BIOGRAPHICAL SKETCH

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

NAME: Robert Keith Naviaux, MD, PhD

eRA COMMONS USERNAME (credential, e.g., agency login): RNaviaux

POSITION TITLE: Professor

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

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Georg August Universität, Göttingen, Germany	Undergrad	06/1978	Biochemistry
University of California, Davis, CA	B.S.	06/1979	Biological Sciences
Indiana University, Bloomington, IN	M.A.	05/1981	Zoology and Microbiology
Indiana University School of Medicine, Indianapolis, IN	M.D., Ph.D.	MD: 06/1986 PhD: 10/1989	Human Genetics and Virology
University of California, Davis Medical Center, Sacramento, CA	Residency	06/1990	Internal Medicine, Clinical Investigator Pathway
The Salk Institute, La Jolla, CA	Postdoc	06/1994	Retrovirology, Gene Therapy
University of California, San Diego Medical Center, San Diego, CA	Fellowship	06/1997	Biochemical Genetics, mtDNA Replication
National Institute of Environmental Health Sciences, Research Triangle Park, NC	Visiting Scholar	04/2003	Biochemistry of the mitochondrial DNA polymerase γ
Scripps Institution of Oceanography, La Jolla, CA. Cal Echoes Expedition; Ocean-going research cruise to study the ecosystems biology of the Santa Barbara Basin	Research Team Member	10/2010	Research Scientist aboard the R/V Melville—Marine Ecosystems Biology

A. Personal Statement

Research in my lab has focused on the role of mitochondria and metabolism in monogenic and complex disorders in children and adults. These disorders range from orphan diseases like Alpers and Leigh syndromes, to common diseases like autism spectrum disorder (ASD), myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), fibromyalgia, post-traumatic stress disorder (PTSD), recurrent major depressive disorder (rMDD), treatment refractory suicidal ideation, traumatic brain injury (TBI), chronic traumatic encephalopathy (CTE), cancer, diabetes, and autoimmune disorders. We also study acute and chronic infectious diseases like Lyme disease and the ecobiology of human herpes virus-6 (HHV-6) infection and latency.

We have a special interest in the molecular mechanisms of healing and tissue regeneration, innate immunity, and the interplay between genetic and environmental (ecogenetic) factors in human health and disease. My lab discovered the molecular basis of Alpers Syndrome—the oldest Mendelian form of mitochondrial disease—and we were the first to show that defects in a human DNA polymerase (the mitochondrial DNA polymerase γ, *POLG*) could cause human disease. We identified the first mitochondrial DNA (mtDNA) mutation associated with autism and were the first to quantify the risk of neurodegeneration with infection in mitochondrial disease. We were also the first to characterize the metabolic features of the cell danger response (CDR), the healing cycle, and to coin the term “ecoallele” to describe gene variations that shape fitness according to environmental conditions.

My lab has helped develop a number of advanced technologies like biocavity laser spectroscopy, mtDNA mutation detection by mass spectrometry, and novel methods for exosome purification and analysis. We developed some of the first methods to isolate metagenomic DNA from beach sand and ocean core sediments for use in the molecular reconstruction of modern and ancient marine ecosystems. This has given us a unique window into the ecosystem biology and metabolic contributions of the gut microbiome to human health. We have developed new tools for deep phenotyping of health and disease by advanced metabolomics and exposomics in samples from a wide array of biofluids, tissues, and cultured cells. These tools, along with state-of-the-art methods in mass spectrometry, stable isotope tracer studies for fluxomics, mitochondrial respiratory chain biochemistry, and polarographic analysis permit us to dissect the metabolomic and molecular features of any disease in any cell type.

Mentoring is an important part of our work. Over the past 10 years, I have mentored 7 high school summer research interns, 13 undergraduate students, 4 graduate students, 12 postdocs and fellows, and 2 junior faculty members.

B. Positions and Honors

Positions and Employment

1976	Undergraduate Research Intern, Tumor Immunology and Natural Killer Cell Biology, National Institutes of Health, NCI, Bethesda, MD
1978-1979	Undergraduate Research Assistant, Experimental Hematology, Radiobiology Laboratory, U.C. Davis
1979-1981	X-ray Crystallographic Analysis, Beck Analytical Services, Bloomington, IN
1986-1990	Intern and Resident, Internal Medicine, American Board of Internal Medicine (ABIM), Clinical Investigator Pathway, University of California, Davis
1997-2003	Assistant Professor, Department of Medicine, Medical Genetics, Biochemical Genetics and Metabolism, University of California, San Diego, School of Medicine
2001-2003	Assistant Professor, Department of Pediatrics, Biochemical Genetics and Metabolism, University of California, San Diego, School of Medicine
2003-2009	Associate Professor, Departments of Medicine and Pediatrics, University of California, San Diego, School of Medicine.
2009-Present	Professor, Departments of Medicine, Pediatrics, and Pathology, University of California, San Diego, School of Medicine.

Other Experience, Professional Appointments, National and International Service

1996-Present	Founder and Co-director, The Mitochondrial and Metabolic Disease Center (MMDC) at the University of California, San Diego School of Medicine
1998-2013	Founder and Co-director, UCSD Biochemical Genetics Molecular Diagnostics Laboratory
1999	Co-Founder and Founding Program Director, The Mitochondrial Medicine Society (MMS)
1999-2006	Scientific Advisory Board, United Mitochondrial Disease Foundation (UMDF)
1999-2012	Founding Associate Editor, *Mitochondrion*
2007-2010	President, Mitochondrial Medicine Society (MMS)
2012-2014	Scientific Advisory Council Member; The Autism Speaks Autism Treatment Network (ATN)
2013-2015	Association Française contre les Myopathies, Plateforme Maladies Rares (AFM—The French Muscular Dystrophy and Rare Disease Council)
2013-2015	Scientific Advisory Council, The James Kirk Bernard Foundation for the Prevention of Youth Suicide

Honors and Awards

1982-1986	***E.B. Rinker Scholarship*** for Academic Achievement and Teaching, Indiana University SOM
1986	***Alpha Omega Alpha*** Medical Honor Society, Graduating with Highest Distinction, Indiana Univ. School of Medicine
1987-1989	***Medical Scholar***, University of California, Medical Scholars Research Program, U. C. Davis School of Medicine

1987 ***Giannini-Bank of America Award*** *for Excellence in Medical Research*, University of California, Davis

1987 *Outstanding Young Men of America Award,* for academic achievement, leadership, and community service

1990 ***Medical Scholar and Resident****,* ABIM Clinical Investigator Pathway, University of California, Davis

1990 ***NIH National Medical Resident of the Year***, Internal Medicine, NIH, NIDDK, Bethesda, MD

1994 ***Fogarty International Scholar***—Organizer, Director, National Gene Therapy Workshop, Bombay, India

2001 Inaugural **Kelsey Wright Award Recipient** for Excellence in Mitochondrial Medicine

2002 Honored in a non-fiction book entitled, *Anna's Friends—Lessons Learned from a Short and Beautiful Life* (336 pp, Rogue River Publications, Belmont MI, 2002, ISBN 0-9718076-3-9), written by John Stuive and Kathleen Feeney, parents of a child with a terminal mitochondrial disease cared for by Dr. Naviaux

2007 **Best Abstract Award,** United Mitochondrial Disease Foundation *Mitochondrial Medicine 2007 Conference*, 2nd Prize for "Lambda Profiling and Biocavity Laser Spectroscopy—Testing A New Technology for Mitochondrial Disease Diagnosis"

2007 **American Physical Society and the American Institute of Physics Showcase** of our 2007 *J Biomed Optics* paper in the November 15, 2007 issue of *Virtual Journal of Biological Physics Research*

2007 **Thomson ESI**, Science Citation Index "**Fast Moving Front Article**" award for our 2004 paper reporting POLG mutations as the cause of Alpers syndrome and mtDNA depletion

2008 **Hailey's Hero Award**, Hailey's Wish Foundation—For Outstanding Research and Clinical Care of children with mitochondrial disease

2011 International **Trailblazer** grant recipient for studies in autism pathogenesis and treatment, Autism Speaks

2014 **Simons Foundation Autism Research Initiative** (SFARI), #1 most viewed paper in autism research in 2013

2018 **Lifetime Achievement Award**, Mitochondrial Medicine Society (MMS)

2019 **Pioneering Achievement Award**, The International Society for Environmentally Acquired Illness (ISEAI).

2019-2020 **Top #1, #2, #3, and #4 most-downloaded papers** in the journal *Mitochondrion*: https://www.journals.elsevier.com/mitochondrion/most-downloaded-articles

2020 **UCSD Faculty Excellence in Stewardship Award**, for work with grassroots philanthropic donors and foundations in support of basic and translational research

C. Contributions to Science

1. Discoverer of the cause of **Alpers Syndrome**. Our work brought a close to a 70-year old medical mystery that began with the first description of Alpers Syndrome by Bernard Alpers in 1931.
    a. **Naviaux RK**, Nyhan WL, Barshop BA, Poulton J, Markusic D, Karpinski NC, Haas RH. Mitochondrial DNA polymerase gamma deficiency and mtDNA depletion in a child with Alpers syndrome. *Annals of Neurology*. 1999;45:54-58.
    b. **Naviaux RK**, Nguyen KV. POLG Mutations Associated with Alpers' Syndrome and Mitochondrial DNA Depletion. *Ann Neurol*. 2004;55:706-712

2. Early contributor and leader in the growth and development of the new field of **Mitochondrial Medicine**
    a. Founder of the Mitochondrial and Metabolic Disease Center (MMDC) at UCSD in 1996
    b. Co-Founder and former President, the Mitochondrial Medicine Society (MMS) in 1999
    c. **Naviaux RK**, *ed*. Mitochondrial Medicine--Developing the Scientific Foundations for the Medical Management of Mitochondrial Disease, *Mitochondrion* 2004; Vol. 4, pp. 349-824, Elsevier, Oxford, UK. *This was the first monograph (475 pp) to review the emerging field of Mitochondrial Medicine.*

3. Inventor and developer of advanced technologies as **new tools and lenses** to examine the roles of the environment, genes, mitochondria, and metabolism in human health and disease
    a. **Naviaux RK** et al. Metabolic features of chronic fatigue syndrome. *Proc Natl Acad Sci USA.* 2016, 113(37):E5472-80.

b. **Naviaux RK,** Costanzi E, Haas M, Verma IM. The pCL vector system: rapid production of helper-free, high-titer, recombinant retroviruses. *Journal of Virology*. 70: 5701-5705, 1996.
c. **Naviaux RK,** Good B, McPherson JD, Steffen DL, Markusic D, Ransom B, Corbeil J. Sand DNA - a genetic library of life at the water's edge. *Marine Ecology-Progress Series*. 2005;301:9-22.
d. Li K, Naviaux JC, Bright AT, Wang L, **Naviaux RK**. A robust, single-injection method for targeted, broad-spectrum plasma metabolomics. *Metabolomics*. 2017;13(10):122. PMID: 28943831

4. First to show the concerted metabolic and redox mechanisms for **mitochondrial control of epigenetics**, and early contributor to the reassessment of oxidative stress as **oxidative shielding**—an evolutionarily conserved cellular defense mechanism in chronic disease
    a. **Naviaux RK**. Mitochondrial control of epigenetics. *Cancer Biology and Therapy* 7:1191-1193, 2008
    b. **Naviaux RK.** Oxidative shielding or oxidative stress? *J Pharmacol Exp Ther* 342:608-618, 2012

5. Discoverer of the role of the **cell danger response** and **purinergic signaling** in autism.
    a. **Naviaux RK.** Metabolic Features of the Cell Danger Response. *Mitochondrion* 16:7-17, 2014.
    b. **Naviaux RK**, Zolkipli Z, Wang L, Nakayama T, Naviaux JC, Schuchbauer MA, Rogac M, Tang Q, Dugan LL, Powell SB. Antipurinergic Therapy Corrects the Autism-Like Features in the Poly(IC) Mouse Model. *PloS one* **8**, e57380 (2013).
    c. Naviaux JC, Schuchbauer MA, Li K, Wang L, Risbrough VB, Powell SB, **Naviaux RK**. Reversal of autism-like behaviors and metabolism in adult mice with single-dose antipurinergic therapy. *Translational Psychiatry* 2014.
    d. **Naviaux RK**, et al. Low-dose suramin in autism spectrum disorder: a small, phase I/II, randomized clinical trial. *Annals of Clinical and Translational Neurology* 2017. PMID: 28695149

A listing of over 100 biomedical publications is available in **PubMed**, and over 150, including ecology and bioengineering publications, in **Google Scholar**. Dr. Naviaux's papers have been cited over 7000 times.

D. Research Support (In past 3 years)

Ongoing Research Support

Naviaux (PI) 10/1/99-Present
UCSD Foundation Christini Fund, La Jolla, CA
Mechanisms of Mitochondrial Disease
This is an annual golf tournament and fund-raiser that provides support for Dr. Naviaux and his continuing studies of Alpers syndrome, mitochondrial disease pathogenesis, and gene discovery from marine metagenomic studies.

Naviaux (PI) 5/1//07-Present
Lennox Foundation, Dallas, TX
Mechanisms of Mitochondrial Disease
This grant provides funding to support Dr. Naviaux's general research into the molecular pathogenesis of mitochondrial disease.

Naviaux (PI) 2/1/13-Present
"The 5k Mito Walk and Roll"
Mechanisms of Mitochondrial Disease
This is a new annual fund-raising event sponsored by Steele Canyon High School students to support mitochondrial research in the Naviaux laboratory.
OVERLAP: None

Naviaux (PI) 12/31/19-12/30/20
The Brain Foundation
Crosstalk Between the Metabolome and Exposome in Autism Spectrum Disorder
This is a clinical research study to examine the impact of the exposome on ASD and metabolism.
OVERLAP: None

Naviaux (PI) 3/23/18-3/22/21
Kuzani Pharmaceuticals
Mechanisms of antipurinergic therapy for autism spectrum disorder
This is a clinical research contract to facilitate the development of suramin for ASD.
OVERLAP: None

Naviaux (PI) 8/5/19-5/1/21
Steven and Alexandra Cohen Foundation
Metabolomic and Exposomic of Acute and Post-Treatment Lyme Disease Syndrome
This is a new award to study the metabolic and environmental factors in Lyme disease.
OVERLAP: None

Naviaux (PI) 7/15/19-7/14/21
Khosla Foundation
Metabolomic and Exposomic Connections between ME/CFS and Lyme Disease
This is a new award to study the metabolic and environmental connections between complex chronic disorders.
OVERLAP: This project provides funding to extend our Lyme work to ME/CFS

<u>Completed Research Support</u> (In past 3 years)

Naviaux (PI) 7/1/16-6/30/17
Open Medicine Foundation
Metabolomic of Chronic Fatigue Syndrome
This is a new grant to complete the clinical validation of NextGen Metabolomics methods in a cohort of patients with chronic fatigue syndrome.
OVERLAP: None

Naviaux (PI) 5/1/16-4/28/17
Sarika Agrawal
Mechanisms and Treatment of Autism
This grant provides support for Dr. Naviaux's studies of autism, the cell danger response, and treatment with suramin.
OVERLAP: None

Naviaux (PI) 1/13/16-1/12/17
N of One Foundation for Autism Research
The Suramin Autism Treatment 1 (SAT-1) Phase I/II Clinical Trial
This was a new grant to help complete the first clinical trial of suramin for the treatment of autism spectrum disorders.
OVERLAP: None; contributed to the $1.2 million cost of this clinical trial