Message from Dr. José G. Montoya

Dear ME/CFS Community,

On behalf of the Stanford ME/CFS Initiative team, we would like to express our most sincere gratitude to all of you who have contributed to our efforts in researching and treating Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS). Our commitment extends beyond understanding of the causes of ME/CFS; we are devoted to delivering individualized care to each and every patient that is affected by this crippling disease.

This year, our newsletter provides a summary of our current projects, and those we will be embarking on in the coming year. Our team of collaborators is ever-growing, including experts from many disciplines who seek to find a biological explanation for ME/CFS. Our most important team members are our supporters—people like you and your family members and friends. Your support fuels our endeavors to prevent this disease and provide a cure to those affected.

Please find enclosed our latest newsletter. We would love to hear from you. Please write to us at The Stanford ME/CFS Initiative, 1000 Welch Road, Suite 202, Palo Alto, CA 94304.

From all of us at the Stanford ME/CFS Initiative, please accept our sincerest appreciation for your support!

Sincerely,

José G. Montoya, MD, FACP, FIDSA
Professor of Medicine
Division of Infectious Diseases and Geographic Medicine
Stanford University School of Medicine

Director,
Palo Alto Medical Foundation Toxoplasma Serology Laboratory
National Reference Center for the Study and Diagnosis of Toxoplasmosis
Meetings, Conferences, and Media Coverage

Chronic Fatigue Syndrome Advisory Committee (CFSAC) meeting
Sponsored by the United States Department of Health and Human Services, the CFSAC meeting was held on August 18-19, 2015. Dr. Montoya joined committee members from across the country to discuss the findings brought to light by the reports individually released by the Institute of Medicine (IOM) and the NIH Pathways to Prevention Workshop (P2P) on the state of ME/CFS in the research and clinical arenas.
For more information on this meeting, please visit: http://www.hhs.gov/advcomcfs/meetings/index.html

United Kingdom ME/CFS Research Collaborative Conference
As part of his ongoing collaborations with physicians and researchers abroad, Dr. Montoya attended the UK ME/CFS Collaborative Conference, held at Newcastle University from October 13-14, 2015. As a keynote speaker in the Neuropathology session, Dr. Montoya highlighted his collaboration with Stanford colleague, Michael Zeineh MD, PhD, which resulted in the preliminary discovery of a brain biomarker for ME/CFS.
For more information on this meeting, please visit: http://www.meassociation.org.uk/2015/10/global-mecfs-research-22-october-2015/

“Is This Why You’re Still So Tired?” – O (Oprah Magazine)
Dr. Montoya’s work is juxtaposed alongside the story of one of his patients, whose life completely changed at the onset of ME/CFS. Dr. Montoya is quoted as saying, “Many physicians and researchers thought patients with CFS didn’t show signs of active inflammation… But when we began to perform more in-depth tests, the results were staggering. A picture of patients with highly inflamed bodies emerged before our eyes and validated what they’ve been telling us for decades.”
To read the complete article, please visit: http://www.oprah.com/health_wellness/Chronic-Fatigue-Syndrome

“Is chronic fatigue syndrome finally being taken seriously?” – The Guardian
As a young doctor, Dr. Montoya was advised to stop treating patients with ME/CFS. His academic mentor told him, “You are committing academic suicide. You’re turning your career into a mess.” Over a decade later, the medical community has finally begun to change its tune.
To read the complete article, please visit: http://www.theguardian.com/lifeandstyle/2016/apr/04/chronic-fatigue-syndrome-cfs-taken-seriously

“Unraveling the mystery of chronic fatigue syndrome” – Palo Alto Weekly
Studies conducted with colleagues at Stanford and Columbia have demonstrated noticeable differences in patients with ME/CFS when compared to healthy counterparts. However, not all ME/CFS patients are the same. “With AIDS, there are different manifestations of the disease, but they are all caused by a single virus,” Dr. Montoya is quoted as saying. On the other hand, ME/CFS may be caused by several different infectious diseases.
To read the complete article, please visit: http://paloaltoonline.com/news/2015/07/10/unraveling-the-mystery-of-chronic-fatigue-syndrome
Ongoing Research

Validating MRI-DTI as a Biomarker for ME/CFS
In October 2014, Dr. Montoya and Dr. Zeineh published exciting neuroradiology research that showed substantial differences in the brains of patients with ME/CFS. The next step is to replicate these early findings by analyzing a larger cohort of ME/CFS patients. To this end, Drs. Montoya, Zeineh, and José R. Maldonado, have resubmitted an application for an R01 research grant to the National Institutes of Health. R01 grants are highly competitive, but if awarded, provide an average of $400,000 a year for 3-5 years. While receiving an R01 grant would likely cover the cost of this project, Dr. Montoya and his team plan to move ahead with this critical study, no matter the outcome.

This study will utilize two important approaches: (1) we will use magnetic resonance imaging (MRI) to identify the changes in the brain that give rise to fatigue, and (2) we will analyze blood samples from patients to determine whether increased inflammation correlates with changes in the brain. Researching both the brain and blood will greatly improve our understanding of this disease, and may lead to new treatments.

For more information on this research, please visit: https://med.stanford.edu/news/all-news/2014/10/study-finds-brain-abnormalities-in-chronic-fatigue-patients.html

Immune and Brain Biomarkers in Gulf War Illness (GWI) Veterans
Upon returning from the Gulf War, a significant number of veterans fell ill to a mysterious sickness, which has been termed “gulf war illness,” or GWI. There is substantial overlap in the symptoms of GWI and ME/CFS. We plan to use MRI-DTI to analyze the brains of GWI veterans, as well as test their blood for distinct cytokine signatures indicative of inflammation.

We have submitted a grant application to the United States Department of Defense to fund this research, and are awaiting their decision. This study will be carried out in collaboration with Dr. Zeineh, and Palo Alto VA Psychiatrist and GWI expert, J. Wesson Ashford, MD, PhD.

Microbial Discovery and Immunity in ME/CFS
Ian Lipkin, MD, and Mady Hornig, MA, MD, of Columbia University are leading this multi-center study to analyze the microbiome of ME/CFS patients. At Stanford, we are in the process of recruiting 25 ME/CFS cases and 25 controls. We will then analyze patients’ blood, saliva, and stool samples at four time points.

Neuroendocrine Study
In an effort to understand the pathogenesis of ME/CFS, we will study how the Hypothalamic–pituitary–adrenal (HPA) axis functions in ME/CFS patients. With the expertise of Laurence Katzenelson MD, endocrinologist at Stanford, we aim to explore how biomarkers for HPA dysfunction might serve as objective markers for the disease. We hope to start recruiting participants by late spring of 2016.
High Throughput Sequencing/Pathogen Discovery
Through our continued partnership with Holden Maecker, PhD, director of the Stanford Human Immune Monitoring Center, and Drs. Lipkin and Hornig at Columbia University, our effort of looking for pathogens present or abundant in ME/CFS patients has yielded exciting results. We are in the process of preparing a manuscript for submission to a peer-reviewed journal.

Gene Expression and Immune System Dynamics-Gene Expression
To more fully understand the immune response and possible immune system dysfunction observed in ME/CFS patients, we are partnering closely with our colleagues at the Stanford Human Immune Monitoring Center, Dr. Maecker and Mark Davis, PhD. We are in the process of finalizing analysis of samples and plan to submit a manuscript shortly.

Cardiovascular Health in ME/CFS Patients
In collaboration with our colleagues, Francois Haddad, MD, and Mehdi Skhiri, MD, we evaluated cardiovascular aging in ME/CFS patients. After extensive analysis, we found that the heart is unlikely to be affected by ME/CFS. Drs. Haddad and Skhiri are continuing this research by looking at endothelial function and cytokine levels in ME/CFS patients before and after physical exercise. Their research is currently being prepared for publication.

Cognitive Impairment in ME/CFS Patients
Dr. Maldonado of Stanford and collaborators, Marcie Zinn, PhD, and Mark Zinn, MM, led two studies utilizing techniques in electroencephalography (EEG) to yield objective measurements for evaluating cognitive impairments in ME/CFS patients. Two manuscripts are currently in preparation for publication.

Subgrouping Chronic Fatigue Syndrome Patients by Genetic and Immune Profiling
Funding from the Department of Defense has enabled us to further explore the immune responses for ME/CFS patients, in comparison to healthy controls. We are continuing a detailed analysis of human leukocyte antigen (HLA) types in ME/CFS patients. The HLA system is responsible for regulating the immune system in humans. These efforts are being undertaken by our new biostatistician Donn Garvert, MS, under the direction of Tyson Holmes, PhD, senior biostatistician at the Stanford Human Immune Monitoring Center. The results of their research are currently being reviewed for publication.

Gene Expression and Immune System-Lyme Disease Cohort
In an effort to expand our knowledge in the realm of chronic disease, our team is working on a new study aimed at understanding the immune profile and gene expression of patients suffering from chronic Lyme disease. Specifically, we will look at gene expression, cytokine profiles, and phosphor-immunoflow, which may help us to identify new biomarkers specific to chronic Lyme disease.

This research is being carried out in conjunction with our colleague, Dr. Davis, professor in the Department of Microbiology and Immunology. Additionally, we are collaborating with physicians at Stanford and other institutions who have extensive clinical experience with patients suffering from Lyme disease.

We are currently recruiting participants. If you would like to participate in this study, please contact Jill Anderson: janders5@stanford.edu
Future Research and Endeavors

ME/CFS Brain and Tissue Bank
It is with some hesitation that we publically announce our decision to begin the regulatory process to accept brain donations from deceased ME/CFS patients. We plan to establish a robust tissue and brain bank to help us better understand the nature of ME/CFS. More information on this effort is forthcoming.

Homebound/Bedbound ME/CFS Patient Study
The Stanford ME/CFS Initiative is committed to improving the lives of all patients with ME/CFS, including those who are home- and bedbound. It is imperative that we conduct studies that seek to address the challenges faced by these severely ill patients and learn more about their treatment needs. Within the next year, we will commence enrolling homebound patients for a formal study.

Universal Pathogen Discovery
Building upon preliminary data we collected from our GEISD-Pathogen Discovery study, we are planning to launch a comprehensive pathogen discovery research. In collaboration with Stephen Quake, DPhil, we will take samples of blood, cerebrospinal fluid, lymph nodes, bone marrow, and NK cell compartments.
With the partnership of Linda Nguyen, MD, gastroenterologist and motility expert at Stanford, we will also collect gastrointestinal biopsies. This study will be the first comprehensive effort to search for pathogens in sites never attempted before.

General Team Updates

Welcome, Jill Anderson and Donn Garvert!
We have expanded our team to include Jill Anderson, our new Clinical Research Coordinator. Jill graduated with a bachelor’s degree from Johns Hopkins University, where she also worked as a research assistant. Jill has expertly managed several of our internal projects and external collaborations. One of the highlights of her role is interacting with ME/CFS patients.

The generosity of a patient’s family has enabled us to add a much-needed biostatistician to our core team. Donn Garvert, MS, conducts statistical analyses for a variety of different research projects. The expertise he brings to the team has allowed us to engage in several new projects in the past year.

Donor Stories featured on Stanford ME/CFS Initiative Website
We are grateful to the donors who make our work possible, and it has been an honor getting to know their personal stories. Mia Anderson was in college when she fell ill with ME/CFS. To spread awareness about her disease, and raise money for vital research, she made and sold bracelets. To read more about her story, please visit: http://med.stanford.edu/chronicfatiguesyndrome/donor-stories.html
If you would like to share your experience, please contact Victoria Muirhead: victoria.muirhead@stanford.edu
Make a Gift

Philanthropic support from our donors is critical to moving ME/CFS research forward. An estimated one million Americans suffer from this debilitating illness, yet only a fraction of the entire National Institutes of Health (NIH) budget goes towards ME/CFS research. The progress we have made in this field has been largely due to passionate advocates and visionary donors.

Donations to Dr. José G. Montoya’s ME/CFS Fund are used to support clinical research. Your gift signifies a vote of confidence in our work.

To make a gift to support our research, please visit:
http://med.stanford.edu/chronicfatiguesyndrome/about/donation.html

If you would like to fund a specific research project, or want more information, do not hesitate to reach out to our partners at Stanford Medical Center Development:

<table>
<thead>
<tr>
<th>Anne Marie Krogh, Director of Major Gifts</th>
<th>Victoria Muirhead, Associate Director of Leadership Giving</th>
</tr>
</thead>
<tbody>
<tr>
<td>650.721.6929</td>
<td>650.497.7084</td>
</tr>
<tr>
<td><a href="mailto:amkrogh@stanford.edu">amkrogh@stanford.edu</a></td>
<td><a href="mailto:victoria.muirhead@stanford.edu">victoria.muirhead@stanford.edu</a></td>
</tr>
</tbody>
</table>

All money donated to Stanford University is tax-deductible in the United States.

A Special Thank You

What sets the Stanford ME/CFS Initiative apart is its numerous and deep collaborations with brilliant and talented colleagues across Stanford Medicine and beyond. We wish to extend a special thank you to the many people whose participation has been key to our success.

Dr. Montoya’s core team: Amity Hall, PA; Aimee Jadav, PA; Jane Norris, PA; Jill Anderson; Donn Garvert, MS; LaMoria Roberts; Luciana Mendiola, MA

Our collaborators: Tyson Holmes, PhD; Lily Chu, MD; Rosemary Fernandez; Francois Haddad, MD; Mady Hornig, MA, MD; Safwan Jaradeh, MD; Xuhuai Ji, PhD; James Kang, MD; Kristopher Kapphahn, PhD; Amit Kaushal, MD, PhD; W. Ian Lipkin, MD; Holden Maecker, PhD; Jose R. Maldonado, MD; Michael Mindrinos, PhD; Linda Nguyen, MD; Stephen Quake, PhD; William Robinson, MD; Yael Rosenberg-Hasson; Mehdi Skhiri, MD; Cristina Tato, MPH, PhD; Rohit Gupta, PhD; Janine Sung; Alaina Puleo; Wenzhong Xiao, PhD; Weihong Xu, PhD; Jared Younger, PhD; Michael Zeineh, MD, PhD

Summer interns: undergraduate students Tullia Lieb, Josie Furbershaw, Anh-Tram Bui; and high school student Tristan Verghese

Thank you, and we look forward to another fruitful year of research!