

A Welcome Letter from Ron Davis

Dear Friends,

I want to personally welcome you to this day of presentations by a group of superb scientists! I greatly respect each of them and am always impressed with their creativity, dedication and rigor. I'm excited to have them all together, analyzing and integrating all of our data, brainstorming and thinking out of the box about how to put it all together, and planning next steps so that the research can move as fast as possible with the most qualified scientists doing work they are good at to cure this horrid disease.

As I look at my son, Whitney, my heart cries for his suffering and then it connects to all of you patients who suffer with him.

As I watch my wife, Janet, caring for our son into the early morning hours, giving up so much of her life, I think of all you caregivers who walk with her on this path caring for your loved ones.

Of course I am constantly thinking of all you doctors and scientists, trying to absorb all the data you have collected, feeling all of our pain at the painstaking process that never moves fast enough, and trying to find the best to join our collaboration.

And to all of you doctors out there – I'm incredibly grateful for your dedication to caring for these patients when it is so hard and so little is known, and I'm thrilled that you are here trying to learn more so you can bring it back to your patients.

Finally, I'm grateful beyond words for the generosity of the donors who have contributed to this research, because you make our progress possible. I'm especially grateful for Linda Tannenbaum and the Open Medicine Foundation for their tireless work in raising the funds that enable us to do this work, and for making this symposium possible. Thank you from the bottom of my heart.

We are all in this together. I have no doubt that we will figure out what has gone wrong in the bodies of patients with this tragic disease, and find treatments that will work to make it better or someday cure it.

I hope you enjoy this wonderful panel of scientists that we have gathered. Many of them are not people you have heard of before in this field. I have chosen them because I believe we need to garner expertise from peripheral, but related, fields of study, open our minds to new thoughts and information, and nurture out-of-the-box thinking in order to break open this field, unravel the mysteries of this disease, and find a cure.

I hope this day leaves you inspired and hopeful!

Sincerely,



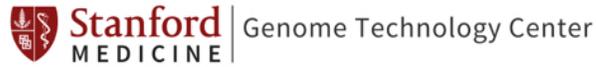
Symposium Chair

Professor of Biochemistry and of Genetics, Stanford University School of Medicine

Director, Stanford Genome Technology Center

Director, Chronic Fatigue Syndrome Research Center at Stanford University

Director, Open Medicine Foundation ME/CFS Scientific Advisory Board

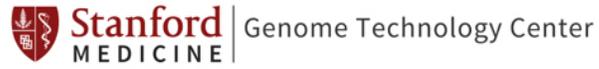


Community Symposium on the Molecular Basis of ME/CFS

Sponsored by the Open Medicine Foundation: <http://omf.ngo/community-symposium>

Saturday, August 12, 2017 at Paul Brest Hall, Stanford University

- 08:00 a.m. Registration**
- 09:00 a.m. Welcome: Linda Tannenbaum, CEO, OMF**
- 09:03 a.m. Symposium Logistics: Ashley Haugen, Event Organizer**
- 09:05 a.m. Opening Remarks: Ronald W. Davis, PhD, Stanford University**
- 09:10 a.m. Keynote Address: Robert K Naviaux, MD, PhD, University of California, San Diego**
The metabolism of the cell danger response, healing, and ME/CFS
- 09:30 a.m. Chris Armstrong, University of Melbourne**
ME, metabolism and I
- 09:50 a.m. Jonas Bergquist, MD, PhD, Uppsala University**
In search of biomarkers revealing pathophysiology in a Swedish ME/CFS patient cohort
- 10:10 a.m. BREAK**
- 10:40 a.m. Maureen Hanson, PhD, Cornell University**
Probing metabolism in ME/CFS
- 11:00 a.m. Neil McGregor, MDSc, PhD, University of Melbourne**
Genome-wide analysis & metabolome changes in ME/CFS
- 11:20 a.m. Alan Light, PhD, University of Utah**
Gene variants, mitochondria & autoimmunity in ME/CFS
- 11:40 a.m. Panel Discussion: Morning Speakers**
- 12:10 p.m. LUNCH**
- 01:30 p.m. Baldomero Olivera, PhD, Howard Hughes Medical Institute & University of Utah**
A novel source of drugs: the biodiversity of oceans
- 01:50 p.m. Mario Capecchi, PhD, Nobel Laureate; Howard Hughes Medical Institute & University of Utah**
The role of microglia in neuropsychiatric disorders
- 02:10 p.m. Mark Davis, PhD, Howard Hughes Medical Institute and Stanford University**
Is CFS/ME an autoimmune disease?
- 02:30 p.m. BREAK**
- 03:00 p.m. Alain Moreau, PhD, University of Montreal**
New research strategies for decoding ME/CFS to improve diagnosis and treatment
- 03:20 p.m. Wenzhong Xiao, PhD, Massachusetts General Hospital, Harvard Medical School**
Big data analysis of patient studies of ME/CFS
- 03:40 p.m. Ronald W. Davis, PhD, Stanford University**
Establishing new mechanistic and diagnostic paradigms for ME/CFS
- 04:00 p.m. Panel Discussion: Afternoon Speakers**



Closing Remarks:

04:30 p.m. Linda Tannenbaum, CEO, OMF

04:35 p.m. Ronald W. Davis, PhD

05:00 p.m. – RECEPTION 6:00 p.m.

Ronald W. Davis, PhD

Establishing new mechanistic and diagnostic paradigms for ME/CFS



Dr. Davis, Symposium Chair, is Professor of Biochemistry and Genetics at Stanford University School of Medicine, Director of the Stanford Genome Technology Center, Director of the Chronic Fatigue Syndrome Research Center at Stanford University, and Director of the Open Medicine Foundation ME/CFS Scientific Advisory Board. Dr. Davis holds a PhD in chemistry from Caltech and is a member of the National Academy of Sciences. Throughout his career he has made numerous seminal discoveries that have accelerated genetics, genomics, and bioengineering, including over 70 patented technologies that

have launched numerous successful companies. His contributions have been recognized by the Gruber Genetics Prize, the Genetics Society of America Medal, the Warren Alpert Prize, and the Personalized Medicine World Conference Luminary Award. In 2013, he was named one of the 7 World's Greatest Inventors by *The Atlantic*.

Robert Naviaux, MD, PhD

The metabolism of the cell danger response, healing, and ME/CFS



Dr. Naviaux is Professor of Medicine, Pediatrics, and Pathology at the University of California, San Diego (UCSD). He is the founder and co-director of the Mitochondrial and Metabolic Disease Center, former President of the Mitochondrial Medicine Society (MMS), and a founding associate editor of the journal *Mitochondrion*. He is an internationally known expert in human genetics, inborn errors of metabolism, metabolomics, and mitochondrial medicine. Dr. Naviaux discovered the genetic basis of Alpers syndrome, the oldest Mendelian form of mitochondrial disease, and developed the first DNA test to

diagnose it. He studied biochemistry at Georg-August University in Göttingen, Germany, and received his MD and PhD in Genetics and Virology from the Indiana University School of Medicine. He is currently the director of the first FDA-approved clinical trial to study the safety and test the effects of suramin on behavior and language in children with autism. Dr. Naviaux is a member of the OMF Scientific Advisory Board.

Chris Armstrong

ME, metabolism and I



Chris Armstrong is a biochemistry researcher at the University of Melbourne. He began research into ME/CFS in 2010 as an honours student. In 2011 he began a PhD to pioneer the applications of metabolomics to study ME/CFS. He published the first comprehensive ME/CFS metabolomics study on blood and urine in 2015. These studies were first to recognise an alteration in energy, amino acid and purine metabolism in ME/CFS patients. Overall, his research has led to biochemical findings that represent the cellular reaction to a chronic stressor in ME/CFS patients. Currently, Chris is monitoring ME/CFS

patients longitudinally to determine how metabolism alters with symptom severity on a case-by-case basis.

Jonas Bergquist, MD, PhD

In search of biomarkers revealing pathophysiology in a Swedish ME/CFS patient cohort



Dr. Bergquist is a Full Chair Professor in Analytical Chemistry and Neurochemistry at the Department of Chemistry at Uppsala University, Adjunct Professor in Pathology at the University of Utah School of Medicine, and Distinguished Professor in Precision Medicine at Binzhou Medical University in Yantai, China. His group is continuously developing general analytical tools for screening and discovery of biomarkers of pathological states. These approaches include identifying relevant clinical applications, advanced sample pretreatment, multidimensional liquid based separation, high resolution mass spectrometry, and

multivariate data analysis. Dr. Bergquist studies numerous conditions, including neurodegenerative disorders. His research into ME/CFS is focused on characterizing the neuroimmunological aspects of the disease using proteomics and metabolomics, with a special interest in cerebrospinal fluid studies.

Maureen Hanson, PhD

Probing metabolism in ME/CFS



Dr. Hanson is the Liberty Hyde Bailey Professor in the Department of Molecular Biology and Genetics at Cornell University. She previously was on the Biology faculty at the University of Virginia, Charlottesville. She holds a Ph.D. in Cell and Molecular Biology from Harvard University. Her lab is currently carrying out collaborative studies on ME/CFS concerning gene expression in immune cells, mitochondrial DNA variation, dysbiosis of the gut microbiome, and metabolomics, and the effect of exercise on inflammatory markers, metabolism and physiology. She is Director of the Cornell Center for

Enervating Neuroimmune Disease. Dr. Hanson is a member of the OMF Scientific Advisory Board.

Neil McGregor, MDSc, PhD

Genome wide analysis & metabolome changes in ME/CFS



Dr. McGregor is a member of the faculty at the [University of Melbourne, Faculty of Medicine, Dentistry and Health Sciences](#). He gained his PhD at the University of Sydney in 2000 and has published over 60 papers in peer reviewed journals. His area of research is metabolomics, microbiomics and genomics. His interest is in documenting the interactions between the biochemistry identified with in each of these methods of analyses of human tissues and how they may relate to the pathophysiology of the disease being studied. He was a co-editor of “The journal of Chronic Fatigue syndrome” along with Prof

Kenny De Meirleir for a period of 6-7 years.

Alan Light, PhD

Gene variants, mitochondria & autoimmunity in ME/CFS



Dr. Light is a Professor of Anesthesiology and Neurobiology and Anatomy at The University of Utah. He is a member of the University of Utah programs in Neuroscience, the Brain Research Institute, and the Pain Research Center. Dr. Light has published over 120 peer reviewed research articles focused on peripheral and spinal cord mechanisms of pain and fatigue processing (20 recently on ME/CFS). He received a Javits Award from NIH for his research on descending control of pain. His current focus is on the mechanisms of the sensations of muscle pain and fatigue, and the plasticity they undergo following inflammation, injury and in disorders such as ME/CFS and Fibromyalgia Syndromes.

Mario Capecchi, PhD

The role of microglia in neuropsychiatric disorders



Dr. Capecchi was awarded the 2007 Nobel Prize in Physiology or Medicine for his pioneering work in developing a gene-targeting technology in mice, which has been used to create mouse models for hundreds of diseases including cancer, revolutionizing mammalian biology and our understanding of disease genetics. He is a Distinguished Professor of Human Genetics and Biology at the University of Utah School of Medicine and a Howard Hughes Medical Institute Investigator. Dr. Capecchi holds a PhD in biophysics from Harvard University, which he carried out in Dr. James Watson's laboratory studying the mechanisms of gene and protein expression. His current research involves investigating the molecular genetic causes underlying human disorders involving the immune system and the brain. In addition to numerous honors and awards, Dr. Capecchi is a member of the National Academy of Sciences, the European Academy of Sciences, the American Academy of Arts and Sciences, and the National Academy of Medicine. He is also a member of the OMF Scientific Advisory Board.

Baldomero Olivera, PhD



Dr. Olivera is a Distinguished Professor of Biology at the University of Utah and a Howard Hughes Medical Institute Investigator. He is also an Adjunct Professor at the Salk Institute, La Jolla, California and at the Marine Science Institute, University of the Philippines. Dr. Olivera researches the ion channels and receptors that mediate signaling in the nervous system. Through his studies of neurotoxins produced by predatory cone snails, Dr. Olivera has been able to develop a number of pain drugs, including one whose synthetic form is now used to treat pain effectively in patients who have become tolerant to morphine.

Dr. Olivera is passionate about interdisciplinary science and education. He holds a PhD in biophysical chemistry from Caltech and is a member of the National Academy of Sciences as well as the OMF Scientific Advisory Board.

Mark Davis, PhD

Is CFS/ME an autoimmune disease?



Dr. Mark M. Davis is the Director of the Stanford Institute for Immunology, Transplantation and Infection (ITI), a Professor of Microbiology and Immunology, and a Howard Hughes Medical Institute Investigator. He received a B.A. from Johns Hopkins University and a Ph.D. from the California Institute of Technology. Dr. Davis is well known for identifying many of the T-cell receptor genes, which are responsible for the ability of these cells to recognize a diverse repertoire of antigens. His current research interests involve understanding the molecular interactions that underlie T cell recognition and the challenges of

human immunology, specifically a “systems level” understanding of an immune response to vaccination or infection. He has received many honors and awards, including memberships in the National Academy of Sciences and the Institute of Medicine, The Paul Ehrlich Prize, The Gairdner Foundation Prize, The King Faisal Prize, the General Motors Alfred P. Sloan Prize, and being elected as Foreign Member to the Royal Society of London. Dr. Davis is a member of the OMF Scientific Advisory Board.

Alain Moreau, PhD

New research strategies for decoding ME/CFS to improve diagnosis and treatment



Dr. Moreau is a Full Professor in the Faculty of Dentistry (Stomatology Department), cross-appointed to the Biochemistry and Molecular Medicine Department in the Faculty of Medicine at Université de Montréal. He served as Director of Research and Chief Scientific Officer of Sainte-Justine University Hospital (2013-2016) and was a member and Vice-Chair of the Advisory Board of the Institute of Musculoskeletal Health and Arthritis of the Canadian Institutes of Health Research (2010-2016). More recently, he was appointed Director of Network for Canadian Oral Health Research. He is an internationally recognized expert on molecular genetics of pediatric scoliosis. His discoveries led

to multiple peer-reviewed papers, international conferences as a guest speaker, several awards as well as 45 patents covering innovative diagnostic tests and therapeutic molecules. Dr. Moreau's main research interests also target complex adult diseases such as osteoarthritis, osteoporosis and myalgic encephalomyelitis.

Wenzhong Xiao, PhD

Big data analysis of patient studies of ME/CFS



Dr. Xiao is Director of the Immuno-Metabolic Computational Center at Massachusetts General Hospital, Harvard Medical School. His research is at the interface of computation, genomics and medicine. A major bottleneck of genome medicine today is around data analysis, interpretation, and integration. His research interest is to develop approaches to address these challenges and to help translate genome technologies to better disease diagnosis, prevention and therapeutics, especially in studies of human immune and metabolic diseases. In collaboration with researchers at Stanford Genome Technology

Center and Open Medicine Foundation, his lab has been analyzing the Big Data Severely Ill Patient Study and other studies on ME/CFS, and comparing ME/CFS with other diseases. Dr. Xiao is a member of the OMF Scientific Advisory Board.

Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS)

Key Facts

What is the prevalence of ME/CFS?

- ME/CFS affects 836,000 to 2.5 million Americans.
- An estimated 84 to 91 percent of people with ME/CFS have not yet been diagnosed, meaning the true prevalence of ME/CFS is unknown.
- ME/CFS affects women more often than men. Most patients currently diagnosed with ME/CFS are Caucasian, but some studies suggest that ME/CFS is more common in minority groups.
- The average age of onset is 33, although ME/CFS has been reported in patients younger than age 10 and older than age 70.

What are the symptoms and other effects of ME/CFS?

- There are five main symptoms of ME/CFS:
 1. Reduction or impairment in ability to carry out normal daily activities, accompanied by profound fatigue;
 2. Post-exertional malaise (worsening of symptoms after physical, cognitive, or emotional effort);
 3. Unrefreshing sleep;
 4. Cognitive impairment; and
 5. Orthostatic intolerance (symptoms that worsen when a person stands upright and improve when the person lies back down).
- Other common manifestations of ME/CFS include pain, failure to recover from a prior infection, and abnormal immune function.
- At least one-quarter of ME/CFS patients are bed- or house-bound at some point in their illness.
- Symptoms can persist for years, and most patients never regain their pre-disease level of health or functioning.
- ME/CFS patients experience loss of productivity and high medical costs that contribute to a total economic burden of \$17 to \$24 billion annually.

What are the challenges in improving diagnosis and care for ME/CFS?

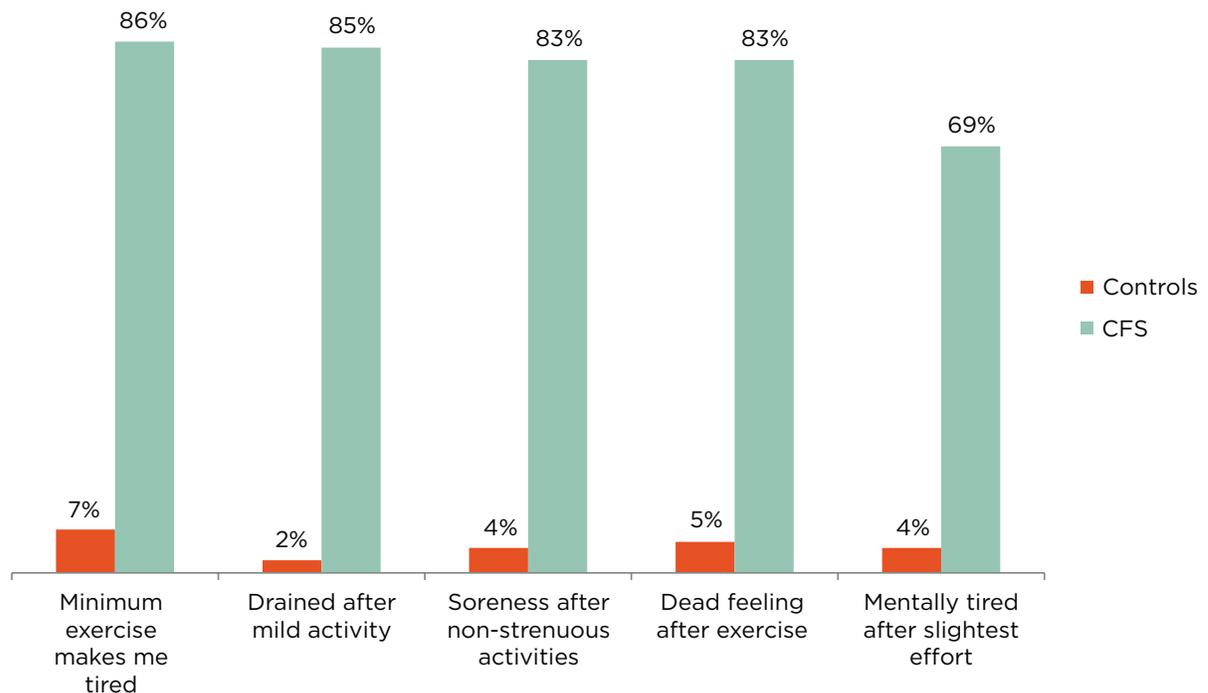
- The cause of ME/CFS remains unknown, although symptoms may be triggered by certain infections.
- Although there are therapies available to manage symptoms of ME/CFS, their efficacy is not known. There is no existing cure for ME/CFS.
- There is an urgent need for more research to discover what causes ME/CFS, understand the mechanisms associated with the development and progression of the disease, and develop effective diagnostic markers and treatments.

Why is a new name for ME/CFS needed?

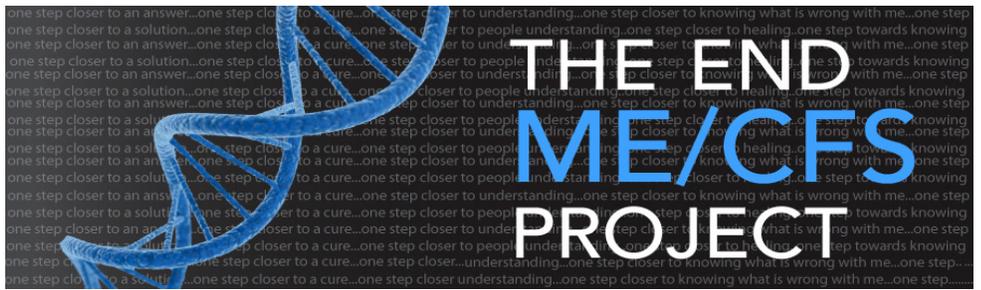
- Several studies have shown that the term “chronic fatigue syndrome” affects patients’ perceptions of their illness as well as the reactions of others, including medical personnel, family members, and colleagues. This label can trivialize the seriousness of the condition and promote misunderstanding of the illness.
- The term “myalgic encephalomyelitis” is not appropriate because there is a lack of evidence for encephalomyelitis (brain inflammation) in patients with this disease, and myalgia (muscle pain) is not a core symptom of the disease.
- The Institute of Medicine (IOM) committee recommends the name **systemic exertion intolerance disease (SEID)** for this disease. This new name captures a central characteristic of this disease—the fact that exertion of any sort (physical, cognitive, or emotional)—can adversely affect patients in many organ systems and in many aspects of their lives.

To learn more, and to access the IOM committee’s proposed diagnostic criteria for ME/CFS, visit www.iom.edu/MECFS. 

FIGURE 1 Percentage of ME/CFS patients and healthy controls reporting post-exertional malaise symptoms of at least moderate severity that occurred at least half of the time during the past 6 months.



NOTE: See the complete report for note and source information (available at www.iom.edu/MECFS).



Open Medicine Foundation® (OMF) is fast-tracking revolutionary research in chronic complex diseases.

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Stanford University
Harvard Medical School

'The word 'hope' is now in my vocabulary again. Thank you Ron and your team for turning on the light at the end of a very, very long tunnel.'

— ME/CFS patient

What is ME/CFS?

Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS), is a devastating and life-altering disease that affects up to 2.5 million people in the U.S. alone. Suffering from a host of symptoms that are chronic and incapacitating, patients with ME/CFS have a lower quality of life and higher rates of disability than patients with AIDS, multiple sclerosis, diabetes and rheumatoid arthritis. No cure or FDA-approved treatment exists.

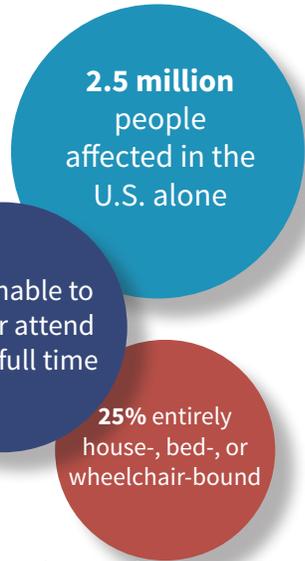
It's invisible. It's pervasive. It's under-researched. We are determined to change this!

The End ME/CFS Project

The Human Genome Project—perhaps the most groundbreaking biomedical project in the last 15 years—succeeded because world-renowned experts in a wide range of disciplines came together and openly shared their research results. Using this model, Open Medicine Foundation has engaged leaders of the Human Genome Project along with researchers from Stanford University, Harvard University, and other leading institutions worldwide to turn their attention to ME/CFS.

Led by Ronald W. Davis, Ph.D.—considered one of the fathers of modern human genetics—and an extraordinary scientific advisory board that includes three Nobel Laureates, six members of the National Academy of Sciences, and other eminent researchers and clinicians, the End ME/CFS Project takes a comprehensive research approach based on collaboration, shared results, and big data analysis. Our lean business model is already fast-tracking revolutionary research and the search for treatments.

The goal of the End ME/CFS Project is to understand the disease at a molecular level. We have already funded the first ever big data study of severely ill ME/CFS patients, using a comprehensive array of cutting-edge molecular, cellular, and clinical technologies. This research has highlighted the complexity of ME/CFS and its metabolic and immunological nature. The ongoing analysis of this rich dataset, and its ongoing expansion to patients of varying severity, will help to identify the molecular defects associated with ME/CFS and potential therapies to correct them. In addition to data generation, this project is also developing low-cost technologies that can diagnose ME/CFS from a blood sample, which would be a game changer for researchers and doctors alike. One of these technologies is already looking promising for both diagnosis and drug screening, and the next step is testing FDA-approved drugs to see which have therapeutic potential. Help us end ME/CFS!



OPEN MEDICINE FOUNDATION'S UNIQUE APPROACH

- **Prestigious Scientific Advisory Board**
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- **Focus on Molecular & Cellular Causes vs. Symptoms Research**
- **Precision Medicine Approach**

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To find out more about OMF and the End ME/CFS Project or to donate, visit our website: www.omf.ngo

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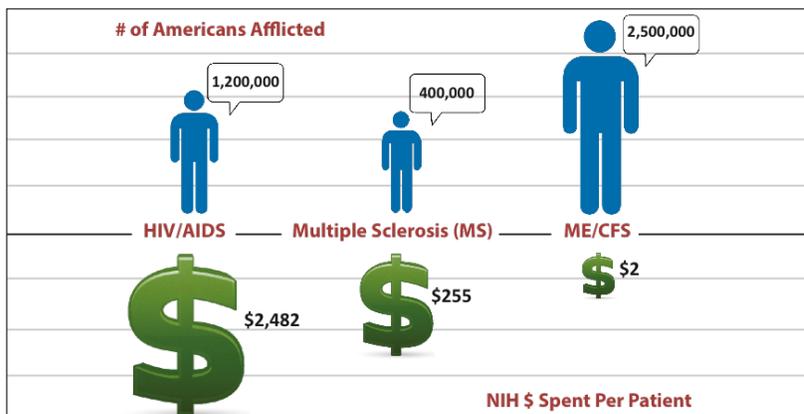
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Linda Tannenbaum
CEO/President
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Let's End ME/CFS Together

According to the recent National Academy of Medicine report, ME/CFS is more common than multiple sclerosis, lung cancer, or AIDS. It likely affects one percent of the population worldwide. Despite the high prevalence of this disease, its research receives remarkably little funding from the National Institutes of Health (NIH). The NIH currently spends an average of just \$2 per patient per year in research dollars for ME/CFS, which will only increase to \$4-\$5 per in 2017/2018. It is a disproportionately underfunded disease.



Although OMF has established a strong relationship with NIH in our efforts to advocate for increased ME/CFS research support, these changes will take longer than we can wait. **Open Medicine Foundation has taken on the challenge of filling the gap to fight this underfunded and under-researched disease.** But a great research strategy is only part of the solution.

To advance this ambitious scientific endeavor, the End ME/CFS Project will require a major financial investment from the private sector. We seek contributions from individuals, corporations, and foundations **to raise a minimum of \$5 million annually for this urgent research.** The funds will be used for:

- Sample collection and testing
- Computational data analysis with an open access platform
- Research project management
- Thought-leader consortiums
- Informing the medical, research, and patient communities
- Fundraising and transparent financial governance

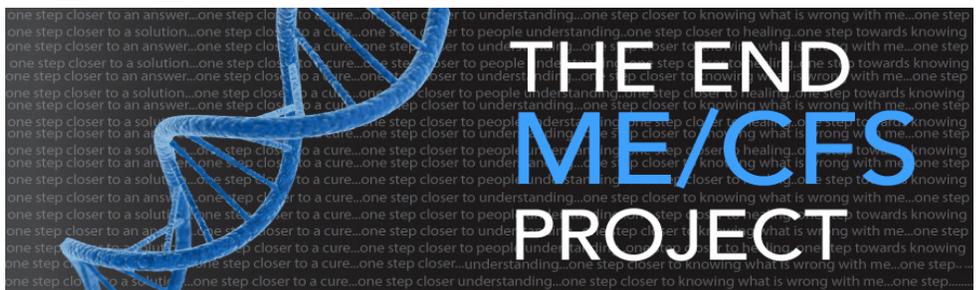
We are determined to reach our goals and with your support, the best minds in their fields will come together in collaboration and groundbreaking research to understand ME/CFS.

Be part of this game-changing effort. Your support will promote revolutionary research to find a diagnostic tool, effective treatments, and ultimately, a cure.

"My son Whitney woke me this morning to inform me that he is dying. He did not say he is dying - he cannot speak. He did not write he is dying - he cannot write. He used Scrabble tiles to spell out his message. He knows he is running out of time. We need research funds TODAY to find answers to save his life and millions of others."



— Ronald W. Davis, PhD
Director, OMF ME/CFS Scientific Advisory Board
One of Today's Greatest Inventors (Atlantic Magazine, 2013)



Open Medicine Foundation® (OMF) is fast-tracking revolutionary research in chronic complex diseases.

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Harvard Medical School

ME/CFS research is progressing faster than ever before, and we have already had some exciting breakthroughs. We are close to understanding the mechanism. I think we can cure this disease.
Dr. Ron Davis

Open Medicine Foundation

Founded in 2012, Open Medicine Foundation (OMF) has built a strong community of researchers, patients, parents and caregivers in over 90 countries working toward a shared goal - to cure ME/CFS. As the leader in ME/CFS research, OMF has invested over \$6 million in research to date.

What is ME/CFS?

ME/CFS, or Myalgic Encephalomyelitis/Chronic Fatigue Syndrome, is a devastating and life-altering disease that affects up to 2.5 million people in the U.S. alone and over 17 million worldwide. ME/CFS can strike anyone, at any age, at anytime. It is a global crisis with 80% of patients unable to work or attend school and 25% of patients are entirely house-bound, bed-bound, or wheelchair bound.

The End ME/CFS Project

The End ME/CFS Project is OMF's first major initiative. Using an open and collaborative model, OMF is leading and funding research to understand the molecular basis of ME/CFS to identify effective treatments and to ultimately find a cure.

Scientific Advisory Board

OMF's Scientific Advisory Board is comprised of world-renowned researchers including 3 Nobel Laureates and 6 members of the National Academy of Sciences.

Complex Chronic Diseases

Starting with ME/CFS, we are confident that the End ME/CFS project will shed light on other chronic complex diseases with similar symptoms (fibromyalgia, chronic Lyme, Gulf War illness, Ehlers-Danlos syndrome, autism, and others).

Join Team OMF

Around the world, people in over 90 countries participate in Team OMF to support research and share hope with patients. We invite you to join Team OMF. Donate. Educate. Invite friends and family to donate. Host a fundraising event. Introduce potential funders to OMF. Get involved and give hope to millions.

Take Action Today

Register to receive our news and stay informed - - www.omf.ngo/newsletter-sign-up
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