

**BIOGRAPHICAL SKETCH**

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NAME: Swerdlow, Russell Howard

POSITION TITLE: Gene and Marge Sweeney Professor of Neurology

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

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

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
New York University, New York, New York	B.A.	05/1987	Psychobiology
New York University, New York, New York	M.D.	05/1991	Medicine
University of Virginia, Charlottesville, Virginia	Clinical Training	06/1992 06/1995	Medicine Intern Neurology Resident
Western State Hospital, Staunton, Virginia/ University of Virginia, Charlottesville, Virginia	Clinical Fellowship	06/1996	Geriatric Neuropsychiatry
University of Virginia, Charlottesville, Virginia	Postdoc (Laboratory)	06/1997	Neurodegenerative Diseases

**A. Personal Statement**

I am a physician-scientist who primarily studies brain energy metabolism and the role brain energy metabolism plays in neurodegenerative diseases. My main area of clinical expertise includes the neurodegenerative diseases that affect cognition, and especially Alzheimer's disease. My research focuses on why brain bioenergetic function declines with advancing age, why brain bioenergetic changes are accentuated in neurodegenerative disease states, and how to repair and reverse age-and-neurodegeneration-related bioenergetic dysfunction. I began this line of investigation as an undergraduate trainee, and as a medical student I continued my research training as part of my university's Research Honors Program. During my post-graduate neurology training I focused on studies of mitochondrial function and genetics in a basic science laboratory. Upon completing my residency I completed additional formal training in cognitive disorders, and a postdoctoral fellowship in a mitochondria-focused laboratory. With the support of a K08 Award I transitioned to an independent investigator, and since then I have continuously pursued my research program. To date my research has covered several research disciplines, including basic, translational, and clinical research and I have served as a PI on multiple types of NIH grants (K08, R03, R01, P30) as well as a Col on multiple other grants. The sum of my experience to date puts me in a good position pursue a broad range of research projects relating to brain bioenergetics, brain aging, and neurodegenerative diseases.

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

1991-95 Internal Medicine Intern and Neurology Resident, University of Virginia, Charlottesville  
 1995-96 Clinical Fellowship, Geriatric Neurology and Neuropsychiatry, Western State Hospital, Staunton, Virginia/ University of Virginia, Charlottesville  
 1995-97 Postdoctoral Research Fellowship, Neurodegenerative Diseases, Dept. Neurology, University of Virginia, Charlottesville  
 1996-97 Clinical Instructor of Neurology, Dept. Neurology, University of Virginia, Charlottesville  
 1997-03 Assistant Professor of Neurology, Dept. Neurology, University of Virginia, Charlottesville

- 1998-07 Neurology Consultant, Western State Psychiatric Hospital, Staunton, Virginia
- 2003-07 Associate Professor of Neurology, Dept. Neurology, University of Virginia, Charlottesville
- 2007- Professor of Neurology and Molecular & Integrative Physiology, School of Medicine, University of Kansas Medical Center, Kansas City, KS
- 2010- Professor of Biochemistry and Molecular Biology, School of Medicine, University of Kansas Medical Center, Kansas City, KS

**Other Experience and Professional Memberships**

- 1992- American Academy of Neurology (1992), Society for Neuroscience (1996)
- 2001-07 Auxiliary Awards Subcommittee, American Academy of Neurology
- 2002- NIH study section reviewer for NIEHS PD Environment-Gene Interactions SEP, CDIN (permanent member 2006-2009), BDCN, NINDS Udall Centers Review Group, NSD-B, NHLBI, CMAD, NIA BSC, NIAAA BSC, Alzheimer's Center Study Section, NST2, NOMD (permanent member 2014-2017); VA Merit study section reviewer for Neurobiology-D (permanent member 2004-2008); reviewer for multiple Foundations
- 2002-07 Alzheimer's Disease and Related Disorders Commission for the Commonwealth of Virginia; Chair of Commission from 2006-2007
- 2004-07 Director, Medical Student Summer Research Program, University of Virginia School of Medicine
- 2004- Board of Directors, CurePSP Foundation (2004-2010); CurePSP Research Committee Chair (2005-2010); CurePSP Vice-Chair (2007-2010); Research Committee Member (2005-2018)
- 2005-07 Director, Telemedicine Memory Disorders Clinic of the Commonwealth of Virginia
- 2005-07 Faculty, Neuroscience Graduate Training Program, University of Virginia
- 2008- Director, Neurodegenerative Disorders Program of the KUMC Institute for Neurologic Discoveries
- 2008-11 Associate Director, KUMC General Clinical Research Center
- 2009- Editorial Board, The Open Pathology Journal (2009-present); Associate Editor, Frontiers in Aging Neuroscience (2009-present); Associate Editor, Journal of Alzheimer's Disease (2010-present); Editorial Board, Biochimica et Biophysica Acta-MBD (2010-present); Editorial Board, Neurology (2010-2017); Chief Clinical Editor, Biochimica et Biophysica Acta-Clinical (2013-2018); Editorial Board, Aging Cell (2019-Present)
- 2010- KUMC IACUC
- 2011- Director, University of Kansas Alzheimer's Disease Center
- 2011- KUMC Institute for Neurologic Discoveries Executive Committee
- 2012-15 KU School of Medicine Research Committee (Chair from 2013-2014)
- 2013-14 KU SOM Faculty Executive Committee; KU Medical Center Faculty Research Council
- 2014-16 KUMC Research Advisory Council
- 2014- Kansas City University of the Biomedical Sciences IRB (non-institutional member)
- 2014- Founding Director, Heartland Center for Mitochondrial Medicine
- 2014- KUMC MD PhD Program Admissions Committee
- 2015- T32 Neuroscience Rehabilitation Training Program Internal Advisory Committee, KUMC
- 2017- NIA Board of Scientific Counselors
- 2019- NIH Center for Alzheimer's and Related Dementias Advisory Group

**Honors**

- 1986-87 Distinguished Undergraduate Research Award; Founders Day Award; Phi Beta Kappa; Magna Cum Laude (New York University College of Arts and Sciences)
- 1987-91 Silverstein Scholarship; Research Honors Program; Medical Degree with Honors in Pathology (New York University School of Medicine)
- 1995 99<sup>th</sup> Percentile, National In-Service Training Examination in Neurology
- 1997 S. Weir Mitchell Award, American Academy of Neurology
- 1998-01 George Cotzias Fellow, American Parkinson's Disease Association
- 2012 University of Kansas 2012 Scholarly Achievement Award
- 2013- Gene and Marge Sweeney Professor of Neurology
- 2014 Chancellor's Club Research Award, Kansas University Medical Center
- 2016 "Meet the Expert" Lecture, Society for Neuroscience Annual Meeting
- 2017- NIA Board of Scientific Counselors
- 2017 Pioneer in Alzheimer's Award, Frontiers in Aging and Regenerative Research ADAR Program
- 2019 NIH Center for Alzheimer's and Neurodegenerative Diseases Planning Meeting

### C. Contributions to Science

1. My work has meaningfully contributed to an emerging appreciation that mitochondria play an important role in common neurodegenerative disease states. My work with cytoplasmic hybrid (cybrid) cell lines prepared through mitochondrial transfer from Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, and progressive supranuclear palsy has over 4100 citations.
  - a. **Swerdlow RH**, Parks JK, Miller SW, Tuttle JB, Trimmer PA, Sheehan JP, Bennett JP, Davis RE, Parker WD. Origin and functional consequences of the complex I defect in Parkinson's disease. Ann Neurol 1996;40:663-670. PMID: 8871587
  - b. **Swerdlow RH**, Parks JK, Cassarino DS, Maguire DJ, Maguire RS, Bennett JP, Parker WD. Cybrids in Alzheimer's disease: A cellular model of the disease? Neurology 1997;49:918-925.
  - c. **Swerdlow RH**, Miller SW, Parks JK, Sheehan JP, Cassarino DS, Maguire DJ, Maguire RS, Bennett JP, Juel VC, Phillips LH, Trimmer PA, Pattee G, Tuttle JB, Davis RE, Parker WD. Mitochondria in sporadic amyotrophic lateral sclerosis. Exp Neurol 1998;153:135-142.
  - d. Silva DF, Selfridge JE, Lu J, E L, Roy N, Huffles L, Burns JM, Michaelis EK, Yan SD, Cardoso SM, **Swerdlow RH**. Bioenergetic flux, mitochondrial mass, and mitochondrial morphology dynamics in AD and MCI cybrid cell lines. Hum Mol Genet 2013;22:3931-3946. PMCID: PMC3888119
2. Based on my cybrid work, I formally proposed the "mitochondrial cascade hypothesis" in an attempt to reconcile mitochondrial function, brain aging, and Alzheimer's disease histopathology. My mitochondrial cascade hypothesis manuscripts have been cited over 1800 times.
  - a. **Swerdlow RH**, Khan S. A "Mitochondrial Cascade Hypothesis" for sporadic Alzheimer's disease. Med Hypoth 2004;63:8-20. PMID: 15193340
  - b. **Swerdlow RH**, Burns JM, Khan SM. The Alzheimer's disease Mitochondrial Cascade Hypothesis. JAD 2010;20 Suppl 2:S265-279. PMCID: PMC2883665
  - c. **Swerdlow RH**, Burns JM, Khan SM. The Alzheimer's Disease Mitochondrial Cascade Hypothesis: Progress and Perspectives. BBA-Mol Biol Dis 2014;1842:1219-1231. PMCID: PMC3962811
3. Based on the hypothesis that manipulating brain energy metabolism may impact neurodegenerative disease progression, I have developed a translational program in brain energy manipulation, or what I have called "bioenergetic medicine". To my knowledge I am the first person to propose the use of ketone bodies for the treatment of Alzheimer's disease. The development of bioenergetic medicine approaches has become an increasing focus in recent years. Relevant papers have been cited over 600 times.
  - a. **Swerdlow R**, Marcus DL, Landman J, Harooni M, Freedman ML. Brain glucose and ketone body metabolism in patients with Alzheimer's disease. Clin Res 1989;37(2):461A.
  - b. E L, Lu J, Selfridge JE, Burns JM, **Swerdlow RH**. Lactate administration reproduces specific brain and liver exercise-related changes. J Neurochem 2013;127:91-100. PMCID: PMC4276250
  - c. Wilkins HM, Harris JL, Carl SM, E L, Lu J, Selfridge JE, Roy N, Huffles L, Koppel S, Morris J, Burns JM, Michaelis ML, Michaelis EK, Brooks WM, **Swerdlow RH**. Oxaloacetate Activates Brain Mitochondrial Biogenesis, Enhances the Insulin Pathway, Reduces Inflammation, and Stimulates Neurogenesis. Hum Mol Genet 2014;23:6528-6541. PMCID: PMC4271074
  - d. E L, Burns JM, **Swerdlow RH**. Effect of high-intensity exercise on aged mouse brain mitochondria, neurogenesis, and inflammation. Neurobiol Aging 2014;35:2574-2583. PMCID: PMC4171347
4. My clinical research has contributed to the genetic understanding of neurodegenerative and mitochondrial diseases. I originally described the kindred that allowed for the discovery that CSF1R mutation causes the disease hereditary diffuse leukoencephalopathy with axonal spheroids (HDLS).
  - a. **Swerdlow RH**, Wooten GF. A novel DDP gene mutation that causes dystonia in female carriers of the Mohr-Tranebjaerg syndrome. Ann Neurol 2001;50:537-540. PMID: 11601506
  - b. **Swerdlow RH**, Miller BB, Lopes BS, Mandell JW, Wooten GF, Damgaard P, Manning C, Fowler M, Brashear RH. Autosomal Dominant Subcortical Gliosis Presenting as Frontotemporal Dementia. Neurology 2009;72:260-267. PMID: 19153373
  - c. Rademakers R, Baker, M, Nicholson AM, Rutherford NJ, Finch N, Soto-Ortolaza A, Lash J, Wider C, Wojtas A, DeJesus-Hernandez M, Adamson J, Kouri N, Sundal C, Shuster EA, Aasly J,

MacKenzie J, Roeber S, Kretzschmar HA, Boeve BF, Knopman DS, Petersen RC, Cairns NJ, Ghetti B, Spina S, Garbern J, Tselis AC, Uitti R, Das P, Van Gerpen JA, Meschia JF, Levy S, Broderick DF, Graff-Radford N, Ross OA, Miller BB, **Swerdlow RH**, Dickson DW, Wszolek ZK. Mutations in the colony stimulating factor 1 receptor (CSF1R) cause hereditary diffuse leukoencephalopathy with spheroids. NatGenet 2011;44:200-205. PMID: PMC3267847

**Complete List of Published Work in my Bibliography:**  
**Over 180 peer-reviewed manuscripts**

<http://www.ncbi.nlm.nih.gov/sites/myncbi/russell.swerdlow.1/bibliography/43469236/public/?sort=date&direction=ascending>

**D. Research Support**

**Ongoing Research Support**

P30 AG035982 Swerdlow (PI) 07/01/11 - 06/30/21  
University of Kansas Alzheimer's Disease Core Center  
The goal of this project is to promote Alzheimer's disease and brain aging research at the University of Kansas.  
Role: PI

R01 AG060733 Swerdlow (PI) 2/1/19-11/30/23  
Validation and Mechanistic Interrogation of Metabolism Targeting for AD  
This project (1) Assesses cognitive effects of a ketogenic diet cognition in Alzheimer's participants in a randomized trial, (2) Determines how the intervention affects bioenergetic, inflammatory, and lipid biology

R01 AG061194 Swerdlow (PI) 2/1/19-11/30/23  
Mechanistic Basis of the mtDNA Haplogroup J-Alzheimer's Disease Association  
This project assesses the effects and determines the mechanistic impact of mtDNA haplogroup J on mitochondrial function and Alzheimer's disease pathology

Department of Defense AZ 170111 Swerdlow and Harris CoPIs 7/1/18-6/30/21  
Does TBI Affect mtDNA Heteroplasmy?  
This project determines whether TBI accelerates accumulation of brain mtDNA heteroplasmy  
Role: Co-PI

R43 AG060817 Michaelis (PI); Swerdlow KUMC PI 9/1/18-3/31/20  
Targeting bioenergetic flux for Alzheimer's disease management  
This project advances the development of compounds that enhance brain bioenergetic fluxes  
Role: KUMC PI

U01 AG016976-15 [741816] Swerdlow (Site PI) 07/01/11 - 06/30/21  
National Alzheimer's Coordinating Center (NACC)  
Continue to provide to NACC designated common data which form the basic level of participation required of all NIA-funded Alzheimer's Disease Centers (ADC's)  
Role: Site PI

Ausio Pharmaceuticals Swerdlow (PI) 04/01/17 - 03/31/20  
S-Equol in Alzheimer's Disease 2 Trial (SEAD2)  
Placebo controlled, biomarker-endpoint defined study to determine if S-equol's increases AD subject platelet mitochondria COX activity.  
Role: PI

Astra-Zeneca Burns and Swerdlow (Co-PIs) 12/01/18-11/30/20  
Randomized Controlled Pilot Trial of Dapagliflozin in Alzheimer's Disease  
This project generates safety, efficacy, and metabolism biomarker data for dapagliflozin in AD participants

Role: Co-PI

KU Frontiers-IAMI Swerdlow (PI) 01/01/18-06/30/19  
Pharmacokinetic Analysis of a Novel Bioenergetic Medicine Ester  
This project generates animal PK data for a novel bioenergetic medicine ester

R01AG061038 Zhao (PI) 02/15/19-01/31/24  
Sporadic Alzheimer's Disease: A Bioenergetic Etiology?  
This project to addresses whether brain bioenergetic dysfunction could underlie sporadic AD  
Role: Col

R01 AG043962 Burns (PI) 07/01/13 – 06/30/19  
Effect of Aerobic Exercise on Alzheimer's Pathophysiology in Preclinical AD  
We assay biospecimens from exercised adults with preclinical AD.  
Role: Col

R01AG054320 Yan (PI) 07/01/18-03/31/23  
Pink1, amyloid pathology, and mitochondrial quality control in Alzheimer's Disease  
This project evaluates mitochondrial quality control in AD  
Role: Col

R21 AG056062 Thyfault (PI) 05/01/17-04/31/19  
Skeletal Muscle Mitochondrial Abnormalities in Alzheimer's Disease  
This project evaluates mitochondrial function in muscle biopsies from AD and non-AD subjects  
Role: Col

K99 AG050490 Morris (PI) 03/01/16-02/28/19  
Metabolic Hormones, Aging, and Alzheimer's Disease  
This project studies metabolism and mitochondrial function in AD models and patient-derived biospecimens  
Role: Advisor

K99 AG056600 Wilkins (PI) 08/01/17-07/31/19  
Relationship between Amyloid beta and Bioenergetics  
This project studies relationships between beta amyloid and bioenergetics  
Role: Mentor

### **Completed Research Support**

R21 NS094945 Zhu (PI) 08/01/16-07/31/18  
Rescue of mt DNA-derived defects by mitochondria-targeted mRNA import and translation  
This project is developing an approach to translate nuclear-expressed mRNA transcripts within mitochondria  
Role: Col

Stop Alzheimer's Now Foundation Swerdlow (PI) 10/01/16-09/30/18  
Ketone Body-Based Interventions for Alzheimer's Prevention and Therapy  
This project determines how ketosis achieved with and without a ketogenic diet affects brain metabolism  
Role: PI

R01 FD003739 Barohn (PI)/Swerdlow (Co-PI) 11/01/12 – 10/31/17  
Phase 2 Study of Rasagiline for Treatment of Amyotrophic Lateral Sclerosis  
We assay biospecimens from rasagiline-treated human subjects for evidence of molecular target engagement  
Role: Col

Kansas Board of Regents EPSCOR Program Swerdlow (PI) 07/01/15—6/30/17  
Bioenergetic Manipulation for the Treatment of Alzheimer's Disease  
Major Goals: Synthesize and validate novel compounds that can enhance brain energy metabolism  
Role: PI