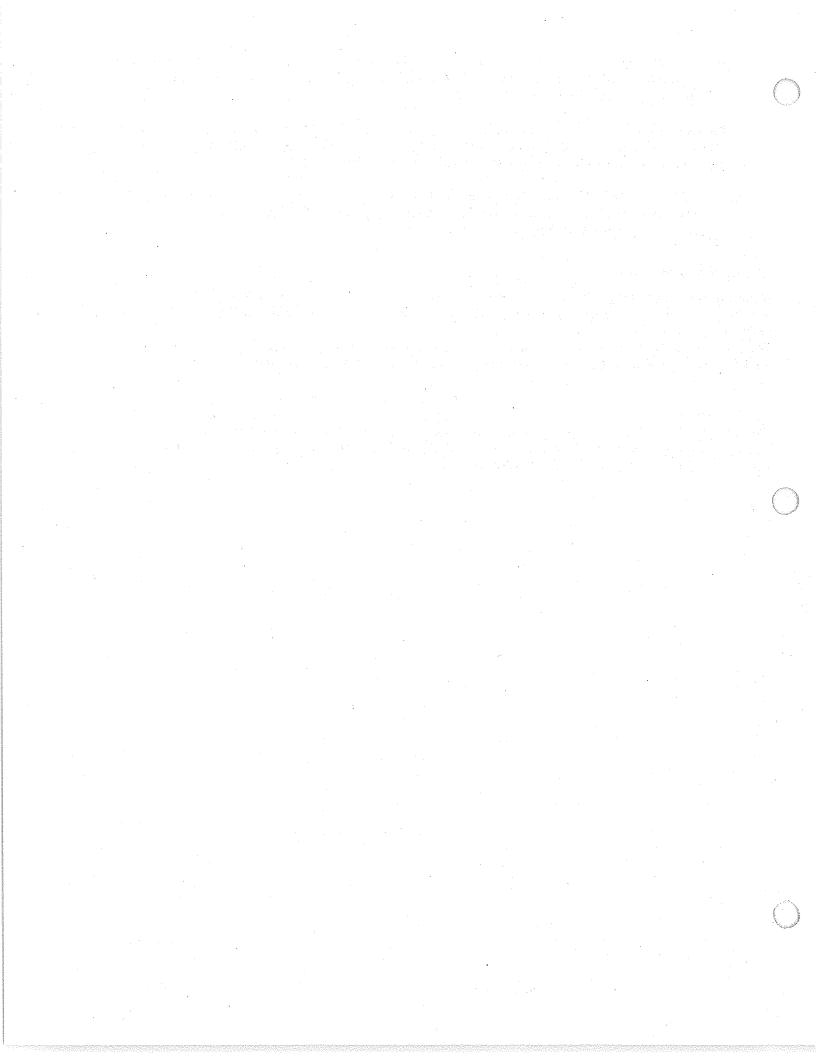
MS Society/Fast Forward Program Katzen (Co-PI) 10/1/12-9/30/15

A Randomized Double-Blind Placebo-Controlled Study of Caprylic Triglyceride for Cognitive Impairment in Multiple Sclerosis

The goal of this study is to examine the safety, tolerability and efficacy of Caprylic Triglyceride for the treatment of executive dysfunction and memory impairment in Multiple Sclerosis.

K23 NS045051 Katzen (PI) 5/10/06-4/30/12

Recovery of Cognitive Functions Following Shunt Placement in Normal Pressure Hydrocephalus
The major goal of this project is to examine cognitive outcome in NPH following placement of programmable shunts. A second goal is to determine whether shunting parameters contribute to cognitive outcome in NPH.



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<br>Bonnie E. Levin, Ph.D.     | POSITION TITLE Associate Professor of Neurology and Psychology |
|------------------------------------|--|
| eRA COMMONS USER NAME bonnie_levin |  |

| EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.) |                        |         |                |  |  |  |
|--|------------------------|---------|----------------|--|--|--|
| INSTITUTION AND LOCATION   | DEGREE (if applicable) | YEAR(s) | FIELD OF STUDY |  |  |  |
| Georgetown University  | BS                     | 1974    | Psychology     |  |  |  |
| Temple University  | Ph.D.                  | 1983    | Psychology     |  |  |  |

### A. PROFESSIONAL EXPERIENCE

| 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-       | Associate Professor, Department of Neurology, University of Miami                   |
|             | 1979-1980<br>1979-1980<br>1980<br>1981-1982<br>1981<br>1986-1992                    |

# 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, NABIS: H II Date Safety of Monitoring Board

Pediatrics; UM Sleep Center, Department of Neurology.

Professional Advisory Board: Epilepsy Foundation of South Florida

Editorial Boards: Neuropsychology, Journal of the International Neuropsychological Society (JINS), Aging, Neuropsychology and Cognition, Journal of Clinical & Experimental, Neuropsychology (JCEN)

## B. SELECTED PUBLICATIONS:

<u>Levin, B.E.</u>, Weiner, W.J.: Psychosocial Aspects of Parkinson's disease. In:W.C. Koller, (Ed), Handbook of Parkinson's Disease. In:M. Decker, Inc., New York, 1987; 465-474.

Levin, B.E., Llabre, M.M., Weiner, W.J.: Parkinson's disease and depression: Psychometric properties of the Beck Depression Inventory. Journal of Neurology, Neurosurgery, and Psychiatry, 1988;51:1401-4.

<u>Levin, B.E.</u>, Llabre, M.M., Weiner, W.J.:Cognitive impairments associated with early Parkinson's disease. Neurology, 1989,39:557-561.

Kramer, J.H., <u>Levin, B.E.</u>, Brandt, J., Delis, D.C.:Differential verbal learning impairments in Alzheimer's, Huntington's and Parkinson'sdisease. Neuropsychology, 1989;3:111-120.

<u>Levin, B.E.</u>,:Organizational deficits in dyslexia: Possible frontal lobe dysfunction. Developmental Neuropsychology, 1990;6(2):95-110.

Levin, B.E., Llabre, M.M., Ansley, J., Brown, M.C., Weiner, W.J., Sanchez-Ramos, J.: Visuospatial Impairments in Parkinson's disease. In: M. Streifler, A. Korczyn (Eds). Parkinson's Disease: Anatomy, Pathology, and Therapy. Advances in Neurology, 1990; 53:624-629.

<u>Levin, B.E.</u>, :Spatial cognition in Parkinson's disease. Alzheimer Disease and Associated Disorders, 1990:4:161-170.

<u>Levin, B.E.,</u> Llabre, M.M., Weiner, W.J., Brown, M.C.:Visuospatial decline in Parkinson's disease. Neurology, 1991:41:365-369.

Levin, B.E., Feldman, E., Duchowny, M.S., Brown, M.C.: Neuropsychological assessment of children with epilepsy. International Journal of Pediatrics, 1991;6:214-219.

<u>Levin, B.E.</u>., Llabre, M.M., Reisman, S., Weiner, W.J., Brown, M.C.:A retrospective study of the effects of anticholinergic medication on memory performance in Parkinson's disease. Journal of Neuropsychiatry and Clinical Neurosciences, 1991;3:412-416.

<u>Levin, B.E.</u>; Duchowny, M.S. Childhood obsessive compulsive disorder and cingulate epilepsy. Biological Psychiatry, 1991;30:1049-1055.

Brown, M.C., <u>Levin, B.E.</u>, Ramsay, R.E., Katz, D.A., Duchowny, M.S.:Characteristics of patients with non-epilpetic seizures. Journal of Epilepsy, 1991;4:225-229.

<u>Levin, B.E.,</u> Tomer, R., Rey, G.J.: Clinical Correlates of Cognitive Impairments in Parkinson's disease. In: S.J. Huber and J.L. Cummings (Eds), Parkinson's Disease: Behavioral and Neuropsychological Aspects: New York: Oxford University Press. 1992; 97-106.

Post, J.M., <u>Levin</u>, B.E., Berger, J.R., Duncan, R., Quencer, R., Calar, G.:Prospective revaluation by cranial MR of both asymptomatic and neurologically symptomatic HIV + subjects. American Journal of Neuroradiology, 1992, 13:359-370.

<u>Levin, B.E., Tomer, R. Rey, G.L.: Clinical Correlates of Cognitive Impairment in Parkinson's Disease:</u> Behavioral and Neuropsychological Aspects. New York: Oxford University Press. 1992;97-106.

Levin, B.E., Tomer,R.: Cognitive Function in Parkinson's disease. In: J. Cedarbaum and S. Gancher (Eds), Neurologic Clinics of North America: Issue on Parkinson's Disease. 1992; 10:471-485.

<u>Levin, B.E.</u>, Berger, J.R., Didona, T., Duncan, R.:Cognition in asymptomatic HIV infection. Neuropsychology, 1992;6:303-313.

Tomer, R., <u>Levin, B.E.</u>, Weiner, W.J.:Obsessive compulsive symptoms and motor asymmetries in Parkinson's disease. Neuropsychiatry, Neuropsychology and Behavioral Neurology, 1993;6:26-30.

Feldman, E., Levin, B.E., Lubs, H.L., Rabin, M., Lubs, M.L., Jallad, B., Kusch, A.: Adult dyslexia: A retrospective developmental and psychosocial profile. Journal of Neuropsychiatry and Clinical Neurosciences, 1993;5:195-199.

Tomer, R., <u>Levin, B.E.</u>: Differential affects of aging in two verbal fluency tasks. Perceptual and Motor Skills, 1993:76:465-466.

Kelley, R.E., Chang, J.Y., Suzuki, S., <u>Levin, B.E.</u>, Reyes-Iglesia, Y.:Selective increase in transcranial doppler velocity during a cognitive task. Cortex, 1993;29:45-52.

Brown, M.C., <u>Levin, B.E.</u>, Ramsay, R.E., Landy, H.J.:Comprehensive evaluation of left hemisphere Type 1 schizencephaly. Archives of Neurology, 1993;50:667-669.

Tomer, R., <u>Levin, B.E.</u>, Weiner, W.J.:Side of motor onset influences cognition in Parkinson's disease. Annals of Neurology, 1993;34:579-584.

Rey, G., <u>Levin, B.E.</u>, Rodas, R., Bowen, B., Nedd, K.:A longitudinal examination of crossed aphasia. Archives of Neurology, 1994;51:95-100.

Duchowny, M., Levin, B.E., Jayakar, P., Resnick, T.: Neurobiologic factors and the selection of children for epilepsy surgery. Journal of Child Neurology, 1994(2);2S42-2S49

Rey, G., Tomer, R., <u>Levin, B.E.</u>, Sanchez-Ramos, J., Bowen, B., Bruce, J.H.: Psychiatric symptoms, atypical dementia and left-visual field inattention in cortico-basal ganglionic degeneration. Movement Disorders, 1995;10(1):106-110.

<u>Levin, B.E., Katzen, H.: Early Cognitive Changes in Parkinson's Disease. In: W. Weiner and A. E. Lang.</u> Behavioral Neurology of Movement Disorders. Advances in Neurology, 1995;65:85-89.

Feldman, E., Levin, B.E., Fleischmann, J., Jallad, B., Kushch, A., Gross-Glenn, K., Rabin, M., & Lubs., H.A.:Gender differences in the severity of adult familial dyslexia. Reading and Writing, 1995;7:155-161. Goldstein, R., Duchowny, M., Jayakar, P., Altman, N., Resnick, J., Levin, B.E., Harvey, A.S., Alvarez, L.: Predictors of seizure relief after temporal lobectomy in children. Journal of Child Neurology, 1996, 11 (6), 445-450.

Duchonwy, M., Jayakar, P., Harvey, S., Resnick, T., Alvarez, L., Dean P. <u>Levin, B.E.</u>:Language cortex representation: Effects of developmental versus acquired pathology. Annals of Neurology, 1996,40:31-38. Shulman, L.M., Singer, C., <u>Levin, B.E.</u>, Weiner, W.J.:Diagnostic testing for dementia patients with Parkinson's disease. Journal of the American Gerontological Society, 1996, 44(2) 214-215.

Katzen, H., Levin, B.E., Llabre, M.: Age of onset inflences dementia in Parkinson's disease. Journal of International Neurosychological Society, 1998, 4, 285-290.

Rey, G.J., Feldman, E., Levin, B.E., Rivas-Vazquez, R., Benton, A.L.: Current trends and future of neuropsychological research with Hispanics. Archives of Clinical Neuropsychology, 1999; 14(7), 593-601. Levin, B.E., Katzen, H.L., Klein, B., Llabre, M. Cognitive decline affects subject attrition in longitudinal research. Journal of Clinical and Experimental Neuropsychology. 22 (5), 580-586.

Klein, B., Levin, B.E., Duchowny, M.S., Llabre, M.: Cognitive outcome of children with epilepsy and

malformations of cortical development . Neurology 2000,55,230-235:
Weiner, WJ, Rabinstein, A, Levin, B.E. Weiner, C. Shulman, LM Cocaine-induced persistent dyskinesias, Neurology2001:564 964-965.

Arena, P., Levin, B., Fleming, L, Friedman, M., Blythe, D. A pilot study of the cognitive and psychological correlates of chronic ciguatera poisoning. Harmful Algae 3 (2004) 51-60.

Grossman, AB, Levin, BE, Katzen, HL., Lechner, S. PTSD symptoms and onset of neurologic disease in elderly trauma survivors. Journal of Clinical and Experimental Neuropsychology, 2004, 26(5), 698-705. Friedman, MA, Levin, BE. Neuropsychological effects of harmful algal bloom (HAB) toxins. Journal of International Neurological Society (2005) 11(3):331-8.

Levin, BE, Katzen, H. Early cognitive changes and nondementing behavioral abnormalities in Parkinson's disease. In: W. Weiner and A. E. Lang. Behavioral Neurology of Movement Disorders. Advances in Neurology, 2005.

Grossman, A. B., Levin, B. E., & Bradley, W. G. (2006). Premorbid personality characteristics of patients with ALS. Amyotroph Lateral Scler, 7(1), 27-31.

Katzen, H. L., Levin, B. E., & Weiner, W. (2006). Side and type of motor symptom influence cognition in Parkinson's disease. Mov Disord, 21(11), 1947-1953.

Scanlon, B. K., Katzen, H. L., Levin, B. E., Singer, C., & Papapetropoulos, S. (2008). A formula for conversion of UPDRS-III scores to Hoehn and Yahr stage. Parkinsonism & Related Disorders, 14(4), 379-

Papapetropoulos, S. Katzen, H., Schrag, A., Singer, C., Scanlon, B. K., Nation, D. Guevara, A. & Levin, B.E.(in press) A questionnaire-based (UM-PDHQ) study of hallucinations in Parkinson's disease. BMC Neurology. 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.

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. 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 (in press). Chou, KL, Amick, M.M., Brandt, J and others (Levin, B.E.) (in press)A recommended scale for cognitive screening in clinical trials of Parkinson's disease. Recommendations of a task force in behalf in the Parkinson Study Group Cognitive Behavioral Working Group, Movement Disorders.

Katzen, H., Myerson, C., Papapetropoulos, S., Nahab, F., Gallo, B. & Levin, B. (in press). Multi-modal hallucinations and cognitive function in Parkinson's disease. Dementia and Geriatric Cognitive Disorders.

Katzen, H., Ravdin, L.D., Assuras, S., Heros, R., Kaplitt, M., Schwartz, T. H., Fink, M., Levin, B.E., & . Relkin, N.R. (in press). Post-shunt cognitive and functional improvement in idiopathic Normal Pressure Hydrocephalus (iNPH). Neurosurgery.

Papapetropoulos, S., Katzen, H., Scanlon, B., Guevera, A., Singer, C., & Levin, B. (in press) Objective quantification of neuromotor symptoms in Parkinson's disease: implementation of a portable, computerized measurement tool. Parkinson's Disease.

# Relevant Refereed Abstracts : .: \* ! .:

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Myerson, C.E., Katzen, H.L., Nahab, F.B., Levin, B.E. (2010, February). Redfining the link between apathy and cognition in Parkinson's disease. Presented at the International Neuropsychological Society, 38th Annual Meeting, Acapulco, Mexico

Marion, I.B., Katzen, H.L., Myerson, C.E., Rodriguez, K., Gallo, B.V., Levin, B.E. (2009, December). Neuropsychological Outcome Following Unilateral STN DBS: A Comparison of English-speakers and Spanishspeakers. Presented at the XVIII World Federation of Neurology World Congress on Parkinson's Disease and Related Disorders, Miami Beach, FL.

Katzen, H. Assuras, S., Raydin, L., Strybing, K., Heros, R., Schwartz, T., Fink, M., Kaplitt, M., Levin, B., Relkin, N. (2009, October). Improvement in Gait and Cognition Following Shunt Placement in Idiopathic Normal Pressure Hydrocephalus. Oral presentation at the annual Hydrocephalus meeting, Baltimore, MD. The second of th

Myerson, C.E., Katzen, H.L., Ledon, J., Mittel, A., McClendon, M., Nahab, F.B., Gallo, B.V., Levin, B.E. (2009, November). Cardio-metabolic co-morbidities and cognitive decline in Parkinson's disease. Poster accepted for presentation at the National Academy of Neuropsychology, 29th Annual Conference, New Orleans, LA.

Myerson, C.E., Katzen, H.L., Papapetropoulos, S., Ledon, J., Nahab, F.B., Gallo, B.V., Levin, B.E. (2009, October). Multi-modal hallucinations and cognitive function in Parkinson's disease. Presented at the American Neurological Association 134th Annual Meeting. Baltimore, MD.

Myerson, C.E., Katzen, H.L., Marion, I.B., Mittel, A.M., Nahab, F.B., Gallo, B.V., Levin, B.E. (2009, December). Profiles of apathy and depression in Parkinson's disease. Presented at the XVIII World Federation of Neurology World Congress on Parkinson's Disease and Related Disorders, Miami Beach, FL.

Levin, B. E. (2007). Neuropsychological predictors of all-cause mortality in Parkinson's disease. Journal of the International Neuropsychological Society, 13(Supplement S1), 96-97.

# RESEARCH SUPPORT ACTIVE:

2U01NS38529-07A1 (Benavente/ Romano, site PI)
NIH/NINDS \$306,8000
Secondary Prevention of Small, Subcortical Strokes (SPS3)

02/01/2008-6/30/2011 3%

1 UO1 NS052478-01A2 (Adelson)
NINDS \$1,627,822 (Site Neuropsychologist)
Pediatric Traumatic Brain Injury Consortium: Hypothermia

7/30/07 – 6/30/2013 4.80 Calendar months

R01 NS055107-04 (Maudsley) NIH/NINDS 6/01/06-12/31/12 (10%) Volumetric MRSI Evaluation of Traumatic Brain Injury \$333,850

R01 NS060874-02 (Govindaraju) NIH/NINDS 9/30/08-8/31/12 (5%) Brain Metabolic Imaging in Amyotrophic Lateral Sclerosis \$301,219

A Pilot Study of Moderate Hypothermia for Severe Traumatic Brain Injury in Children, N.I.H., P. Davis Adelson (PI) Univ. of Pittsburgh.

Role: Site Neuropsychologist.

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

| NAME<br>Nahab, Fatta B.                                       | POSITION TITLE Assistant Professor of Neurology and Neuroscience       |
|---|--|
| eRA COMMONS USER NAME (credential, e.g., agency login) fnahab | Director, Functional Imaging of Neurodegenerative Disorders Laboratory |

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<br>(if applicable)                 | MM/YY                               | FIELD OF STUDY                               |
|---|---|-------------------------------------|--|
| La Sierra University (Riverside, CA)<br>Loma Linda University (Loma Linda, CA)    | B.S.<br>M.D.                              | 1992-1996<br>1996-2000              | Biology<br>Medicine                          |
| Loma Linda University Medical Center (Loma Linda, CA)                             | Internship<br>Residency<br>Chief Resident | 2000-2001<br>2001-2004<br>2003-2004 | Int. Medicine/Psychiatry Neurology Neurology |
| Human Motor Control section, NINDS<br>National Institutes of Health, Bethesda, MD | Fellowship                                | 2004-2008                           | Movement Disorders and Functional MRI        |
| ·   | 1   | 1                                   | ± 1  |

# A. Personal Statement:

N/A

# **B.** Positions and Honors

# Positions and Employment

2004-2008 Neurology Consultant, NIH Clinical Center, Bethesda, MD

2005-2008 Director, NIH Botulinum Toxin Clinic, Bethesda, MD

2005-2007 General Medical Hospitalist, Shady Grove Adventist Hospital, Rockville, MD

2007-2008 Assistant Clinical Investigator, NINDS, NIH, Bethesda, MD

2008-present Assistant Professor of Neurology, University of Miami, Miami, FL

2008-present Director of Research, Section of Movement Disorders, Dept. of Neurology, University of Miami

2008-present Director, Functional Imaging of Neurodegenerative Disorders Laboratory

2011-present Assistant Professor of Neuroscience, University of Miami, Miami, FL

#### **Patents**

12/083,141 Pending Title: OctanolFormulations and Methods of Treatment (USA,CAN,EUROPE)

Inventors: FB Nahab, M Hallett, J Serbin, J McLane

12/867,702 Pending Title: Octanoic AcidFormulations and Methods of Treatment

Inventors: FB Nahab, M Hallett, J Mclane

Provisional Filing Title: Context Differential Autocorrelation Mapping Of Functional MRI

Inventors: FB Nahab, P Kundu (Filed Sept 21, 2010).

#### Other Experience and Professional Memberships

Brain; Clinical Neurophysiology; Human Brain Mapping Conference; Journal of Psychiatric Research; Movement Disorders; Neurolmage; Parkinsonism & Related Disorders; Neurosurgery, Brain Topography; Cognitive, Affective, and Behavioral Neuroscience

# Professional Memberships:

2001-present American Academy of Neurology

2004-present Movement Disorder Society

# 2009-present Organization of Human Brain Mapping

# Honors and Awards (selected):

1997 Summer Research Scholarship, MacPherson Society

1998 Excellence in Research Award, Western Medical Student Research Forum

1998 Outstanding Service Award, Iacono Movement Disorder and Neuroscience Group

2002-2004 Academic Development Award, Loma Linda University Dept of Neurology

2004 Resident Scholarship, American Academy of Neurology

2004 Alpha Omega Alpha Medical Honor Society Membership

2008 J. Stephen Fink, MD PhD American Society for Experimental NeuroTherapeutics (ASENT) Fellow

2010 Chairman's Award for Teaching Excellence

#### C. Peer-reviewed Publications

1. Nahab FB, Peckham E, Hallett M. Pilot study of botulinum toxin type A for the treatment of refractory restless legs Syndrome. *Neurology* 2008; 71 (12): 950-.

2. Nahab FB, Hattori N, Saad ZS, Hallett M. Contagious yawning and the frontal lobe: An fMRI study. *Human Brain Mapping* 2009 (30): 1744-1751

- 3. Edwards T, Scott B, Almonte C, Burt A, Powell E, Beecham G, Wang L, Zuchner S, Konidari I, Wang G, Singer C, Nahab FB, Scott B, Stajich J, Martin ER. Genome-wide association study confirms SNPs in SNCA and the MAPT region as common risk factors for Parkinson disease. Ann Hum Genet, 2010; 74: 97-109
- 4. Nahab FB. Exploring yawning with neuroimaging. Front NeurolNeurosci. 2010; 28: 128-33
- 5. Nahab FB, Kundu P, Gallea C, Kakareka J, Pursley R, Pohida T, Milletta N, Friedman J, Hallett M. The neural processes underlying self-agency. Cerebral Cortex 2010; 21: 48-55
- 6. Nahab FB and Hallett M. In: Yousry T, ed. Neuroimaging Clinics of North America. The role of fMRI in the diagnosis of movement disorders. NeuroimagClin N Am 2010; 20: 103–110
- 7. Katzen H, Myerson C, Papapetropoulos S, Nahab FB, Gallo B, Levin B.Multi-modal hallucinations and cognitive function in Parkinson's disease. Dement GeriatrCognDisord 2010;30:51-56
- 8. Nahab FB, Wittevrongel L, Ippolito D, et al. An open-label, single-dose, crossover study of the pharmacokinetics and metabolism of two oral formulations of 1-octanol in patients with essential tremor. Neurotherapeutics 2011; 8 (4): 753-762
- 9. Haubenberger D, Kalowitz D, Nahab FB, Toro C, Ippolito D, Wittevrongel L, Hallett M. Validation of computerized essential tremor spiral analysis as outcome parameter for clinical trials in Essential Tremor. Movement Disorders 2011;26(11):2073-80
- 10. Wallace DM, Shafazand S, Carvalho DZ, Nahab FB, Sengun C, Moore HP, Singer C. Sleep-related falling out of bed in Parkinson's disease. ClinNeurol 2012; 8(1): 51-57
- 11. Pankratz N, Beecham GW, DeStefano AL, et al. (collaborator: Nahab FB). Meta-analysis of Parkinson's disease: identification of a novel locus, RIT2. Ann Neurol 2012; 71(3):370-84
- 12. Nahab FB, Handforth A, Brown T, Shin C, Quesada A, Dong C, Haubenberger D, Hallett M. Octanoic Acid Suppresses Harmaline-Induced Tremor in Mouse Model of Essential Tremor. Neurotherapeutics 2012 (Epub Ahead of Print)
- 13. Wallace DM, Shafazand S, Carvalho DZ, Nahab FB, Sengun C, Russell A, Moore HP, Singer C. Sleep-related falling out of bed in Parkinson's disease. J ClinNeurol 2012; 8(1): 51-57.
- 14. Levin BE, Katzen HL, Maudsley A, Post J, Myerson, Govindaraju V, Nahab FB, Scanlon B, Mittel A. Whole-brain Proton MR Spectroscopic Imaging in Parkinson's Disease. J Neuroimag (in press)
- 15. Haubenberger D, McCrossin G, Lungu C, Considine E, Toro C, Nahab FB, Auh S, Buchwald P, Grimes G, Starling J, Potti G, Scheider L, Kalowitz D, Bowen D, Carnie A, Hallett M. Safety and efficacy of octanoic acid in alcohol-responsive essential tremor. A randomized controlled study. Neurology (Accepted, minor revisions, 10/18/12)

# D. Research Support

**Active Research Support** 

Functional Imaging of Tremor Circuits and Mechanisms of Treatment Response

Nahab FB - PI

Funding Entity: NINDS/NIH

Grant Period: 7/11-3/16

Grant #: R01-NS-073683-01A1

Topic: The major goals of this project are to define the brain networks responsible for tremor generation, identify imaging correlates of various tremor phenotypes and elucidate the mechanisms of treatment response. Dr. Nahab is involved with all aspects of this project.

#### The Genetics of Parkinsonism

Vance J - PI, Nahab FB - Col

Funding Entity: NINDS/NIH Grant Period: 9/11-8/16

Grant #: 2P50NS071674-02 (Udall Center)

Topic: The overall goal of the center is to identify genes or genetic mechanisms that cause or contribute to an individual's susceptibility to Parkinson Disease (PD) and to translate these discoveries into early detection of risk or disease, as well as provide therapeutic targets for PD.

Dr. Nahab assists in subject enrollment, clinical adjudication, and manuscript revision.

# Clinical Biomarker Assessment of Efficacy of Cognitive Remediation in Patients with Schizophrenia Stabilized on Lurasidone (TENETS)

Steinbeck R - PI, Nahab FB - Col

Funding Entity: The Research Foundation for Mental Hygeine

Topic: The purpose of this study is to conduct a scientifically rigorous clinical trial that optimizes the likelihood of meaningful improvement in cognitive and psychosocial functioning in patients with schizophrenia. Subjects receive Lurasidone, an antipsychotic agent, during the study and a subpopulation undergoes two functional MRI studies to characterize changes in cognition (memory, attention, problem solving, etc.). My responsibilities in this study include data collection, imaging quality control, and sub-study management.

**Completed Research Support** 

International Essential Tremor Foundation Nahab (PI)

7/08-6/11

Identification of the neural generator(s) in essential tremor using functional magnetic resonance imaging.

This study will identify the neural network responsible for generating essential tremor.

Role: PI

Total Award: \$25,000

NIH 5P50NS039764-10

Vance (PI)

9/30/2009 - 5/31/2010

Genetics of Parkinsonism

This study is a Udall Center grant intended to study the genetics of Parkinsonisms.

Role: Co-Investigator on Core B (0.16 calmo)

Total Cost: \$947,606

Intramural NIH 07-N-0160

Nahab (PI)

2007-2008

NINDS/NIH

Pilot study of botulinum toxin, type A for the treatment of restless legs syndrome

Intramural NIH 07-N-0117

Nahab (PI)

2006-2008

NINDS/NIH

BOLD-fMRI of the Perception of Volition in Functional Movement Disorders

Intramural NIH 06-N-0243

Hallett (PI)

2006-2008

NINDS/NIH

Brain Connectivity between visual input and motor output.

Intramural NIH 06-N-0139

Peckham (PI)

2006-2008

NINDS/NIH

Treatment for Psychogenic Movement Disorders.

Intramural NIH 06-N-0128

Hallett (PI)

2006-2008

NINDS/NIH

fMRI studies of task specificity in Focal Hand Dystonia.

Intramural NIH 06-N-0084

Hallett (PI)

2006-2008

NINDS/NIH

Brain Networks Responsible for Sense of Agency: An EEG study.

Intramural NIH 06-N-0023

Nahab (PI)

2005-2008

NINDS/NIH

Brain networks responsible for self-agency: An fMRI study.

Intramural NIH 05-N-0092

Nahab (PI)

2004-2008

NINDS/NIH

Clinical Trial Characterizing the Bioavailability of 1-Octanol in Adults with Ethanol-responsive Essential Tremor.

Intramural NIH 05-N-0032

Nahab (PI)

2004-2006

NINDS/NIH

Functional MRI Study of Brain Activation with Observation of Facial Expressions.

Intramural NIH 04-N-0153

Pirio Richardson (PI)

2004-2006

NINDS/NIH

Timing of Voluntary Movement in Patients with Tourette Syndrome and Chronic Tic Disorder Using EEG and Surface EMG.

Intramural NIH 04-N-0151

Pirio Richardson (PI)

2004-2006

NINDS/NIH

Timing of Voluntary Movement in Patients with Schizophrenia Using EEG and Surface EMG.

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>TATJANA</b> | RUNDEK. | MD | PhD |

eRA COMMONS USER NAME (credential, e.g., agency login) TR89XX

POSITION TITLE

**Professor of Neurology** 

**Director, Clinical Translational Research Division** Miller School of Medicine, University of Miami, FL

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<br>(if applicable) | MM/YY     | FIELD OF STUDY              |
|---|---------------------------|-----------|-----------------------------|
| University of Zagreb, College of Mathematics, Croatia | B.S.                      | 1979-1983 | Applied Mathematics         |
| Medical School University of Zagreb, Croatia          | M.D.                      | 1984-1989 | Medicine                    |
| Medical School University of Zagreb, Croatia          | M.S.                      | 1989-1991 | Epidemiology/Bioinformatics |
| Ludwig-Maximillian University, Munich, Germany        | Ph.D.                     | 1991-1995 | Neuroscience                |
| Medical School University of Zagreb, Croatia          | Residency                 | 1991-1994 | Neurology                   |
| Grossharden Spital Munich, Germany                    | Fellowship                | 1994-1995 | Stroke                      |
| Columbia University, New York, NY                     | Fellowship                | 1998-2000 | Stroke/Neuroepidemiology    |

### A. Personal Statement: N/A

# **B.** Positions and Honors POSITIONS AND EMPLOYMENT

|  | a |  |  |  |  |  |
|--|---|--|--|--|--|--|
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| 100           | IMILOCOLLIN        | 7.  |  |
|---------------|--------------------|---|--|
|               | 1990-91            | Medicine Internship                       | Clinical Hospital for Pulmonary Diseases, Zagreb, Croatia  |
| Carlo Par     | 1991-94            | Neurology Residency                       | Grossharden Spital Munich, Germany   |
| Countries     | 1995-96            | Neurosonology Post-Doctoral Fellow        | Neurosonolgy Laboratory University of Ulm, Germany   |
| in the second | 1998-00            | Stroke Fellow (Epidemiology)              | Columbia University, New York, NY  |
| A             | <u> Academic A</u> | Appointments:                             | in de la Martin de la companya de la Carlo de Martin de la companya de la companya de la companya de la compan<br>Notae de la companya |
|               | 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   |
|               | 2000-02            | Associate Research Scientist              | Columbia University, New York, NY  |
|               | 2002-07            | Assistant Professor of Neurology          | Columbia University, New York, NY  |
|               | 2007-              | Associate Professor of Neurology          | Miller School of Medicine, University of Miami, Miami, FL  |
| Į             | Hospital Ap        | ppointments:                              |  |
| -             | 1994-00            | Stroke Attending                          | Department of Neurology, University of Zagreb, Croatia   |
|               | 1995-98            | Director, Neurosonology Laboratory        | Department of Neurology, University of Zagreb, Croatia   |
|               | 2002-07            | Director, Neurosonology Laboratory        | Columbia University, New York, NY  |
|               | 2007-              | Director, Clinical Translational Research | Department of Neurology, Miller School of Medicine,  |
|               |                    | Division in Neurology                     | University of Miami, Miami, FL   |
|               |                    |   |  |

#### OTHER EXPERIENCE AND PROFESSIONAL MEMBERSHIPS

Editorial Board Member of the Professional Journals: Stroke, Neurology, Journal of CardioMetabolic Syndrome Ad Hoc Reviewer for the Professional Journals: Stroke, Neurology, Neuroepidemiology, Cerebovascular Diseases, Scandinavian Journal of Rheumatology, Circulation, American Journal of Ultrasound in Medicine, Headache

#### 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             |
| JONODS |   |

#### HONORS

| 1997 | Fulbright Award and Scholarship, Neurological Institute, Columbia University, New Yorl | k, NY |
|------|--|-------|
| 1996 | George Soros Scholarship, Neurology Seminars, University of Krems, Austria             |       |

Humbolt Award, Neurosonology Laboratory, University of Ulm, Germany

2006 Nassau Women Physicians Foundation Award for Stroke Research in Women; Long Island, NY

2009 President Elect, Neurosonology Community Practices of the American Institute of Ultrasound in Medicine

#### C. Selected Peer-reviewed Publications

(from 11 book chapters, 22 invited articles, 135 peer-reviewed articles).

- 1. Rundek T, Sacco RL. New models of successful academic mentoring. Neurology. 2011 Jul 27. [Epub ahead of print] PMID: 2179566
- 2. Dong C, Della-Morte D, Wang L, Cabral D, Beecham A, McClendon MS, Luca CC, Blanton SH, Sacco RL, **Rundek T**. Association of the sirtuin and mitochondrial uncoupling protein genes with carotid plaque. PLoS One. 2011;6(11): e27157. PMCID: PMC3210138
- 3. 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):889-96. PMCID: PMC3116444
- 4. 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;42(3):588-92. PMCID: PMC3042493
- 5. **Rundek T**, Katsnelson M. Is frequent ultrasound monitoring of spontaneous cervical artery dissection clinically useful? Neurology. 2010;75(21):1858-9. PMID: 20962293
- 6. 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(10):1195-200 PMCID: PMC2954671
- 7. **Rundek T**, Salameh MJ. Carotid plaque assessment: a bumpy road to improved risk prediction. J Am Coll Cardiol. 2010;56(13):1069; PMID:20846614
- 8. 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(4):264-8. PMCID: PMC2907549
- Della-Morte D, Gardener H, Denaro F, Boden-Albala B, Elkind MS, Paik MC, Sacco RL, Rundek T. Metabolic syndrome increases carotid artery stiffness: the Northern Manhattan Study. Int J Stroke. 2010;5(3):138-44. PMCID: PMC2980500
- 10. Gardener H, Della Morte D, Elkind MS, Sacco RL, **Rundek T**. Lipids and carotid plaque in the Northern Manhattan Study (NOMAS). BMC Cardiovasc Disord. 2009;9:55. PMCID: PMC2804671
- 11. Gutierrez J, Hossam A, Lazarezcu R, Kay E, **Rundek T**. Effect of beta blockers on sepsis outcome. Med Sci Monit. 2009;15(10):CR499-503. PMID: 19789508
- 12. Ratchford EV, Jin Z, Di Tullio MR, Salameh MJ, Homma S, Gan R, Boden-Albala B, Sacco RL, Rundek T. Carotid bruit for detection of hemodynamically significant carotid stenosis: the Northern Manhattan Study. Neurol Res. 2009;31(7):748-52. PMCID: PMC2727568
- 13. Godia EC, Madhok R, Pittman J, Trocio S, Ramas R, Cabral D, Sacco RL, Rundek T. Carotid artery distensibility: a reliability study. J Ultrasound Med. 2007;26(9):1157-65. PMCID: PMC2677175
- 14. Prabhakaran S, Singh R, Zhou X, Ramas R, Sacco RL, Rundek T. Presence of calcified carotid plaque predicts vascular events: the Northern Manhattan Study. Atherosclerosis. 2007;195(1):e197-201. PMCID: PMC2654324
- Rundek T, Elkind MS, Di Tullio MR, Carrera E, Jin Z, Sacco RL, Homma S. Patent Foramen Ovale and Migraine. A Cross-Sectional Study from the Northern Manhattan Study. Circulation. 2008;118(14):1419-24. PMCID: PMC2737546
- 16. Salameh MJ, Rundek T, Boden-Albala B, Jin Z, Ratchford EV, Di Tullio MR, Homma S, Sacco RL. Self-reported peripheral arterial disease predicts future vascular events in a community-based cohort. J Gen Intern Med. 2008;23(9):1423-8. PMCID: PMC2518027
- 17. Rundek T, Arif H, Boden-Albala B, Elkind MS, Paik MC, Sacco RLS. Carotid plaque thickness predicts ischemic stroke, myocardial infarction and vascular death: The Northern Manhattan Study. Neurology 2008;70(14):1200-7. PMCID: PMC2831775

## D. Research Support

#### **Ongoing Research Support**

Novel Factors for Unexplained Phenotypes of Subclinical Carotid Atherosclerosis NIH/NINDS R01 NS 065114

PI: T. Rundek

07.01.10-06.3.15

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

# 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, and enhance career development in genetic epidemiology.

# 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 homocysteine, carotid intima-media thickness and carotid stiffness among the families of high-risk Caribbean Hispanics.

# University 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 09.30.11-08.31.15

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 University 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 (ISGC) that will bring together the world's leading clinician-scientists in stroke genetics.

# The Albert Einstein Study Program Project in Aging

NIA 2P01 AG003949-26; Pls: Lipton, Derby; Albert Einstein, NY,

T. Rundek, PI for the TCD Core Laboratory

07/1/11-06/30/15

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.

#### **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 erythomatosus.

Clopidogrel versus Aspirin Carotid Ultrasound Stroke Study (CASS); Sanofi-Aventis/BMS; PI: T. Rundek (7.01.05-12.30.08). This as a 3-year single center clinical trial aimed to test the hypothesis whether clopidogrel was superior to aspirin in improving carotid artery wall properties in the patients with non-disabling stroke from a multi-ethnic community.

STARR (The STudy of Atherosclerosis with Ramipril and Rosiglitazone); Canadian Institutes of Health Research, Aventis Pharma, King Pharmaceuticals and GlaxoSmithKline; Pl: Eva Lonn, Mcaster University, Hamilton, Canada; T. Rundek, CU Site Pl (01.01.02-12.31.07). STARR was a multi-centre, international, randomized controlled clinical trial aimed to evaluate the effects of ramipril and of rosiglitazone on atheroscleorsis progression, as determined by B-mode carotid ultrasound. It is a substudy of DREAM (Diabetes REduction Assessment with Ramipril and Rosiglitazone Medication) trial.

Carotid Artery Distensibility and Risk of Stroke; *The Gilbert Baum Memorial Grant and the American Institute of Ultrasound in Medicine Award;* Pl: 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 Effect of Atorvastatin on Carotid Plaque Morphology Assessed by Gray Scale Ultrasound Densitometry; *Pfizer, Inc.* PI: T. Rundek (7.01.05-06.30.06). This was a 1-year single center study clinical trial aimed to assess the effect of atorvastatin on carotid artery plaque density within 30 days of treatment with a single dose of atorvastatin.

A Pilot Study to Evaluate Potential Screening Factors for Atherosclerosis in Survivors of Childhood and Young Adult Hodgkin's Disease; *The Columbia Cancer Institute;* PI: K. Kelly, Co-Investigator: T. Rundek (7.01.05-06.30.06). The main objective of this study was to obtain pilot data to evaluate the prevalence and severity of asymptomatic carotid artery disease in a cohort of survivors of childhood or young adult Hodgkin's disease.

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 substudy 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.

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   | POSITION TITLE   |
|--|--|
| Ralph Lewis Sacco  | Chairman and Professor of Neurology,                           |
| eRA COMMONS USER NAME (credential, e.g., agency login) SACCORL | Epidemiology & Public Health, Human Genetics, and Neurosurgery |

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

| INSTITUTION AND LOCATION                      | DEGREE<br>(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   |

#### B. Positions and Honors

| 1989-97 | Asst Professor of Neurology & Public Health (Epidemiology) in the Sergievsky Center                    |
|---------|--|
| 1997-02 | Assoc 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 Human |
|         | Genetics (with tenure) and Chairman of Neurology, Miller School of Medicine, University of Miami       |
|         |  |

| 1982              | Alpha Omega Alpha                             | 2001 | Fellow of the American Heart Association    |
|-------------------|---|------|---|
| <sup>7</sup> 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          |
| 2011              | Henry I Russek Lecture 2011                   | 2012 | Robert Wartenberg Lecture AAN               |
| Odlan Dual        | factional Experience                          |      |   |

#### Other Professional Experience

| Other Flor | essional Expensive  |   |
|------------|---|---|
| 1999-05    | American Academy of Neurology - Clinical Research Subcommittee, Chair | ٢ |
| 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                                      |   |
| 2005-08    | ASA, Chair Stroke Advisory Committee                                  |   |
| 2005-09    | American Academy of Neurology, Board of Directors                     |   |
| 2010-11    | President, American Heart Association, National Board of Directors    |   |
|            |   |   |

# C. Selected Peer-reviewed Publications

- 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.Highdensity lipoprotein cholesterol and ischemic stroke in the elderly. **JAMA** 2001;285:2729-35 PMID: 11386928
- 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
- 6. Sacco RL, Anand K, Lee HS, Boden-Albala B, Stabler S, Allen R, Paik MC. Homocysteine and the Risk of Ischemic

- Stroke in a Triethnic Cohort. The Northern Manhattan Study. Stroke 2004; 35:2263-9 PMID: 15345803
- 7. 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 Jul;40(7):2307-12. Epub 2009 Jun 4. PubMed PMID:19498180
- 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 (NOMASS). **Stroke.** 2010 Sep;41(9):1896-900. Epub 2010 Jul 29. PubMed PMID: 20671256; PubMed Central PMCID: PMC2932858.
- Dhamoon MS, Moon YP, Paik MC, Boden-Albala B, Rundek T, Sacco RL, Elkind MS. Quality of life declines after first ischemic stroke. The Northern Manhattan Study. Neurology. 2010 Jul 27;75(4):328-34. Epub 2010 Jun 23. PubMed PMID: 20574034; PubMed Central PMCID: PMC2918891.
- 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. Epub 2011 Aug 11. PubMed PMID: 21836088; PubMed Central PMCID: PMC3189513
- 11. 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 Dec 19:1-11. [Epub ahead of print] PubMed PMID: 22182463
- 12. Wang L, Beecham A, Zhuo D, Dong C, Blanton SH, Rundek T, Sacco RL. Fine Mapping Study Reveals Novel Candidate Genes for Carotid Intima-Media Thickness in Dominican Families. **Circ Cardiovasc Genet**. 2012 Mar 14. [Epub ahead of print] PubMed PMID: 22423143.
- 13. Gardener H, Scarmeas N, Gu Y, Boden-Albala B, Elkind MS, Sacco RL, DeCarli C, Wright CB. Mediterranean diet and white matter hyperintensity volume in the Northern Manhattan Study. **Arch Neurol**. 2012 Feb;69(2):251-6. PubMed PMID: 22332193; PubMed Central PMCID: PMC3281550.
- 14. 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. Epub 2012 May 22. PubMed PMID: 22619283; PubMed Central PMCID: PMC3396556.
- Boden-Albala B, Roberts ET, Bazil C, Moon Y, Elkind MS, Rundek T, Paik MC, Sacco RL. Daytime Sleepiness and Risk of Stroke and Vascular Disease: Findings from the Northern Manhattan Study (NOMAS). Circ Cardiovasc Qual Outcomes. 2012 Jul 1;5(4):500-7. Epub 2012 Jul 10. PubMed PMID: 22787063.

#### D. 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.

#### **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.

#### 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.

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

Role: Co-I; PI: Koch (local); Woo (study); Agency: NIH/NINDS; Type: R01 (NS069763); Period: 07.01.10-07.31.13 Aims: The goal of this study is to identify the relative importance of leading risk factors for ICH in blacks and Hispanics, determine differences in outcomes based on race and ethnicity and leading predictors of poor outcome, and determine differences in neuroimaging characteristics by race and ethnicity. 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:04.01.07-02.14.15:

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: 10.01.07-10.01.13

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

# Clinical and Translational Science Award (PI, J. Szapocznik)

Role: CTSA Executive Committee, Agency: NIH/NCRR/NIMHD

Period: 07/01/12-6/30/17; Aims: The goal of this CTSI is to facilitate translational research at UM.

#### 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.

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

Role: Co-I; PI: Romano; Agency: NIH/NINDS; Type: R01 (NS 069938); Period: 04.15.10-03.31.12

Aims: This is an ancillary study of SAMMPRIS to study the mechanisms that underlie ischemic stroke in stented and non-stented patients with intracranial atherosclerosis.

#### 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.

#### 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.

#### 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.

#### Inflammation and Infection as Risk Factors in Stroke

Role: Mentor; PI: Elkind; Agency: NIH/NINDS; Type: K23 (NS 42912); Period: 01.15.02-12.31.06

Aims: This K23 award is a nested case-control study to evaluate inflammation and other infection exposures as a risk factor for ischemic stroke in the Northern Manhattan Study.

# Inflammation, Leukocyte activation and Stroke Risk

Role: Co-I; PI: M Elkind; Agency: AHA/Grant-In-Aid (0355596T); Period: 07.01.03-06.30.06

Aims: This is a study to evaluate inflammatory markers as risk factors for vascular outcomes within NOMAS.

#### 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

#### Vascular predictors of cognitive impairment and decline in a tri-ethnic community

Role: Mentor; PI: Clinton Wright; Agency: NIH/NCRR; Type: K12 RR017648; Period: 08.01.03-07.31.06.

Aims: To identify vascular risk factors that contribute to cognitive abnormalities.

#### Familial Intracranial Aneurysm Study

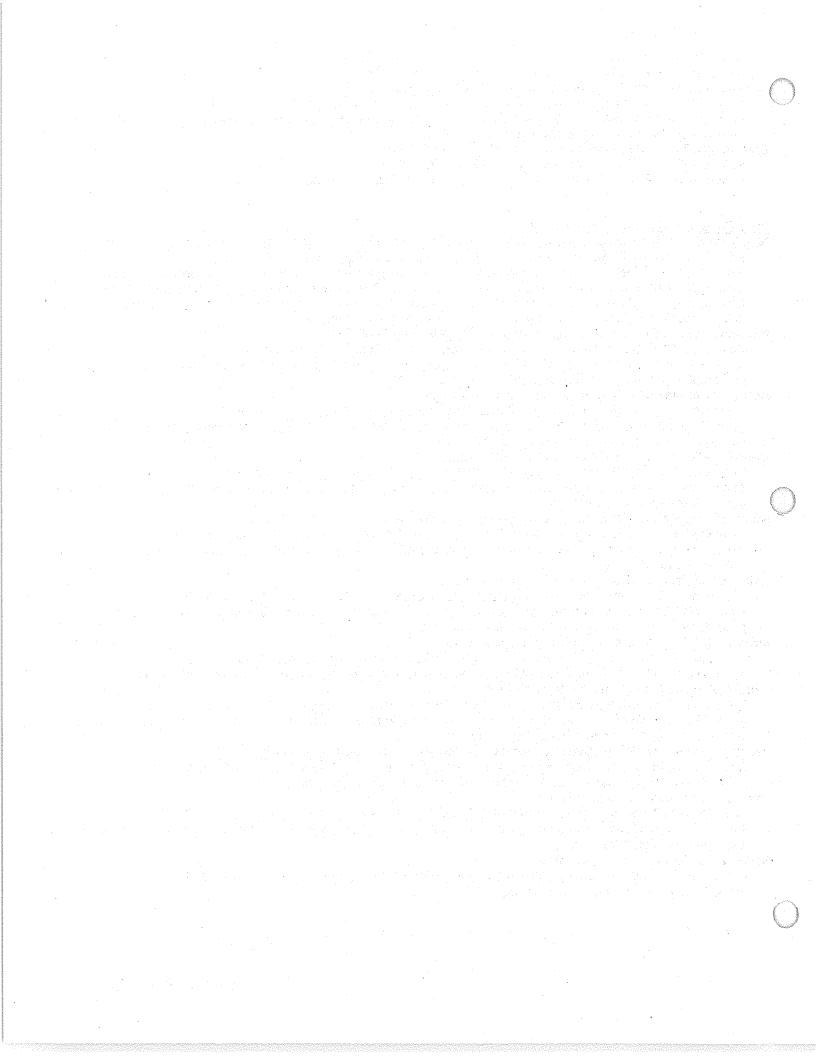
Role: Co-I; PI: Broderick; Agency: NIH/NINDS; Type: R01 (NS 39512); Period: 07.01.02-06.30.07

Aims: This is a multicenter epidemiological family study to investigate the genetic determinants of familial intracranial aneurysms through linkage analysis.

#### **Neuroepidemiology Training Program**

Role: Co-PI; PI: Hauser; Agency: NIH/NINDS; Type: T32 (NS 07153); Period: 07.01.04-06.30.09

Aims: To train neurologists in epidemiology.



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<br>Clinton B. Wright                                       | POSITION TITLE Scientific Director, Evelyn F. McKnight Center for |
|---|---|
| eRA COMMONS USER NAME (credential, e.g., agency login) WRIGHTCL | Age Related Memory Loss Associate Professor of Neurology          |

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

| INSTITUTION AND LOCATION                                | DEGREE<br>(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. **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; 40:3466-71. **PMCID: PMC3114944**
- 9. 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**
- 10. 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**
- 11. 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**
- 12. 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**
- 13. 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**
- 14. 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**
- 15. Whitcomb DC, Larusch J, Krasinskas AM, Crocco E, Wright CB et al. Common genetic variants in the CLDN2 and PRSS1-PRSS2 loci alter risk for alcohol-related and sporadic pancreatitis. *Nat Genet*. 2012; 44: 1349-54. **PMCID: PMC3510344**

# 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

Program Director/Principal Investigator (Last, First, Middle): Wright, Clinton B.

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.

# K02 NS059729 (PI: Wright)

09/01/2008 - 08/31/13

**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 multiethnic 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

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)

AHA 0735387N (Pl: 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.

NS 049060-03 (PI: Marshall)

09/30/04 - 07/14/08

NIH/NINDS

New York Columbia Collaborative Specialized Program of Translational Research in Acute Stroke (SPOTRIAS: Project 1)

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.

Program Director/Principal Investigator (Last, First, Middle): Wright, Clinton B.

NS 049060-03 (Pl: Marshall)

NIH/NINDS

09/30/04 - 07/14/08

New York Columbia Collaborative Specialized Program of Translational Research in Acute Stroke (SPOTRIAS: Project 3)

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.

NS 049060-03 (Pl: Marshall)

09/30/04 - 07/14/08

NIH/NINDS

New York Columbia Collaborative Specialized Program of Translational Research in Acute Stroke (SPOTRIAS: Core C)

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.

# Collaborators

Antonio Barrientos, Ph.D.

Elizabeth Crocco, M. D.

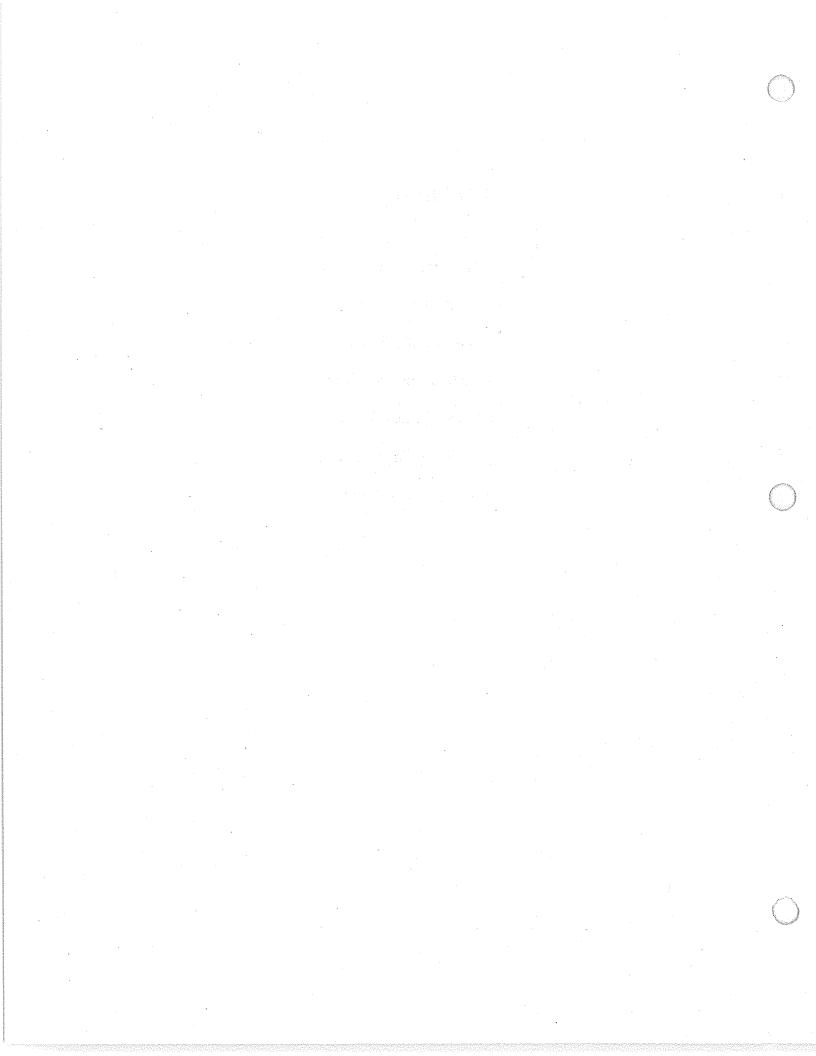
Sara Czaja, Ph.D.

Hannah Gardener, Ph.D.

Carlos Moraes, Ph.D.

Miguel Perez-Pinzon, Ph.D.

Ami P. Raval, Ph.D.



| NAME                  | POSITION TITLE      |
|-----------------------|---------------------|
| BARRIENTOS, Antoni    |                     |
| eRA COMMONS USER NAME | Associate Professor |
| abarrientos           |                     |

| EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.) |                           |           |   |
|--|---------------------------|-----------|---|
| INSTITUTION AND LOCATION   | DEGREE<br>(if applicable) | YEAR(s)   | FIELD OF STUDY                                |
| Univ. of Barcelona. Teachers' School. SPAIN  | B.S.                      | 1981-1984 | Science Education                             |
| Univ. of Barcelona. School of Biology. SPAIN   | B.S.                      | 1986-1992 | Fundamental Biology                           |
| Univ. of Barcelona. School of Medicine. SPAIN  | Ph.D.                     | 1993-1997 | Mitochondrial Genetics and Biochemistry       |
| Uni. of Miami. School of Medicine. FL. USA   | Post-doctoral fellow      | 1997-1999 | Mitochondrial Genetics and Biochemistry       |
| Columbia University. New York. NY. USA   | Post-doctoral fellow      | 1999-2000 | Yeast mitochondrial Genetics and Biochemistry |

#### A. 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)

#### 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** 

- Stage 1 reviewer for The Fellowships ZRG1 **F05-Cell Biology and Development** study section (NIH) (since 2010)
- Stage 1 reviewer for Recovery Act RC1 (2009) and RC4 (2010) applications (NIH)
- Adhoc reviewer for the Membrane Biology and Protein Processing (MBPP) study section (NIH) (since 2011)

Program Director (Last, first, middle): Barrientos, Antoni

- Adhoc reviewer for the Cellular Mechanisms in Aging and Development (CMAD) study section (NIH) (since 2012)

## 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).

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

- 1- Ocampo A., Liu J.J., Schroeder E.A., Shadel G.S. and <u>Barrientos A</u>. Mitochondrial respiratory thresholds regulate yeast chronological life span and its extension by caloric restriction. Cell Metab 16(1):55-67 (2012)
- 2- Liu J. and <u>Barrientos A</u>. Transcriptional regulation of yeast OXPHOS hypoxic genes by oxidative stress. Antiox Redox Signal [Epub ahead of print] (2012)
- 3- Soto IC, Fontanesi F, Myers RS, Hamel P and <u>Barrientos A</u>. A Heme-sensing mechanism in the translational regulation of mitochondrial cytochrome c oxidase biogenesis. Cell Metab. 16 (6): 801-813
- 4- Soto I.C., Fontanesi F., Liu J., <u>Barrientos A</u>. Biogenesis and assembly of eukaryotic cytochrome c oxidase catalytic core. Biochim Biophys Acta. 1817:883-97 (2012)
- 5- Bourens M., Dabir D.V., Tienson H.L., Sorokina, I., Koehler C.M. and <u>Barrientos A</u> 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)
- 6- Bourens M, Fontanesi F, Soto IC, Liu J, and <u>Barrientos A</u>. (2012) Reactive Oxygen Species and Redox Regulation of Mitochondrial Cytochrome c Oxidase Biogenesis. Antioxid. Redox Signal. (2012 Sep 3) [Epub ahead of print]
- 7- Moreno-Lastres D., Fontanesi F., García-Consuegra I., Martín M.A., Arenas J., <u>Barrientos A.</u>, Ugalde C. Mitochondrial Complex I plays an Essential Role in Human Respirasome Assembly (2012) Cell Metab 15(3):324-35 (2012)
- 8- Yong Pan Y., Schroeder E.A., Ocampo A., <u>Barrientos A.</u> and Shadel G.S. Regulation of yeast chronological life span by TORC1 via adaptive mitochondrial ROS signaling. *Cell Metab.* 13(6): 668-678 (2011)
- 9- Ocampo A. and <u>Barrientos A.</u> 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]
- 10-Fontanesi F., Clemente P., <u>Barrientos A.</u> 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)
- 11-Horn D., Zhou W, Trevisson E., Al-Ali H., Harris T.K., Salviati L., and <u>Barrientos A.</u> (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
- 12-Fontanesi F., Soto I.C., Horn D. and <u>Barrientos A.</u> (2009) Mss51 and Ssc1 facilitate translational regulation of cytochrome *c* oxidase biogenesis. *Mol Cell Biol.* 30: 245-259. PMCID2798308
- 13- Soto I.C., Fontanesi F., Valledor M., Horn D., Singh R. and <u>Barrientos A</u>. (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. PMCID2764804
- 14-Ocampo A., Zambrano A. and <u>Barrientos A.</u> (2009) Suppression of polyglutamine-induced cytotoxicity in Saccharomyces cerevisiae by enhancement of mitochondrial biogenesis. *FASEB J.* 24(5):1431-41 PMCID in progress.
- 15- Soto I.C., Fontanesi F., Valledor M., Horn D., Singh R. and <u>Barrientos A</u>. (2009) Synthesis of cytochrome *c* oxidase subunit 1 is translationally down-regulated in the absence of functional F₁F₀-ATP synthase. *Biochim. Biophys. Acta (Mol. Cell. Res.)* 1793:1776-86

# C. Research Support

# Ongoing Research Support

#### RO1 GM071775-06A1

1-1-2012 / 12-31-2015.

"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

Muscular Dystrophy Association.

1-1-2011 / 12-31-2013.

"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.

2 R01 GM071775-06A1 (Supplement)

1-1-2013 / 12-31-2015.

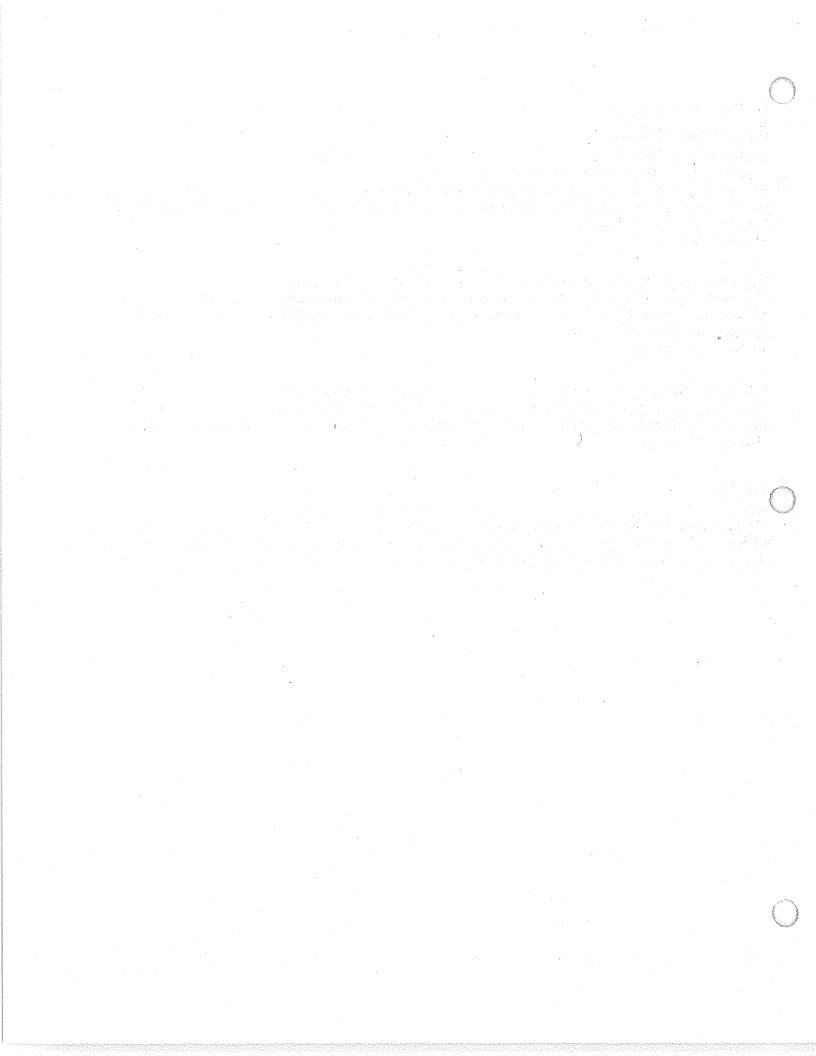
"Macromolecular assemblies in cells". We use the human cell culture models to study cytochrome c oxidase assembly and how it is regulated at the translational level though dynamic protein-protein interactions. PI: Antoni Barrientos.

# Pending:

NIH

7-1-2013 / 6-31-2018

"Mitochondrial Regulation of Neurodegenerative Proteotoxicities". We use the yeast chronological aging models of Parkinson disease and Huntington disease to study the role of mitochondrial respiration and reactive oxygen production in proteotoxicity and their modulation by nutritional cues. PI: Antoni Barrientos.



Provide the following information for the key personnel in the order listed for Form Page 2. Follow the sample format for each person, **DO NOT EXCEED FOUR PAGES**.

NAME

POSITION TITLE

Elizabeth A. Crocco, M.D.

**Clinical Assistant Professor** 

| INSTITUTION AND LOCATION                                    | DEGREE<br>(if | YEAR(s) | FIELD OF STUDY |
|---|---------------|---------|----------------|
|   | applicable)   |         |                |
| Douglas College, Rutgers University, NJ                     | B.S.          | 1989    | Biology        |
| UMDNJ-Robert Wood Johnson Medical<br>School, Piscataway, NJ | M.D.          | 1993    | Medicine       |

#### A. Personal Statement

N/A

# **B.** Positions and Honors.

# **Positions and Employment**

| President and desired and analysis and an arrangement of the second of t | Consideration of the Constitution of the Const |
|--|--|
| 1993-1997<br>1993-1998   | Residency in Psychiatry, Mount. Sinai Medical Center, New York, N.Y  |
| 1995-1997  | Administrative Chief Resident, Mount Sinai Medical Center, New York, N.Y.  |
| 1997-1998  | Chief Fellow, Geriatric Psychiatry, Jackson Memorial Hospital, Mimai, 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-prese   | nt Director, Memory Disorder Center, Department of Psychiatry and Behavioral Sciences, Miller School of Medicine at University of Miami, FL  |
| ) 2/2009-prese   | ent 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 American Psychiatric Association American Association of Geriatric Psychiatry

#### **Honors**

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

Ralph Kaufman Memorial Award for most outstanding resident, Mt. Sinai Medical Center, NYC.

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

Whitcomb DC, Larusch J, Krasinskas AM, Crocco E, Wright CB et al. Common genetic variants in the CLDN2 and PRSS1-PRSS2 loci alter risk for alcohol-related and sporadic pancreatitis. Nat Genet. 2012; 44: 1349-54. PMCID: PMC3510344

**Crocco EA**, Castro, K, Loewenstein D. How late-life depression affects cognition: neural mechanisms. *Current Psychiatric Reports*. 2010;12(1): 34-38.

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.

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.* 

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.

**Crocco E**, Loewenstein DA. Psychiatric aspects of mild cognitive impairment. *Current Psychiatric Reports*. 2005; 7: 32-36.

Ownby RL, Rodríguez L, **Crocco E**, Duara R. Patient and caregiver reports of medication adherence. *International Psychogeriatrics*. 2003;15(Supp 2):310.

Ownby RL, **Crocco E,** Duara R. Memory disorder clinic patients' reports of medication adherence. *Journal of Clinical Psychiatry*. 2002;63:1076.

# D. Research Support <u>Active</u>

XZ003 (PI: Wright/ Crocco) State of Florida, Division of Elder Affairs University of Miami Memory Disorder Clinic 07/01/12-06/30/13

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.

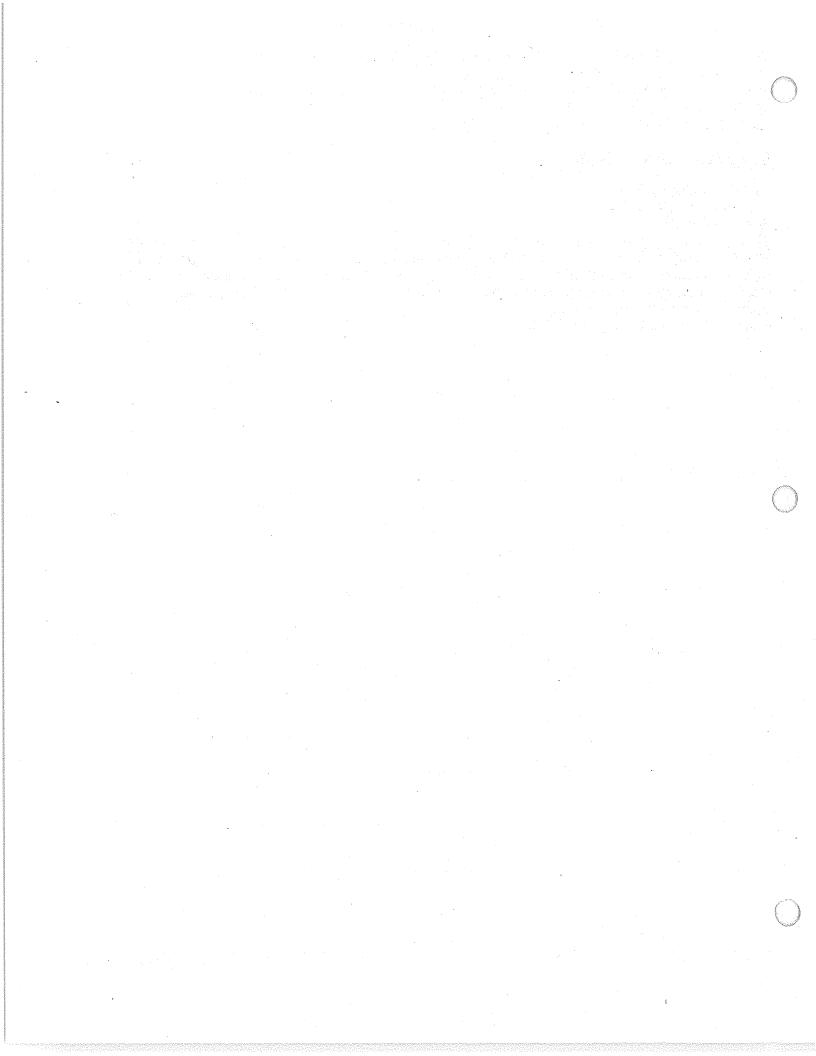
Status of Candidate on Grant: Principal Investigator

## **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, 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.

Role: Co-Investigator: Elizabeth Crocco, M.D.,



| NAME                                     | POSITION TITLE |                       |
|--|----------------|-----------------------|
| Sara J. Czaja, Ph.D.                     | Professor      | and the second second |
| eRA COMMONS USER NAME (credential, e.g., |                |                       |
| agency login)                            |                |                       |

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as

| INSTITUTION AND LOCATION  | DEGREE<br>(if<br>applicable) | YEAR(s)              | FIELD OF STUDY   |
|---|------------------------------|----------------------|--|
| State University of NY College at Buffalo, NY<br>State University of NY at Buffalo, NY<br>State University of NY at Buffalo, NY | B.S.<br>M.S.<br>Ph.D.        | 1975<br>1976<br>1980 | Psychology<br>Industrial Engineering<br>Human<br>Factors/Industrial<br>Engineering |

# A. Personal Statement

N/A

#### **B.** Positions and Honors

| 1980-1982    | Senior Research Associate, Buffalo Organization for Social and Technological Innovation, Inc   |
|--------------|--|
| 1984-1988    | Assistant Professor, Department of Industrial Engineering, SUNY at Buffalo                     |
| 1988-1991    | Associate Professor, Tenured, Department of Industrial Engineering, SUNY at Buffalo            |
| 1989-1990    | Research Associate, Professor, Department of Industrial Engineering, University of Miami       |
| 1988-1993    | Research Director, Stein Gerontological Institute, Miami, FL                                   |
| 1991-1994    | Associate Professor, Department of Industrial Engineering, University of Miami                 |
| 1993-1999    | Director, Center on Human Factors & Aging Research, University of Miami School of Medicine     |
| 1994-present | Professor, Dept. of Psychiatry and Behavioral Sciences, University of Miami School of Medicine |
| 1994-present | Professor, Department of Industrial Engineering, University of Miami, Coral Gables, FL         |
| 1999-present | Director, Center on Aging and Technology Research, University of Miami School of Medicine      |
| 2002-present | Co-Director, Center on Aging, University of Miami, Miami, FL                                   |
| 2010-present | Scientific Director, Center on Aging, University of Miami Miller School of Medicine            |

#### Other Experience and Professional Memberships

Member, The National Academies, Committee on the Role of Human Factors in Home Healthcare, March 2009-June 2011

Member, Technical Expert Panel, Evidence Based Practice Center, Johns Hopkins University, March 2008-present

Member, Board of International Society for Gerontechnology, June 2008

Member, Advisory Committee, National Alliance for Caregiving, Spring 2008

Member, Program Committee for the International Association of Science and Technology for Development (IASTED), June 2007 – June 2008

Member, Subcommittee, Ely Award, Human Factors and Ergonomics Society, 2007 - present

Faculty Affiliate, Department of Biomedical Informatics, Columbia University, April 2008 - present

Member, Program Committee for the International Association of Science and Technology for Development (IASTED), June 2007–June 2008

Member, Subcommittee, Ely Award, Human Factors and Ergonomics Society, 2007

Member, Program Committee Ninth International ACM SIGACCESS Conference of Computers and Accessibility, 2007-2008

#### Honors

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. Keates S, Adams R, Bodine C, Czaja SJ, Gordon W, Gregor P et al. Cognitive and learning difficulties and how they affect access to IT systems. Univ Access Inf Soc. 2007; 5: 329-339.
- 2. Schulz R, Hebert RS, Dew MA, Brown SL, Scheier MF, Beach SR, Czaja SJ, Martire LM, Coon D, Langa KM, Gitlin LN, Stevens AB, Nichols L. Patient suffering and caregiver compassion: New opportunities for research, practice, and policy. Gerontologist 2007; 47(1): 4-13.
- 3. Nair S, Czaja SJ, Sharit J. A multilevel modeling approach to examining individual differences in skill acquisition for a computer-based task. J Gerontol B Psychol Sci Soc Sci. 2007; 62B: 85-96.
- 4. Ownby R, Czaja SJ, Loewenstein D, Rubert M. Cognitive abilities that predict success in a computer-based training program. Gerontologist 2008; 48(2): 170-180.
- 5. Pak R, Czaja SJ, Sharit J, Rogers WA, Fisk AD. The Role of Spatial Abilities and age in Performance in an Auditory Computer Navigation Task. Comput Human Behav 2008; 24: 3045-3051.
- 6. Czaja SJ, Sharit J, Nair SN. Usability of the medicare health website. JAMA 2008; 300 (7): 790-792.
- 7. Lee CC, Czaja SJ, Sharit J. Training older workers for a technology-based jobs. Educ Gerontol. 2009; 35: 15-3
- 8. Schulz R, Czaja SJ, Lustig A, Zdaniuk B, Martire LM, Perdomo D. Improving the quality of life of caregivers of persons with spinal cord injury: A randomized controlled trial. Rehabil Psychol. 2009; 54(1): 1-15
- 9. Sharit J, Hernandez M, Czaja SJ, Pirolli P. Investigating the roles of knowledge and cognitive abilities in older adult information seeking on the Web. ACM Trans Comput Hum Interact 2009; 15(1): Article 3
- 10. **Czaja SJ**, Sharit J. The aging of the population: Opportunities and challenges for human factors engineering. The Bridge 2009; 39(1): 34-40.
- 11. Czaja SJ, 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.
- 12. **Czaja SJ**, Gregor P, Hanson VL. Introduction to the special Issue on aging and information technology. ACM Transactions on Accessible Computing 2009; Vol. 2, No.1, Article 1.
- 13. Sharit J, **Czaja SJ**, 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.
- 14. Taha, J., Sharit, J., Czaja, S.J.. Use of and Satisfaction with Sources of Health Information Among Older Internet Users and Non-Users. The Gerontologist 2009, Vol. 49, No. 5, 663–673
- 15. Schulz, R., Monin, J.K., Czaja, S.J., Lingler, J., Beach, S.R., Martire, L.M., Dodds, A., Hebert, R., Zdaniuk, B., Cook, T.B. (2010). Measuring the Experience and Perception of Suffering. *The Gerontologist*, Vol. 50, No. 6, 774-784.

# D. Research Support. Ongoing research

# 1UL1TR000460-01A1 (Szapocznik, J)

7/27/2012 - 5/31/2017

**NCATS** 

Title: "Miami Clinical and Translational Science Institute"

#### 1R21AG041740-01

4/01/2012 - 03/31/2014

<u>Principal Investigators</u> Sara J. Czaja, Phillip Harvey, David Loewenstein NIH/NIA

Title: "Improving the Functional Outcomes in Older Adults with Schizophrenia"

Principal Investigator Raymond Ownby, M.D.

4/1/11-9/30/12

S. Czaja. Investigator

NIH/National Heart, Lung & Blood Institute, Subcontract from Nova University

This is a project examining health literacy and creating new tools to assess health literacy in English-speaking

Biographical Sketch Format Page

Program Director/Principal Investigator (Last, First, Middle): Czaja, Sara J.

and Spanish-speaking older adults.

Dan Santisteban, Ph.D., Principal Investigator

9/30/09 - 9/29/11

Sara Czaja, Ph.D., Investigator

National Center for Minority Health and Health Disparities

This project is examining the efficacy of a family-based educational intervention delivered via technology for troubled adolescents.

1 R01 NS0072599-01 Antoni, Michael (PI)

8/16/10-5/31/15

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.

2 PO1 AG017211-11 Czaja (PI)

8/1/09 -7/31/14

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.

1 R21 HS018831-01A Czaja (PI)

4/01/11-9/30/12

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.

VA247-P-1116 Ruggiero, Kenneth (PI)

10/25/10-9/24/11

Subcontract: Augusta VAMC and Medical Univ of South CA

Research and Development Services that will develop and evaluate a web-based intervention of OIF-OEF Veterans with mental health problems associated with PTSD, MDD, and/or substance abuse for the VA Medical Center, Charleston, SC

1 RCI MD004703 Daniel Santisteban (PI)

9/24/09 - 8/31/11

A Culturally Informed Tele-Intervention for Minority High Risk Youth and Parents

The study is designed to enhance, refine, and test using a randomized trial, a culturally informed and tailored intervention for high risk minority adolescents and their parents that will be delivered primarily via a mobile/wireless system using a multi-media format that includes text, audio, video and graphics

101UM-Czaja (PI)

9/16/10-7/31/11

Alzheimer's Disease Supportive Service Project (ADSS) REACH

AOA - Alliance on Aging

This project represents the formation of a collaborative partnership with the State of Florida, Dept of Elder Affairs, namely Alzheimer's Disease Supportive Services Project (ADSSP). It will benefit our community by utilizing and translating the evidence base into community programs to develop how-to manuals for replication of community REACH II training in conjunction with ADSSP Resource Center.

Retirement Research Foundation Czaia (PI)

10/01/08 - 9/31/11

A Psychosocial Intervention Program for Working Caregivers

To implement and test the effectiveness of a multi-component psycho-social technology-based intervention aimed at reducing the risk for adverse health outcomes and enhancing work performance and quality of life of working caregivers of older adults; and to refine and package the intervention program for working caregivers so that it can be implemented in a wide variety of work settings.

**Biographical Sketch Format Page** 

1R21CA133487-02 Zarcadoolas, Christina (PI)

12/1/08-11/30/10

# Developing Evidence-Based Guidelines for Patient Accessible Medical Record

Mount Sinai School of Medicine/NIH

Electronic Health Applications. Development of protocols for focus groups and oversight of usability testing. This project includes data analysis and manuscript preparation.

The OASIS Institute Czaja (PI)

2/01/09 - 7/31/10

**Oasis Connections Effectiveness Study** 

Evaluate the effectiveness of the OASIS Connections curriculum in teaching older adults basic computer and Internet skills so that they are able to successfully adapt to today's technology environment.

1 R01 NS055672-01Antoni, Michael (PI)

10/01/06 - 9/30/10

Cognitive Behavioral Stress Management for Chronic Fatigue Syndrome

4-year study that uses a 10-week telephone based cognitive behavioral stress management intervention (T-CBSM) to illuminate neuroimmune mechanisms underlying the effects of stress and stress management on physical health and immune regulation in individuals with chronic fatigue syndrome (CFS) relative to participants receiving a health promotion telephone (T-HP) intervention.

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   | POSITION TITLE        |  |
|--|-----------------------|--|
| Hannah Gardener  | Assistant Scientist   |  |
| eRA COMMONS USER NAME (credential, e.g., agency login) | and the second second |  |

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<br>(if applicable) | MM/YY     | FIELD OF STUDY                      |
|--|---------------------------|-----------|-------------------------------------|
| Dartmouth College, New Hampshire               | AB                        | 1996-2000 | Psychological and Brain<br>Sciences |
| Harvard School of Public Health, Massachusetts | ScD                       | 2003-2007 | Epidemiology                        |
|  |                           | 1         |                                     |

#### A. Personal Statement: N/A

#### B. Positions and Honors

# Research and Professional Experience

## Positions and Employment

| 12/ 2009- present | Assistant Scientist, Department of Neurology, University of Miami Miller School of Medicine, Miami, FL                       |
|-------------------|--|
| 4/2009- 9/2009    | Research Assistant Professor, Department of Pediatrics, University of Miami Miller School of Medicine, Miami, FL             |
| 9/ 2007- 4/2009   | Post-doctoral Associate, Department of Neurology, University of Miami Miller School of Medicine, Miami, FL                   |
| 7/ 2002- 9/2004   | Senior Research Assistant, Department of Society, Human Development, and Health, Harvard School of Public Health, Boston, MA |

# C. Selected Peer-reviewed Publications (in chronological order)

- 1. 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*. (in press)
- 2. **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*. (in press)
- 3. **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. (in press)
- 4. 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)
- 5. 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
- 6. 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

- 7. **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.
- 8. **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.
- 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
- 10. **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
- 11. 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
- 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
- 13. 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
- 14. **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
- 15. 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

## D. Research Support

Active

None

Completed: N/A

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                  | POSITION TITLE |  |
|-----------------------|----------------|--|
| Carlos T. Moraes      | Professor      |  |
| eRA COMMONS USER NAME |                |  |
| cmoraes               |                |  |

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

| INSTITUTION AND LOCATION                                       | DEGREE<br>(if applicable) | YEAR(s) | FIELD OF STUDY         |
|--|---------------------------|---------|------------------------|
| Escola Paulista de Mediclna, Sao Paulo, Brazil                 | B.Sc.                     | 1983    | Biomedical Sciences    |
| Escola Paulista de Mediclna, Sao Paulo, Brazil                 | M.Sc.                     | 1987    | Molecular Biology      |
| Department of Genetics and Development,<br>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 APPOINTMENT | P | R | O | F | E | S | S | 1 | O | N | 1/ | Á١ | L | A | P | P | O | I | N | 7 | 'N |  |  | V. | T | S |
|--------------------------|---|---|---|---|---|---|---|---|---|---|----|----|---|---|---|---|---|---|---|---|----|--|--|----|---|---|
|--------------------------|---|---|---|---|---|---|---|---|---|---|----|----|---|---|---|---|---|---|---|---|----|--|--|----|---|---|

| <sup>1</sup> 2005 - | Professor (Tenured). | Dept. of Neurology, | University of Miam | i, 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:**

| 2010 - present | NIH Scientific Review Panel Member (NOMD Review Group)                                   |
|----------------|--|
| 2002 - 2006    | NIH Scientific Review Panel Member (GHD Review Group)                                    |
| 2007 - Present | Scientific Advisory Committee member, Muscular Dystrophy Association                     |
| 1999 - 2004    | Scientific Advisory Committee member, Muscular Dystrophy Association                     |
| 2007 - 2012    | Scientific and Medical Advisory Board (SMAB) Chair, United Mitochondrial Disease         |
| Foundation     |  |
| 2005 - 2012    | SMAB member, United Mitochondrial Disease Foundation                                     |
| 2005           | Provost Award for Scholarly Activity, University of Miami                                |
| 2002 - 2006    | NIH Scientific Review Panel Member (Genetics of Health and Disease Review Group)         |
| 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).

### **MOST RELEVANT PUBLICATIONS (5)**

- 1. Bacman SR, Williams SL, Hernandez1 D, Moraes CT. Modulating mtDNA heteroplasmy by mitochondria-targeted restriction endonucleases in a "differential multiple cleavage-site" model. *Gene Therapy*, 14:1309-1318 (2007)
- 2. Sion AR, Williams L, Moraes CT. *In vivo* methylation of mtDNA reveals the dynamics of protein-mtDNA interactions. *Nucl. Acid Res.* 37:6701-6715 (2009)
- 3. Wenz T, Rossi SG, Rotundo RL, Spiegelman B, Moraes CT. Increased muscle PGC-1α expression protects from sarcopenia and metabolic disease during aging. *Proc. Natl. Acad. Sci. USA* 106:20405-20410 (2009)
- 4. 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)
- 5. Bacman SR, Williams SL, Duan D, Moraes CT. Manipulation of mtDNA heteroplasmy in all striated muscles of newborn mice by AAV9-mediated delivery of a mitochondria-targeted restriction endonuclease. *Gene Therapy*;19:1101-6 (2012)

# **ADDITIONAL RELEVANT PUBLICATIONS (10)**

- 6. Moraes CT, Shanske S, Trishler H-J, Aprille JR, Andreetta F, Bonilla E, Schon EA, 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)
- 7. Moraes CT, Ciacci F, Bonilla E, Ionascescu V, Schon EA, DiMauro S. A mitochondrial tRNA anticodon swap associated with a muscle disease. *Nature Genetics*, 4:284-287 (1993)
- 8. Bayona-Bafaluy MP, Blits B, Battersby B, Shoubridge EA, Moraes CT. 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)
- 9. Wenz T, Luca C, Torraco A, Moraes CT. MTERF2 regulates oxidative phosphorylation by modulating mtDNA transcription. *Cell Metabolism* 9:499-511 (2009)
- 10. Srivastava PS, Diaz F, Iommarini L, Aure K, Lombes A, Moraes CT. GC-1α/β induced expression partially compensates for respiratory chain defects in cells from patients with mitochondrial disorders. *Human Molecular Genetics* 18:1805-12. (2009)
- 11. Fukui H, Moraes CT. Mechanisms of formation and accumulation of mitochondrial DNA deletions in aging neurons. Human Molecular Genetics 18:1028-36 (2009)
- 12. Williams SL, Huang J, Edwards YJK, Ulla R, Dillon L, Prolla T, Vance J, Moraes CT, Züchner S. The mtDNA mutation spectrum of the progeroid Polg mutator mouse includes abundant control region multimers. *Cell Metabolism*, 12:675-82. (\*co-corresponding authors) (2010)
- 13. Fukui H, Diaz F, Garcia S, Moraes CT. 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)
- 14. Wenz T, Diaz F, Spiegelman BM, Moraes CT. Activation of the PPAR/PGC-1α pathway prevents a bioenergetic deficit and effectively improves a mitochondrial myopathy phenotype. *Cell Metabolism* 8:249-56. (2008)
- 15. Pickrell AM, Fukui H, Wang X, Pinto M, Moraes CT. The striatum is highly susceptible to mitochondrial oxidative phosphorylation dysfunctions. *J Neurosci.*, 31:9895-904. (2011)

#### C. Research Support.

Active

5R01EY010804 Moraes

12/01/94-4/30/13

NIH/NEI (This proposal is an application for continuing funding of this project)

"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: Pl

# 1R01AG036871 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

# 1R01NS079965 Moraes

06/01/2010 - 05/31/2015

NIH/NINDS

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

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

Role:PI

# **Completed Research**

# R56NS041777-09 Moraes

09/15/2010-09/14/2011

NIH/NINDS

"Creating Animal Models with Oxidative Phosphorylation Defects in the CNS"
The objective of this project is to create mouse models of mitochondrial diseases.
Role: Pl

#### 2 R01 CA085700-05A1 Moraes

04/1/2005-12/31/2010

NIH/NCI

"Oxidative phosphorylation in cell growth and death"

The objective of this project is to investigate the role of cytochrome c in apoptosis.

Role: PI

#### 09KW-02 Barrientos and Moraes

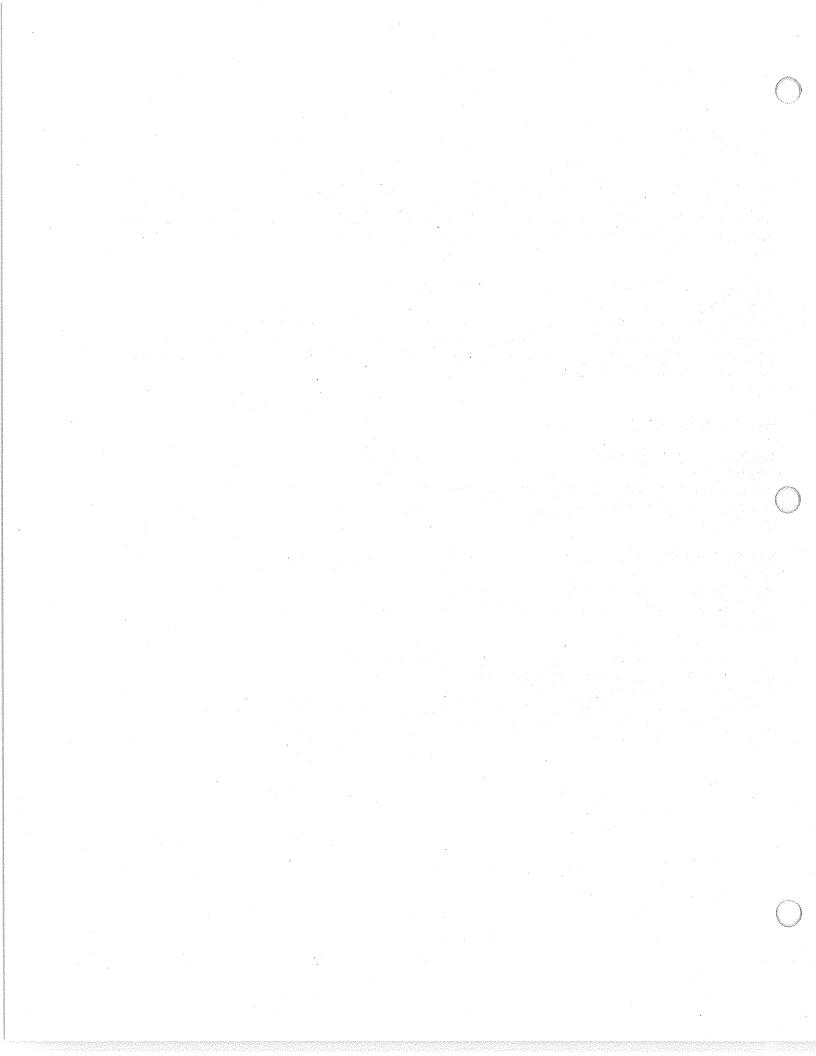
01/01/2010-12/31/2011

FSDH James and Esther King Biomedical Research Program

Project Title: Slowing Dengenerative Processes by Bolstering Cellular Bioenergetics

The goals of this project are to use different transcription factors that stimulate mitochondrial biogenesis to reduce the impact of OXPHOS defects in degenerative processes.

Role: Co-PI



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<br>Miguel A. Perez-Pinzon   | POSITION TITLE<br>Professor  |                                 |             |
|--|------------------------------|---------------------------------|-------------|
| eRA COMMONS USER NAME (credential, e.g., agency login) mperezpinzon                                  |                              |                                 |             |
| EDUCATION/TRAINING (Begin with baccalaureate or other initial pro residency training if applicable.) | fessional education, such as | nursing, include postdoctoral t | raining and |

| INSTITUTION AND LOCATION | DEGREE<br>(if applicable) | 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

I direct the Cerebral Vascular Disease Research Center at the University of Miami since 2005, which was established approximately 45 years ago. I am Professor of Neurology and Neuroscience and I am Vice-Chairman of Basic Sciences in the Department of Neurology. My main research expertise is in the area of cerebral ischemia, which results from cardiac arrest or a stroke. My research focuses on the areas of synaptic, vascular and mitochondrial dysfunction that ensue following cerebral ischemia. Over the last 17 years, my laboratory has investigated the signaling pathways that lead to neuroprotection against ischemia following ischemic preconditioning (IPC). Our goal is to develop new therapies for pre- and post-preatment in stroke and acute myocardial infarction patients.

#### **B.** Position and Honors

| Positions and E | <u>mployment</u>  |
|-----------------|---|
| 1982-1983       | Research assistant: Smithsonian Tropical Research Institute. Dr. Peter W. Glynn (Supervisor). |
| 1985            | Research Assistant: Smithsonian Tropical Research Institute. Drs. Jeffrey Graham and          |
|                 | Ira Rubinoff (Supervisors)  |
| 1988            | Teaching Assistant, Physiology of Marine Organisms; University of Miami, Miami, Fl            |
| 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, Fl

Honors, Awards, and Professional Societies

1982, 1983 Fellowships (2), Smithsonian Tropical Research Institute (STRI).

1986 Fellowship, Fishing and Conservation Trust. Miami, Fl

1989 - present Member of Society for Neuroscience (1989), International Society on Oxygen Transport to Tissues (1996), International Society of Cerebral Blood Flow and Metabolism (1995), American Association for the Advancement of Science (1996) and American Heart

American Association for the Advancement of Science (1990) and American nea

Association (2000)

Koczy Fellowship, (Student of the year) for excellence in graduate research and

education, Rosenstiel School of Marine and Atmospheric Science, University of Miami,

Miami, Fl

1991 Invited speaker at the Society for Experimental Biology in Birmingham, U.K.

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)

# C. Publications (out of 105)

- 1. Garbayo E, Raval AP, Curtis KM, Della-Morte D, Gomez L A, D'Ippolito G, Reiner T, Perez-Stable C, Howard GA, **Perez-Pinzon M A**, Montero-Menei CN, Schiller PC. 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*. doi:10.1111/j.1471-4159.2011.07272.x (2011)
- 2. Curtis KM, Gomez LA, Rios C, Garbayo E, Raval AP, **Perez-Pinzon MA**, Schiller PC. EF1alpha and RPL13a represent normalization genes suitable for RT-qPCR analysis of bone marrow derived mesenchymal stem cells. *BMC Mol Biol* 11, 61, (2010)
- 3. Defazio R A, Levy S, Morales CL, Levy RV, Dave KR, Lin HW, Abaffy T, Watson BD, **Perez-Pinzon M A**, Ohanna V. A protocol for characterizing the impact of collateral flow after distal middle cerebral artery occlusion. *Transl Stroke Res* 2, 112-127, doi:10.1007/s12975-010-0044-2 (2011)
- 4. Lin HW, Defazio RA, Della-Morte D, Thompson JW, Narayanan SV, Raval AP, Saul I, Dave KR, **Perez-Pinzon MA**. Derangements of post-ischemic cerebral blood flow by protein kinase C delta. *Neuroscience* 171, 566-576, (2010)
- 5. Dezfulian C, Alekseyenko A, Dave KR, Raval AP, Do R, Kim F, **Perez-Pinzon MA** Nitrite therapy is neuroprotective and safe in cardiac arrest survivors. Nitric Oxide. (*in press*)
- 6. Perez-Pinzon M, Stetler R and Fiskum G (2012) Novel mitochondrial targets for neuroprotection. J Cereb Blood Flow Metab. (in press)
- 7. Koch S, Sacco R, **Perez-Pinzon M**. Preconditioning the brain: moving on to the next frontier of neurotherapeutics. *Stroke*. (*in press*)

- 8. 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**. Differential effects of delta and epsilon protein kinase C in modulation of postischemic cerebral blood flow. *Adv Exp Med Biol* 737:63-9; 2012
- 9. Ding D, Enriquez-Algeciras M, Dave KR, **Perez-Pinzon M**, Bhattacharya SK .The role of deimination in ATP5b mRNA transport in a transgenic mouse model of multiple sclerosis. *EMBO Rep*. (in press) 2012
- 10. Dave KR, Bhattacharya SK, Saul I, DeFazio RA, Dezfulian C, Lin HW, Raval AP, 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). PMCID: PMC3137627
- 11. Morris KC, Lin HW, Thompson JW, **Perez-Pinzon MA**, Pathways for ischemic cytoprotection: Role of sirtuins in caloric restriction, resveratrol, and ischemic preconditioning. *J Cereb Blood Flow Metab*, 2011. 31(4): p. 1003-19. PMCID:PMC3070983
- 12. Lin, HW, Thompson JW, Morris KC, **Perez-Pinzon MA**. Signal Transducers and Activators of Transcription: STATs-Mediated Mitochondrial Neuroprotection. *Antioxid Redox Signal*, 2011. 14(10): p. 1853-61. PMCID:PMC3078497
- 13. Defazio RA, Levy S, Morales CL, Levy RV, Dave KR, Lin HW, Abaffy T, Watson BD, **Perez-Pinzon MA**, Ohanna V. A protocol for characterizing the impact of collateral flow after distal middle cerebral artery occlusion. *Transl Stroke Res.* 2011. 2(1):112-127. PMCID:PMC3095390
- 14. Koch S, Katsnelson M, Dong C, **Perez-Pinzon M.** Remote ischemic limb preconditioning after subarachnoid hemorrhage: a phase lb study of safety and feasibility. *Stroke*. 2011. 42(5):1387-91. PMCID:PMC3082628
- 15. Lin, HW, Defazio RA, Della-Morte D, Thompson J, Narayanan SV, Raval AP, Saul I, Dave KR, **Perez-Pinzon MA.** Derangements of post-ischemic cerebral blood flow by protein kinase C delta. *Neuroscience*, 2010. 171(2): p. 566-76. PMCID:PMC2981031

# D. Research Support

# Ongoing Research Support

RO1 NS45676-05 **Pérez-Pinzón (PI)** 6/1/07-5/31/15 NIH/NINDS

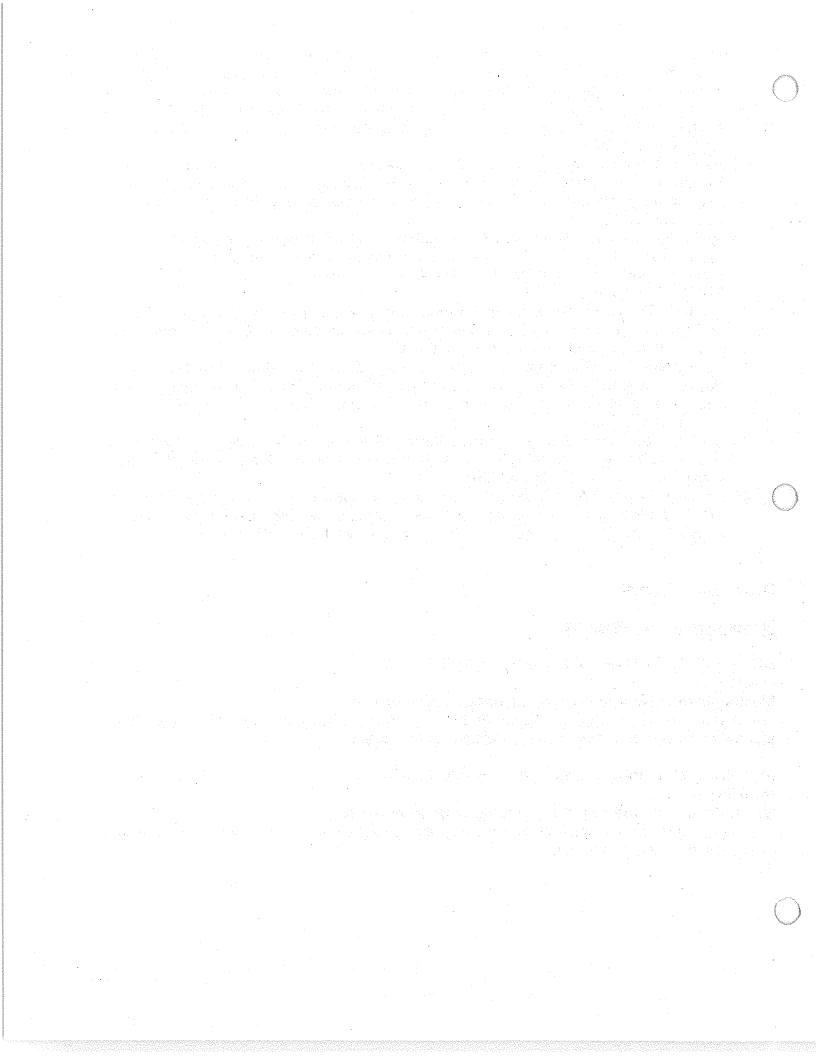
# Mechanisms of Neuroprotection against Cardiac Arrest

The major goal of this project is to study the mechanisms of synaptic and vascular dysfunction and putative neuroprotective agents following cardiac arrest.

RO1 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



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

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

POSITION TITLE
Research Assistant Professor

| EDUCATION/TRAINING (Begin with baccalaurea | te or other initial pro | ofessional education, s | such as nursing, and include postdoctoral training.) |
|--|-------------------------|-------------------------|--|
|  | DEGREE                  |                         |  |

| INSTITUTION AND LOCATION         | DEGREE<br>(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                      |

# 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.

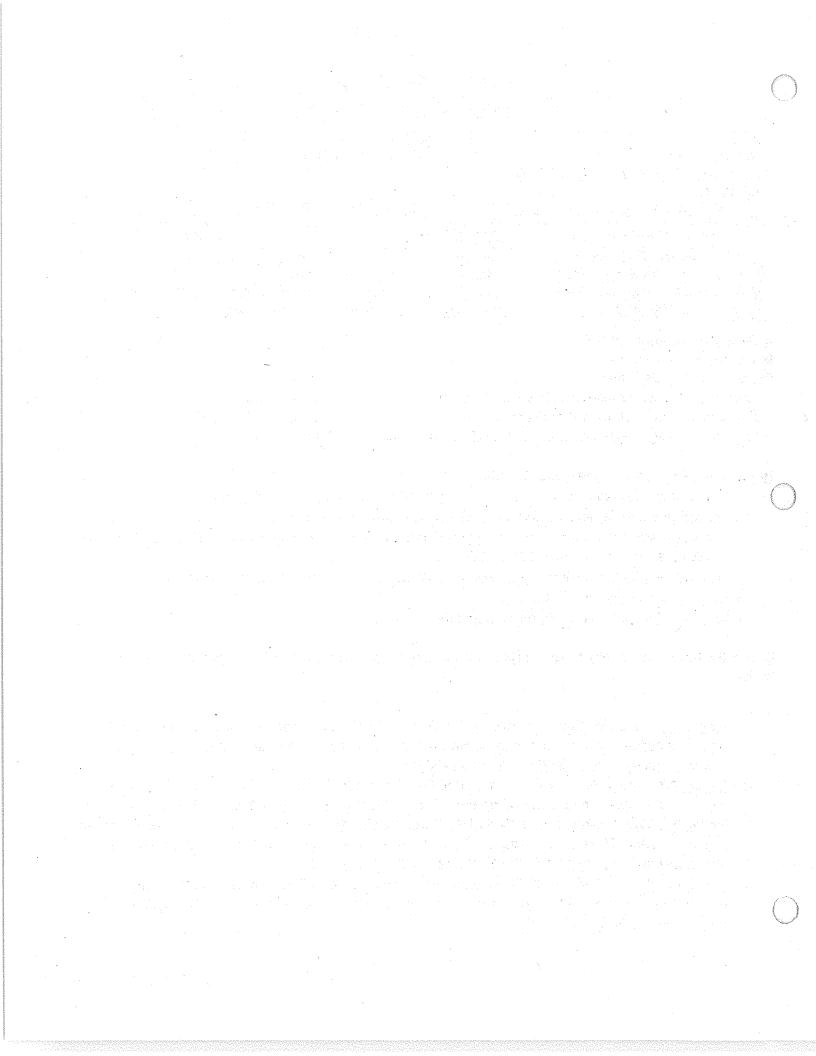
Lecturer: Zoology, M. S. University of Baroda, Gujarat, India. 07/1994 to 11/2000.

# 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-β 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, Saul I, Dave KR, DeFazio RA, Perez-Pinzon MA, Bramlett H. (2009) Pretreatment with a single estradiol-17β bolus activates CREB and protects CA1 neurons against global cerebral ischemia. Neuroscience. 160; 307–318. (PMID: 19272413; PMCID: 2711690)
- Raval AP, Bhatt A, Saul I. (2009) Chronic nicotine exposure inhibits 17β-estradiol-mediated protection of the hippocampal CA1 region against cerebral ischemia in female rats. Neuroscience letters. 458(2):65-69. (PMID: 19442878)



- 5. Raval AP, Bramlett H and Perez-Pinzon MA. (2006) Estrogen preconditioning protects the hippocampal CA1 against ischemia. Neuroscience. 141(4):1721-1730. (PMID: 16777351)
- 6. Raval AP, Dave KR, Mochly-Rosen D, Sick TJ, Perez-Pinzon MA. (2003) εPKC 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)
- 7. Lange-Asschenfeldt C\*, Raval AP\*, Dave KR, Mochly-Rosen D, Sick TJ, Pérez-Pinzón MA. (2004) εPKC 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)
- 8. Bright R, Raval AP, Dembner JM, Pérez-Pinzón MA, Steinberg GK, Yenari MA, Mochly-Rosen D. (2004) Protein kinase C delta mediates cerebral reperfusion injury in vivo. J. Neuroscience. 24 (31): 6880-6888. (PMID: 15295022)
- 9. 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)
- 10. 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)
- 11. 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)
- 12. 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. Journal of Neuroscience. 16; 28(16):4172-4182. (PMID: 18417696; PMCID: 2678917)
- 13. Kim E, 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. Journal of Cerebral Blood Flow & Metabolism. 28(7):1329-1340. (PMID: 18398416; PMCID: 2645802)
- 14. <u>Raval AP</u>. (2011) Nicotine addiction causes unique detrimental effects on female brain. Journal of Addictive Diseases. Review 30(2):149-58. (PMID: 21491296)
- 15. Raval AP, Sick JT, Gonzalez GJ, Defazio RA, Dong C and Sick TJ. Chronic nicotine exposure inhibits estrogen-mediated synaptic functions in hippocampus of female rats. Neuroscience letters 2012; 517(1):41-6

# D. 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.

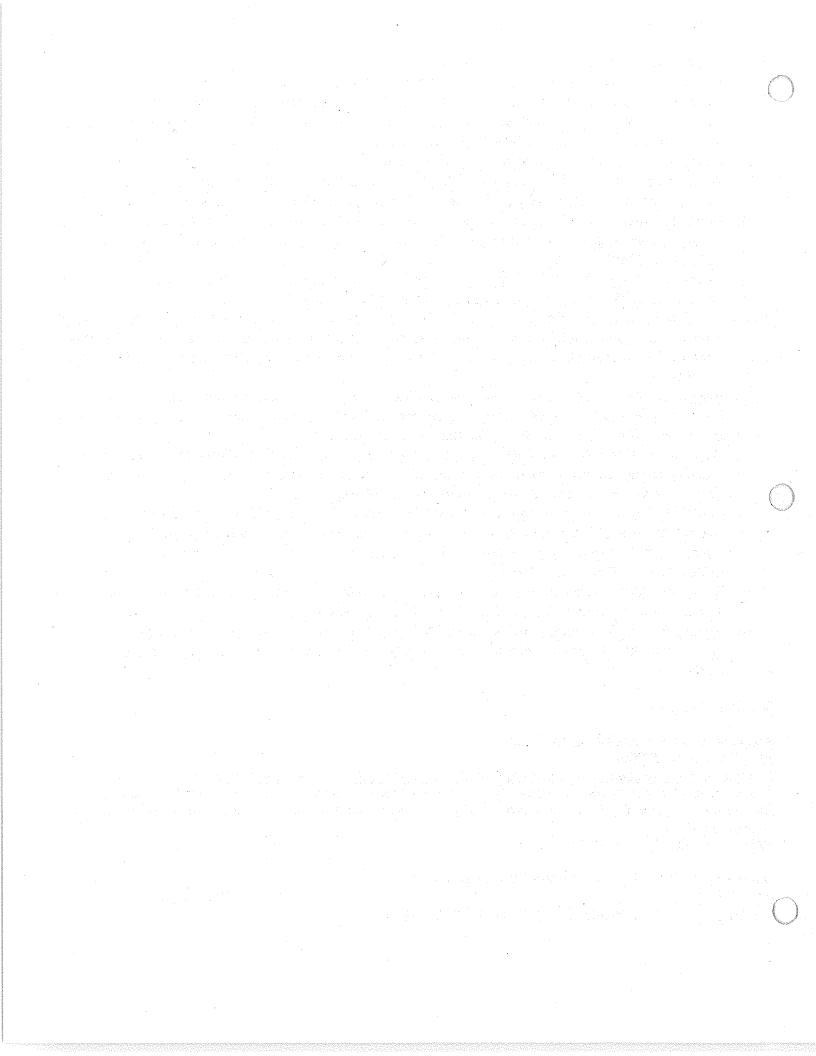
The major goal of this project is to study the effects of chronic nicotine usage on synaptic functions in female rats. There is no scientific/ financial overlap between NIH-R01 application under consideration and the funded AHA-grant-in-aid.

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

Florida Department of Heath#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, Adolescents (UM-SCOR) 10/1/2011-3/31/2013

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

Role: Pl. 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 Heath

#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, Pl. % 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 EPKC protect neuronal mitochondria whereas δPKC 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

