**BIOGRAPHICAL SKETCH**

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NAME: Robert Keith Naviaux, MD, PhD

eRA COMMONS USER NAME (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 |
| NIH- and NIDDK-Sponsored Workshop on Isotope Tracers in Metabolic Research, Little Rock, AK | Participant | 03/2013 | Stable isotope tracers in metabolic phenotype analysis |

## 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, chronic fatigue syndrome (CFS), post-traumatic stress disorder (PTSD), depression, traumatic brain injury (TBI), chronic traumatic encephalopathy (CTE), cancer, diabetes, malaria, tuberculosis, and autoimmune disorders. We have special interests in tissue regeneration, innate immunity, and the interplay between genetic and environmental factors in human health and disease (Ecogenetics). 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 were the first to quantify the risk of neurodegeneration with infection in mitochondrial disease. My lab has developed 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 NextGen metabolomics and targeted mass spectrometry of 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 flux metabolomics, mitochondrial respiratory chain and polarographic analysis, permit us to dissect the metabolomic and molecular features of any disease in any cell type.

## B. Positions and Honors

### Positions and Employment

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|---|---|
| 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 | 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** for Autism Research Institute (SFARI), #1 most viewed paper in autism research in 2013

## 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. Jan 1999. Mitochondrial DNA polymerase gamma deficiency and mtDNA depletion in a child with Alpers syndrome. *Annals of Neurology*. 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 tools and **new 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, Epub ahead of print.
    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. Jiang Y, Hall TA, Hofstadler SA, **Naviaux RK**. Mitochondrial DNA mutation detection by electrospray mass spectrometry. *Clin Chem.* 53:195-203, 2007
    e. Gourley PL, Hendricks JK, McDonald AE, Copeland RG, Yaffe MP, **Naviaux RK**. Reactive biomolecular divergence in genetically altered yeast cells and isolated mitochondria as measured by biocavity laser spectroscopy: A rapid diagnostic method for studying cellular responses to stress and disease. J Biomed Optics 12:1-14, 2007.

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, Schucbauer 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 JC, Wang L, Li K, Bright AT, Alaynick WA, Williams KR, Powell SB, **Naviaux RK**. Antipurinergic Therapy Corrects the Autism-Like Features in the Fragile X (*Fmr1* knockout) Mouse Model. *Molec Autism* 6:1-19, 2015.

A complete listing of 88 Naviaux publications is available in **PubMed**, and 124 in **Google Scholar**. Google Scholar contains additional Naviaux publications in physics and engineering that are not indexed in PubMed. Dr. Naviaux's top 20 papers have been cited over 4000 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) 4/11/16-8/30/16
Autism Research Institute, San Diego, CA
**A Phase I/II Clinical Trial of Suramin for the Treatment of Autism Spectrum Disorders**
This study will develop our understanding of the role of purinergic signaling and suramin treatment in children with autism.

Naviaux (PI) 9/1/08-8/30/16
The William Wright Foundation, Vernon, TX
**Nucleotide Signaling in Mitochondrial Disease and Dysfunction**
This study will develop our understanding of the role of purinergic signaling in mitochondrial disease, healing, and tissue regeneration. In 2015, this gift will help support a clinical trial of suramin in children with autism.

Naviaux (PI) 5/1//07-4/28/16
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.

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

Naviaux (PI) 7/1/11-6/30/14
Jane Botsford-Johnson Foundation, New York, NY
**Autism Metabolomics**
This study will develop the methods of advanced metabolomics for monitoring autism and response to treatment.

1DP3DK094352-01 Sharma (PI) 11/1/11-6/31/14
NIH/NIDDK
**Novel Paradigms in Diabetic Complications**
Role: Co-PI
This is a multidisciplinary program project designed to investigate the role of mitochondria and reactive oxygen homeostasis in diabetic complications. Mass spectrometry-based metabolomics and NextGen DNA sequencing and methylomics methods will be used to evaluate mouse models and up to 3000 urine samples archived from clinical trials and natural history studies of diabetic kidney disease.

Dewleen Baker (PI) 11/1/12-10/31/13
NIMH/DOD
**Metabolomic Signatures of Stress Resilience and Risk**
Naviaux Role: co-PI
This is a 1-year demonstration project that is part of the larger NIMH- and DOD-funded Marine Resilience Study II. It will use the tools of quantitative metabolomics, neuropeptide, and oxidative marker analysis to identify biomarker signatures that are predictive for Post Traumatic Stress Disorder (PTSD) among marines deploying to and returning from Iraq and Afghanistan.

Judy Van De Water (PI) 7/1/11-6/30/12
Autism Speaks, New York, NY
**Evaluation of the immune and physiologic response in children with autism following immune challenge**
Role: Coinvestigator
This was a consortium project grant directed by Dr. Van De Water at the UC Davis MIND Institute to study the metabolic effects of immunization in children with autism and typically developing controls.

Naviaux (PI) 4/1/11-3/31/12
Autism Speaks Trailblazer Award, New York, NY
**Nucleotide Signaling in the Genesis and Treatment of Autism**
This is a multidisciplinary study of the role of purinergic signaling and mitochondria in synaptogenesis and neuroinflammation in a mouse model of autism spectrum disorders (ASDs).