



# The Solve ME/CFS CHRONICLE

SUMMER 2017

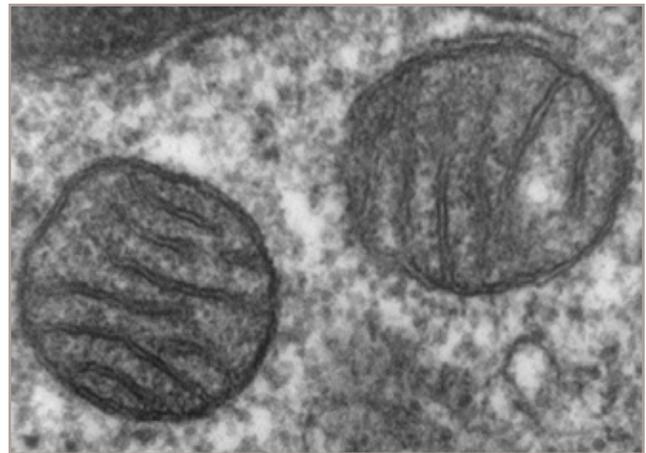
## What's in a Mitochondrion and Why Does It Matter for ME/CFS?

We often hear in the field of ME/CFS (myalgic encephalomyelitis/chronic fatigue syndrome) and in the scientific literature about these mysterious structures called the mitochondria (plural of mitochondrion). That is for good reasons!

Mitochondria are present in almost all cells in our bodies and are vital to produce energy in the form of ATP, a currency that our body can use on a cellular level. In fact, the bulk of the energy produced for any mental or physical function we need comes from mitochondria. A mitochondrion is often dubbed the “power house” of the cell and it is no surprise that this area of biology continues to be of great relevance to our disease space. In ME/CFS, the lack of energy is a key symptom. In addition, “Post Exertional Malaise” or PEM (which we qualify as a misnomer since this is not a malaise, but a full-on crash) is also a cardinal problem in the disease.

So, because lack of energy production is a key attribute of ME/CFS, there is a great deal of interest in these critical sources of energy production in our bodies. Many studies are occurring to better understand the differences in mitochondrial function between people with ME/CFS and healthy controls.

This rather technical article is deep background on mitochondria for those who want a better understanding.



*Transmission electron microscope image of a thin section of mammalian lung tissue, showing two mitochondria.*

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# SMCI This Quarter: A Summary of Our Work

In this recurring section of *The Solve ME/CFS Chronicle*, SMCI summarizes the highlights of our work. Every quarter you see your SMCI team in action and our unceasing efforts to make ME/CFS understood, diagnosable, and treatable.

## RESEARCH work in recent months

*SMCI seeks to engage the entire ME/CFS community in research and works to accelerate the discovery of safe and effective treatments.*

- SMCI announced new ME/CFS research program with Dr. David System at Brigham's and Women Hospital
- SMCI sponsored the publication of new ME/CFS Pediatric Primer with Dr. Peter Rowe
- SMCI Research Advisory Council members Drs. Anthony Komaroff and Jose Montoya co-authored ME/CFS gut bacteria study with Dr. Ian Lipkin at Columbia University
- Deadline for Ramsay Award closed with applications from 6 countries submitted
- SMCI expanded substantive biotech research partnership with Metabolon, conducted at Cornell
- Dr. Nahle presented at global ME/CFS conference Invest in ME Research, in London

## INFLUENCE and EDUCATION work in recent months

*SMCI is the go-to source of trusted, up-to-date medical information, current research, and policy work on ME/CFS and seeks to disseminate this information effectively.*

- Cort Johnson of Health Rising featured Dr. Zaher Nahle and our SMCI Bioenergetics Research Program
- Dr. Nahle participated in the technical development workgroup (TDW) resulting in the revisions released this quarter to the CDC public webpage on ME/CFS, removing references to controversial treatments
- SMCI leaders hosted ME/CFS Panel at Precision Medicine World Conference at Duke University
- Dr. Nahle teamed up with rare disease legislative advocates at Capitol Hill information session
- Carol Head was nominated for a WEGO Health Award for a Community and Patient Leader Hero awards

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*Each board member is a patient or has a family member affected by this disease.*

## ADVOCACY work in recent months

*Through government advocacy, SMCI strives enhance programs that serve patients and researchers alike and for an aggressive expansion of funding for research that will lead to a cure.*

- SMCI issued an action alert to restore ME/CFS funding with over 1,850 messages sent to Congress by advocates
- SMCI co-hosted a Congressional briefing on ME/CFS with #MEAction and Senator Ed Markey
- 52 ME/CFS advocates met with 80+ members of congress and their representatives in Washington DC as part of ME/CFS Advocacy Week
- SMCI met in DC with the Acting Director of the Bureau of Health Workforce at the Health Resources and Services Administration to discuss ME/CFS education for health care providers
- SMCI collaborated to pass a state-wide resolution on ME/CFS in California and spoke at an ME/CFS rally at the state capitol in Sacramento
- Working with local advocates Rivka Solomon and Bobbi Ausubel, SMCI helped to secure the political collaboration of the National Organization for Women to advocate for ME/CFS ■



*Senator Ed Markey of Massachusetts delivers opening remarks at May Congressional Briefing on ME/CFS in Washington, DC*



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## What's in a Mitochondrion and Why Does It Matter for ME/CFS? (cont'd)

It is important to point out upfront that mitochondria are very complex entities. This is partly because they have complicated structures which include many compartments, twists and layers; and partly because they have many other biological functions. These other functions of mitochondria are also vital in human health and can be related to the onset of diseases, in addition to producing energy. We list and summarize these activities below, but first here are some quick and simple facts about the mitochondria.

### Quick facts about the mitochondria:

#### **THEY ARE NOT INDEPENDENT CELLS BUT INDEPENDENT STRUCTURES WITHIN A CELL!**

These intact structures vary in numbers among different cell types. Typically, cells with more energy demand have more mitochondria. For instance, a red blood cell has no mitochondria at all while a liver cell have more than a 1000 per cell.

#### **THEY HAVE THEIR OWN DNA CALLED MITOCHONDRIAL DNA AKA, mtDNA!**

What is unique about the mitochondria is that they have their own genome. No other structure except our own cells has its own DNA. So any given cell in our body that has mitochondria will have two distinct DNA sources (genomes) at the same time. One source is the "classic" human genome that we all know about (known as genomic DNA and that consists of 23 pairs of chromosomes). This DNA source is shared in quantity, mutations and predisposition with all other cells in an individual. The second source is the mitochondrial genome (referred to as mtDNA to distinguish it from genomic DNA). mtDNA resembles more a bacterial genome than a human genome.

#### **MITOCHONDRIAL DNA (mtDNA) IS INHERITED FROM THE MOTHER, NOT THE FATHER!**

The genome in the mitochondria is exclusively inherited from the mother. In fact, all the paternal mtDNA are destroyed upon fertilization, leaving only mitochondrial DNA genome to be passed down in reproduction.

#### **NOT ALL MITOCHONDRIA ARE CREATED EQUAL!**

In other words, not all mitochondria in the body perform the same function. Some perform additional functions based on the type of tissue where they live. For instance, a mitochondrion in a liver cell has additional enzymes that enables them to detoxify certain harmful byproducts., But a mitochondrion in muscle tissue does not have these exact enzymes. Additionally, even in the same tissue, muscle for instance, different type of muscle cells can have different numbers of mitochondria based on their energetic and the specific needs of the organ and tissue they call home.

### Solve ME/CFS Initiative science and discovery programs investigating mitochondria include:

- **2016 Ramsay Award Team 2:** Metabolic Analysis of B-Cell Maturation in ME/CFS with Dr. Geraldine Cambridge, Fane Mensah, and Chris Armstrong.
- **2016 Ramsay Award Team 3:** The Bioenergetic Health Index of NK Cells as a Diagnostic Tool for Chronic Fatigue Syndrome with Drs. Isabel Barao-Silvestre, Ruben Dagada, and Victor Darley-Usmar
- **2016 Ramsay Award Team 5:** HHV-6 Mediated Mitochondrial Modulation and Its Association to ME/CFS with Dr. Bhupesh Prusty
- **SMCI's Directed Research Study:** Pathways and Biomarkers with Metabolon and Drs. Maureen Hanson and Susan Levine

## Mitochondria are critical in these key roles:

### ENERGY PRODUCTION AND CONVERSION:

Mitochondria are equipped with special proteins and factors that allow them to transform nutrients (e.g., glucose and fat) into energy currency (known as ATP). The process of nutrient breakdown would have either started earlier before reaching the mitochondria or is initiated directly in the mitochondria based on the quality and type of the nutrient source. For instance, carbohydrates (complex sugars) must be broken down into simple sugar molecules. These in turn get processed inside the cell before getting fully transformed into ATP by the mitochondria.

### REACTIVE OXYGEN SPECIES (ROS) BALANCE:

ROS are chemical structures that included many species containing oxygen. They are often the product of normal metabolism, especially in mitochondria, and are important for cellular signaling and chemical balance. However, they can also cause damage when they accumulate in an abnormal fashion either due to external factors (e.g., UV radiation) or a genetic mutation or other dysfunction. Deregulated ROS is implicated in many chronic diseases including cancer and are associated with inflammation, aging and DNA damage.

### CELL DEATH CONTROL AND SURVEILLANCE:

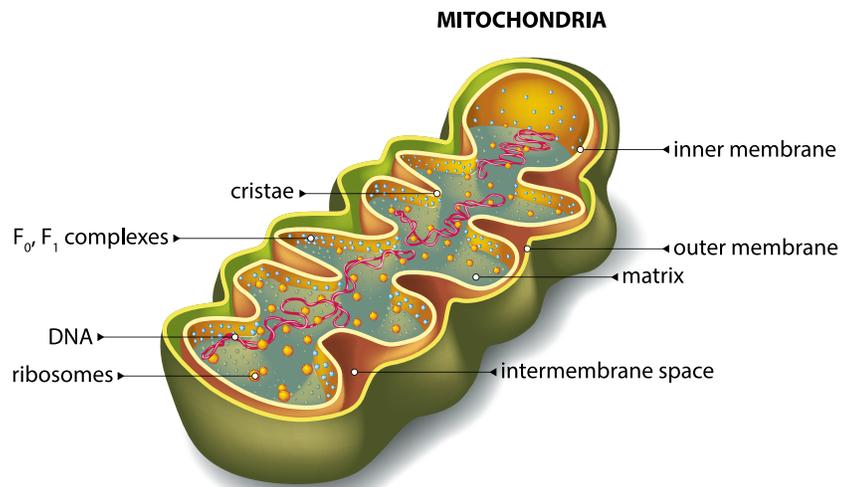
Programmed cell death (also known as apoptosis) is also key function executed by the mitochondria. A specialized apparatus inside the mitochondria signals the process of cellular self-destruction as part of the normal turn around and surveillance process. When this apoptotic machinery as it is called is defective (either hyperactive or inactive) many pathologies ensue as a result of abnormal cellular function. This includes uncontrolled proliferation (like tumors and cancer) and potential harmful cell shut down or destruction.

In addition to these functions, mitochondria are involved in a number of other critical functions, from hormonal control, to calcium signaling (important for proper cell regulation and survival), to cell cycle regulation, to heat production to macromolecule synthesis (e.g., steroids).

Here we only scratched the surface in discussing this important cellular component often mentioned in ME/CFS. We will shed more light in future publications on the many pathologies associated with mitochondrial diseases and their possible relation to ME/CFS.

In conclusion, SMCI and others seek to understand ME/CFS at a molecular level and this is quite complex. Appropriately studying the very complex mitochondria **alone** would cost millions upon millions of dollars. And mitochondria is only one of many avenues of inquiry in understanding ME/CFS that warrant in-depth investigation. All this work falls into the category of basic, rather than translational, research.

Bioenergetics including the function of mitochondria is a key research priority for our organization. SMCI continues to explore the function of this cellular “power-house” in multiple initiatives including our Ramsay Awards and Directed Research programs. ■



# A Letter from Zaher Nahle, PhD, MPA

Dear Friends,

New developments on all fronts!

We reported in our last edition of the *Chronicle* (Spring 2017) on the pre-submission status of many proposals competing through the National Institutes of Health (NIH) Collaborative Research Centers (CRCs) and Data Management and Coordinating Centers (DMCCs) mechanisms. Although still meager in total dollars, these new NIH funding opportunities, announced on January 27, 2017, represent an important step to concretize NIH support for ME/CFS research. This constitutes meaningful momentum following the announcement made by NIH Director Francis Collins in late 2015 and affirmed repeatedly by Dr. Collins, as well as Dr. Walter J. Koroshetz, the Director of the National Institute of Neurological Disorders and Stroke (NINDS), who is overseeing this initiative. We are gratified to update our community that the review process is now well underway, with outcomes expected in late September 2017.

There have been additional recent developments of note regarding ME/CFS. For instance, new updates to the ME/CFS information page on the Centers for Disease Control and Prevention (CDC) website (as of July 7, 2017), are a key step forward in refining the narrative about ME/CFS and purging the disease space from noxious and dated inaccuracies. To this end, the CDC website has been streamlined and improved, notably with the removal of the cognitive behavioral therapy (CBT) and graded exercise therapy (GET) as recommended treatments for ME/CFS. This has been a longstanding point of contention between the CDC and the patient community.

SMCI-wise, although we continue to throttle on all cylinders, we recognize that it is never enough. In the spring we launched another cycle of the Ramsay grant award competition in basic, clinical, translational and epidemiology research. In response, we again received international participation from six countries - underscoring once again the universality of our plight.




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Zaher Nahle, Chief Scientific Officer and Vice President for Research

Peer-review is underway with the winning proposals expected to be announced in the next two months. We also organized, alongside partners and stakeholders, dozens of advocates and patients for an intense advocacy week on Capitol Hill in May that featured a dedicated, even extraordinary, congressional briefing. Moreover, we convened an expert panel dedicated to ME/CFS at the prestigious Precision Medicine World Conference (PMWC), raising the visibility of our disease amongst industry leaders. Our work was also presented at an annual meeting organized by Invest in ME-Research (InME) in London, enabling us to forge new partnerships. All of the aforementioned was undertaken in addition to the numerous features and highlights described throughout this issue.

As always, I look forward to hearing from you. Importantly, please tell us how we did and how can we improve!

A handwritten signature in black ink, appearing to read 'Zaher Nahle'.

Zaher Nahle, PhD, MPA  
Chief Scientific Officer and Vice President for Research  
Solve ME/CFS Initiative

# Research ABCs

Many people with ME/CFS have become their own experts through independent research and sharing information with other patients and loved ones in the ME/CFS community. This patient-based knowledge has grown organically through online and in-person communities as a consequence of the knowledge gap and “expert desert” created by miniscule funding for ME/CFS. SMCI celebrates the patient experts and the exceptionally high engagement found in the ME/CFS community.

Ours is a disease community like no other.

Yet, the world of research is complex with its own language. To help decode and access the increasing work in science and discovery, we offer a collection of research terms and their application in the real-world, authored by our own Chief Scientific Officer and Vice President for Research, Dr. Zaher Nahle.

**BASIC RESEARCH:** a branch of scientific investigation, typically conducted in a laboratory, which involves specialized detection techniques, tools and methodologies. The aim is to uncover the communication, cross-talk (see definition below), structure or function within our cells, tissues, and organs, including the interactions between all these entities amongst each other as well as with the external environment. Basic science research can be done in both healthy and disease states. It is interdisciplinary and incorporates disciplines such as chemistry and physics, in addition to medicine. It is “basic” in that it is foundational, driven purely to understand a function, without a specific focus on clinical trials, therapies or cures.

**BIOENERGETICS:** the examination of the biological systems responsible for generating energy in any organism. The bulk of the energy production in a human cell that is needed for all functions, physical or cognitive, occurs in specialized structures inside the cells called mitochondria (singular: mitochondrion).

**BIOINFORMATICS:** a field of study that collects and extracts knowledge from complex biological data. Typically, it is computer-assisted and relies on modeling, algorithms (mathematical equations) and the processing of massive quantities of data (big data) and information to make sense of it all.

**CHANNELOPATHIES:** diseases that develop because of defects in ion channel subunits (see definition below) due to either genetic or acquired factors.

**CLINICAL TRIALS:** studies conducted on human participants, with the goal of establishing whether a medical approach, treatment, or device is safe and effective for humans. Different from “basic research” scientific investigation which seeks to discover underlying functions. Clinical trials are very expensive (typically funded by pharmaceutical companies) and highly regulated to protect human participants.

**CO-MORBIDITY:** diseases or symptoms that occur simultaneously. (e.g. Fibromyalgia and ME/CFS are often co-morbid).

**CROSS-TALK:** instances in which one or more components of one molecular signaling pathway impacts another, affecting a common biological output. Can be characterized by mutual antagonism, co-regulation, or both positive and negative feedback loops. Cross-talk increases research complexity and difficulty in defining clear results.

**EPIDEMIOLOGY:** the study of the spread of diseases and other health-related factors or events and the application of this study to develop potential interventions.

**EPIGENETICS:** genetic control or alteration by external and environmental factors that do not involve changes to the underlying DNA—essentially biological mechanisms that switch genes on and off.

**GENETICS:** the study of our genes as organized with chromosomes, as well as genetic predispositions to disease or

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## Research ABCs (cont'd)

genetic variation, hereditary or familial associations or relationships between living organisms.

### **INSTITUTIONAL REVIEW BOARDS**

**(IRB):** entities that review, approve, and monitor research. IRB approval is necessary for human subject research.

**ION CHANNELS:** proteins in the membrane (outer wall) of a cell that allow ions (an atom or a molecule) to pass into or out of a cell. Ion channels are present in the membrane of all cells and control cell electrical signals, volume, and function.

**METABOLOMICS:** the study of small metabolic products and related chemical processes of a biological system (organism, cell, or tissue).

**MICROBIOME:** a set of organisms that make up an ecological community, found in other organisms. The human microbiota includes bacteria, viruses, protozoa, fungi. These microbes are deeply integrated with our physiology and can impact health. For example, the “gut microbiome” is the collection of bacteria, viruses, protozoa and fungi found in the digestive tract.

### **NATURAL HISTORY (OF A DISEASE):**

a story or collection of facts about the course of a disease from its onset through its resolution (e.g., severity, onset, demographics, comorbidity). An Institute of Medicine report (Feb 2015) states that given the dearth in studies, especially those that are large in scale, it is hard to define the natural history of ME/CFS. This requires longitudinal study of large numbers of patients.

**PEER-REVIEW:** the evaluation of grants or proposals undertaken by experts with knowledge relevant to the field of study. The “gold-standard” of scientific rigor in making decisions regarding funding.

**PERIPHERAL BLOOD MONONUCLEAR CELL (PBMC):** any peripheral blood cell with a single, round nucleus. These populations of immune cells are collected from the peripheral (circulating) blood, and include lymphocytes, monocytes and dendritic cells. One track of ME/CFS research evaluates altered PBMC production of selected cytokines and immunoglobulins.

**POST-EXERTIONAL MALAISE (PEM):** the hallmark symptom of ME/CFS, PEM is profound fatigue following mental or physical exertion that is not alleviated by sufficient rest, which can impede daily functioning.

### **POSITRON-EMISSION TOPOGRAPHY**

**(PET):** a type of imaging scan that involves the injection of dyes with a radioactive tracers (molecules) that absorb into organs and tissues. In ME/CFS, PET scans have been used to explore the hypothesis that brain inflammation plays a role in the illness. There are many variations to this technology but with the same principles.

### **POSTURAL ORTHOSTATIC TACHYCARDIA SYNDROME (POTS):**

a condition that impacts flow of blood through the body and results in an unusual increase in heart rate when someone stands up. The cluster of symptoms includes fatigue, dizziness and brain fog.

**PREVALENCE STUDIES:** Population studies to understand how many people have a disease, often done by geographic area.

**REGISTRY:** an organized system (database) that collects and stores uniform, detailed data to evaluate populations defined by a specific disease, condition or exposure. Individuals voluntarily provide information about themselves to these registries. Registries support research, including understanding the natural history of a disease.

**TRANSLATIONAL RESEARCH:** the application of basic research into practice for the benefit of humans. Within a medical context, the goal is to transfer knowledge from basic research to clinical application to improve health outcomes, i.e. treatments and cures. ■

# Dr. Rowe: A Leading Voice for Children & Adolescents with ME/CFS

**DR. PETER ROWE** is a professor of pediatrics at the Johns Hopkins University School of Medicine and a member of the SMCI Research Advisory Council (RAC). He serves as the director of the chronic fatigue clinic at Johns Hopkins Children's Center.

Dr Rowe has had a long and distinguished career and is one of the most respected voices in the ME/CFS disease space. His work has been supported by SMCI as well as other federal and private sources. After receiving his undergraduate degree from the University of Toronto, Dr. Rowe earned his medical degree at McMaster University Medical School in Ontario and completed his residency and fellowship in pediatrics at Johns Hopkins and the Robert Wood Johnson General Pediatric, respectively. He has been on the Johns Hopkins faculty since 1991.

Notably, Dr. Rowe is the lead author on the "ME/CFS Diagnosis and Management in Young People: A Primer" published in the journal *Frontiers in Pediatrics* and "Neuromuscular Strain Increases Symptom Intensity in Chronic Fatigue Syndrome" published in *PLoS One* and sponsored for publication by SMCI. What follows is a transcript of our conversation with Dr. Rowe.

## How do you evaluate the ME/CFS field and the progress (or lack thereof) you see right now?

I started working on ME/CFS in the early 1990s. There has been substantial progress since then, although we have a long way to go before any of us can be satisfied. We have a much better understanding of the importance of post-exertional malaise in ME/CFS, including the gene expression changes that accompany this problem. We have much better tools for helping patients manage their symptoms than were available 20-25 years ago. Some of that progress comes from general advances in medicine, such as more effective medications and techniques to manage pain, headaches, and sleep dysfunction. Some comes from research specific to ME/CFS.

For example, in my practice, the practical clinical advances have been the introduction of medications and other management strategies for treating co-morbid orthostatic intolerance, managing common biomechanical movement restrictions using manual therapy techniques, recognizing the role of Ehlers-Danlos syndrome and joint hypermobility, and looking for

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## Dr. Rowe: A Leading Voice for Children & Adolescents with ME/CFS (cont'd)

evidence of milk protein intolerance in the subset with that problem. As a result of these kinds of advances, I think we are quicker to achieve better function for some. That stands in stark contrast to the desperate need for improved understanding of the pathophysiology of severe forms of ME/CFS, and the need for more effective treatments overall.

### Why are you so dedicated to the MECFS population and what sparked your interest in this disease in the first place?

I was working in a general pediatric diagnostic clinic in the early 1990s. That provided a unique opportunity to see patients who had recurrent spells of fainting back-to-back with those who had ME/CFS. What struck me was the similarity in the physical conditions (i.e. in quiet upright postures) that led up to lightheadedness in the fainters and to increased symptoms in those with ME/CFS.

At that time, only the fainters were being evaluated using tilt table testing. When we investigated ME/CFS patients using tilt table tests, we found, somewhat surprisingly, that they had much worse control of blood pressure and heart rate than the fainters. When we began treating the ME/CFS patients with medications that worked for recurrent fainting, it opened up new possibilities for improving daily function. Treating the circulatory problems in many instances helped their cognitive fogging, improved energy and lightheadedness, and enabled them to tolerate exercise. These were exciting and gratifying changes, and I became fascinated by the challenges of trying to find better explanations for the genesis of ME/CFS symptoms and also better treatment approaches.

### If you had a magic wand, what are the top three barriers you would remove first in order to accelerate the discovery process or improve the lives of patients?

First of all, I think a better linkage between clinical care and scientific investigation is critical to advancing



*Peter Rowe, MD, Professor, Johns Hopkins Medical Center. Director of the Chronic Fatigue Clinic at Johns Hopkins Children's Center; Professor of Pediatrics, Johns Hopkins Children's Center, Baltimore, MD*

understanding. Right now we have a striking mismatch between the number of patients needing care and the number of experienced ME/CFS providers. The more clinicians we can attract to the field, the greater the chance that new treatment strategies will emerge. Good clinical observation will almost certainly refine the scientific questions we need to ask.

Second, I think we need better funding for practical treatment trials that can more rapidly assess the efficacy of current or proposed treatments, or replicate the more promising studies done before. It is shameful that 20 years later we have still not had a replication of Kathy Rowe's randomized controlled trial that demonstrated the effectiveness of intravenous immunoglobulin in adolescents with ME/CFS. Another barrier to overcome is the lack of consistent funding to enable us to attract and retain young CFS investigators.

### Tell us about the new pediatric primer.

In June of 2017, the journal *Frontiers in Pediatrics* published a primer on diagnosis and best practices for symptom management in ME/CFS adolescents and young adults. Initiated by an invitation from Ken Friedman, Alan Gurwitt, and Rosemary Underhill and authored by an international group of ME/CFS experts, the Primer contains an abundance of practical clinical advice—including tips on diagnostic criteria, ways to distinguish ME/CFS from other fatiguing illnesses, strategies for addressing symptoms, and specifics on the unique aspects of ME/CFS in children and adolescents. It also provides detailed suggestions on how to diagnose and manage orthostatic intolerance, one of the most treatable contributors to pediatric ME/CFS symptoms.

*Disclosure: The Solve ME/CFS Initiative sponsored the publication of “Myalgic Encephalomyelitis/Chronic Fatigue Syndrome Diagnosis and Management in Young People: A Primer” in the journal Frontiers in Pediatrics.*

### You are an expert in ME/CFS but also in Orthostatic Intolerance (OI) and Ehlers-Danlos syndrome (EDS). Can you describe the overlap a bit and how knowledge of OI and EDS is helping us understand ME/CFS?

Chronic fatigue had long been recognized as a prominent, often unavoidable symptom in EDS – a heterogeneous condition characterized by joint hypermobility, skin fragility, and connective tissue laxity. In the pediatric ME/CFS clinic, we noticed that we had significantly more EDS patients than expected, most of whom had not been diagnosed with EDS. Similarly, in the Genetics clinic, many EDS patients met the criteria for CFS, but had not been given that diagnosis.

Even in the absence of full-blown EDS, 60% of our pediatric ME/CFS patients had joint hypermobility on examination, compared to just 24% of healthy controls. Having connective tissue laxity thus increases the risk of developing CFS, although the mechanism isn't

entirely understood. One observation that has emerged from studying the EDS patients is that, like those with CFS, they have a higher prevalence of lightheadedness and orthostatic intolerance than healthy individuals. The mechanism might be that their blood vessels are as stretchy as their skin and ligaments. When we stand, and blood shifts to the lower half of the body, the blood vessels of those with EDS dilate more readily in response, allowing more gravitational pooling of blood, which in turn predisposes them to postural tachycardia syndrome (POTS) and neurally mediated hypotension (NMH). Treatments and PT practices that help those with EDS can help us treat those with ME/CFS more effectively, and the same goes for clinical insights from ME/CFS that are now being made available to those with EDS.

### Is there a particular line of investigations that you see missing or need more emphasis? What do you think are the most promising areas right now?

I'd like to see more attention to the ability of orthostatic stress to aggravate cognitive dysfunction, PEM, and other symptoms of ME/CFS. I'd also like to see more work on the role of auto-immunity, following up on the interesting preliminary work on antibodies directed against autonomic receptors in POTS and ME/CFS (see for example work by Kem D, 2014; Loebel M, 2015). This may overlap with the work by Fluge and Mella on rituximab and other therapies that have been used in auto-immune illnesses.

The EDS/joint hypermobility overlap with ME/CFS has been relatively neglected in the ME/CFS world and I think we need to more seriously investigate this interaction.

We need more investigation of the interaction of nerve movement and nerve function, especially given that adding tension to nerves and soft tissue can increase the intensity of symptoms in ME/CFS. We need to understand how the nervous system gets mechanically sensitized in ME/CFS and further treatment in this area.

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## Dr. Rowe: A Leading Voice for Children & Adolescents with ME/CFS (cont'd)

A relatively new observation that warrants more attention is that mast cell activation syndrome (MCAS) symptoms overlap a great deal with CFS. A subset of those with POTS and syncope have mast cell disorders. There has been very little investigation of this overlap, despite the potential for improved understanding of the mechanisms of symptoms, and some very practical therapeutic options for those with ME/CFS.

### How do you evaluate the work SMCI is doing in the field?

Research funding can be fairly conservative, often favoring low-risk/low-reward projects. SMCI has been essential to investigators with new ideas and hypotheses, providing money for seed projects that allow collection of preliminary data in support of larger NIH applications. It takes a while for new findings to gain traction in the scientific community. Many of the investigators who have made the greatest impact on the field have had early funding from SMCI. Importantly, SMCI is not only facilitating funding for ME/CFS medical

research but is also generating new data and findings proactively to share with the broader community and is filling knowledge gaps and giving visibility to the disease throughout. I am impressed with the work of this committed organization and pleased to be serving on its RAC.

### Tell us a little bit about your personal life and hobbies, if you wish.

My wife Carla and I have one child, Ian, who was a long-distance swimmer in high school and college, and is now a full-time swim coach with the Nation's Capital Swim Club in the Washington DC suburbs. Carla is an amateur landscape photographer, and I have picked up that interest from her. I like to do a bit of vegetable gardening, although the fruits of those labors are usually enjoyed more by the animals that steal the produce than by our family. And I am a big Orioles fan, always hoping for a return to the glory days of their 1960s teams. ■



## Solve ME/CFS Initiative partners with Jennifer Brea's film "Unrest"

We are pleased to announce that SMCI has joined forces with the impact campaign for the ground-breaking documentary film, "Unrest," directed by and starring Jennifer Brea. SMCI is now an official partner of "#TimeForUnrest," a global impact campaign to change the way the world sees, supports, treats, understands, and funds ME. The campaign officially launches in September; stay tuned for more announcements.

If you are interested in volunteering or supporting this effort, please e-mail Emily Taylor at [ETaylor@SolveCFS.org](mailto:ETaylor@SolveCFS.org).

# New Leader, Same Passion



Just a few short months ago, Vicki Boies (pictured left) completed her term as Chair of the Board of Directors of the Solve ME/CFS Initiative. Dr. Boies continues on in the role of Vice-Chair and her leadership has been instrumental in effecting the many positive developments at SMCI over the recent years.

We are pleased to introduce our new Chair, John Nicols (CEO of Silicon Valley biotech firm Codexis), and share a few words from Dr. Boies. ■

## FROM VICE-CHAIR VICKI BOIES

Dear Friends,

Like all of you who are patients or caregivers for a patient, ME/CFS has been an unfortunate fixture in my life for too many years. My family member became ill in the late 80's, was diagnosed in the early 90's, and is still ill today. During those early years, little was known about the illness and there were too few scientists or physicians interested in ME/CFS. The situation felt very desperate.

While there are still no reliable treatments and there is much to be done, today's landscape looks much more hopeful. SMCI has been one of the important factors in making this change.

For the past 8 years, I have had the privilege of serving on the SMCI Board including the past 3 plus years as the board chair. It has been an exciting time. Under the very able leadership CEO Carol Head has brought to the organization, we have made great strides in research, both in-house and supporting others' work in science and discovery. We have seen measured success in making ME/CFS much more visible on the national scene through our greatly increased advocacy and education efforts. Our staff is currently made up of a group of highly effective and dedicated people who accomplish so much more than our resources would seem to support. We have been especially fortunate to have Dr. Zaher Nahle join SMCI two years ago; he has transformed our research program into the very powerful multi-pronged strategic approach we have today.

I know that our leadership team, along with our new chairperson, John Nicols, will ably continue to lead the organization in our mission to diagnose, treat and cure ME/CFS.

Fondly,

Vicki Boies, Psy.D  
Vice-Chair and former board Chair  
Solve ME/CFS Initiative



John Nicols, pictured above, serves as President and CEO of Codexis Inc., a leading San Francisco Bay Area biotechnology company that engineers and markets proprietary proteins for the world's pharmaceutical industry. Prior to Codexis, John worked in strategic development for 22-years at Albemarle Corporation, a globally leading specialty chemical company headquartered in Baton Rouge, La.

A native of New York City, John earned an MBA from the M.I.T. Sloan School of Management, and a Bachelor of Science in Chemical Engineering from the NYU Polytechnic University.

John is married with two children and four grandchildren. His wife has suffered for over 20 years with Myalgic Encephalomyelitis (ME/CFS) and Fibromyalgia. ■

# Sharing the Success of ME/CFS Advocacy Week May 2017

This May, the events in Washington, DC marked the culmination of five months of planning as SMCI led two weeks of actions online, locally, and the Capitol building itself. In partnership with #MEAction, we built a national coalition to drive action in key areas of US policy and make the voices of people with ME/CFS heard in Washington, DC.

This monumental advocacy effort included actions for patients of every energy level and ability to participate, from a social media post, to a Capitol Hill face-to-face meeting with Congressional leaders. The goal of our efforts is to educate, empower, and deliver our message to Congress to take action on ME/CFS, and set the stage for 2018 advocacy. Our SMCI staffer Emily Taylor brings deep experience, having succeeded in similar advocacy for autism, prior to joining SMCI.

As part of ME/CFS Advocacy week, 52 ME/CFS advocates (composed ME/CFS patients and their loved ones) met with 712 members of congress and their representatives in Washington DC. Our efforts represented 56 states, districts, and territories from across the country. Additionally, over 25 local district meetings took place to supplement our Washington, DC-based efforts.

Effective advocacy is a slow, strategic, step by step process. With our eyes on the prize, our goal is to build foundations for sustained, effective policy work in the future. The most successful advocacy campaigns are layered with short term and long term goals folded together, with “easy” goals and more difficult long-term asks working together.

As one congressional staffer told our team, “we don’t fund by need, we fund by noise.” The Solve ME/CFS Initiative advocacy strategy in 2017 and beyond is specifically designed to make a lot of noise. And we need to make the **right kind** of noise in the **right places**; this is how experience strengthens our work.



*Pictured above left to right, ME/CFS Advocate Naomi Edelson, Congressman Jim McGovern, SMCI Director of Advocacy and Public Relations Emily Taylor*

## **DURING A TWO WEEK PERIOD IN MAY, WE SUCCESSFULLY COMPLETED, WITH #MEACTION:**

- 71 meetings with Washington, DC congressional offices
- 8 meetings face-to-face with members of congress
- A sponsored Capitol Hill briefing with remarks from Senator Ed Markey (MA)
- 2 online actions resulting in over 3,327 messages to congress about ME/CFS
- 3 FREE online training webinars for ME/CFS advocates
- Over 25 local district meetings across the country
- A nationwide call-in day to members of congress
- Three successfully passed state resolutions on ME/CFS (thanks to Bobbi Ausubel, Mark Camenzind, and Laura Bucholtz)
- 1,161 advocates who took action on ME/CFS
- 6 tweets from politicians

## Think Global - Act Local

The Solve ME/CFS Initiative was pleased to support many local advocates in securing proclamations from state and local governments acknowledging ME/CFS.

The State of California passed SCR 40 unanimously becoming the 6th state to pass an awareness resolution for ME/CFS. The California resolution led by Senator Steve Glazer and Assemblywoman Katherine Baker declared every May in California as ME/CFS Awareness Month. A special thank you to **Marilyn Yu** for leading the charge in Sacramento.

Local advocates **Laura Bucholtz**, **Mark Camenzind**, and **Bobbi Ausubel** led the charge in their home towns to pass three city proclamations for ME/CFS in Sarasota, FL, Palo Alto, CA and Walnut Creek, CA.



ME/CFS Advocates take a break in the patient rest area in Cannon House office building (top). Pictured above from left to right, SMCI's Chief Scientific Officer and Vice President for Research Dr. Zaher Nahle, Congressman Ryan Costello, and ME/CFS Advocate Michelle Roy (above).

## Winning Friends and Influencing Congress

In early August, the House Appropriations Subcommittee on Labor-HHS finally released their vision of federal spending for Fiscal Year 2018 in House Resolution 3358. We are disheartened to report that the accompanying committee report, again, zeroed out the \$5.4 million line item for Chronic Fatigue Syndrome at the CDC's Center for Emerging and Zoonotic Infectious Diseases.

Seeing this bad news for ME/CFS, within a week SMCI launched a nationwide action alert turn to the Senate to restore the funding for these critical research, education, and awareness programs. At the time of writing this piece, the congressional messaging campaign has resulted in approximately 1,850 messages to congress calling for the funding to be restored in the Senate bill.

Joining us in this campaign was one of the largest women's organizations in the country, the National Organization for Women (N.O.W.). It was a significant victory for SMCI to collaborate with N.O.W. who stepped up to call out congress on their unjust and discriminatory treatment of ME/CFS.

*Many thanks to Rivka Solomon and her mother Bobbi Ausubel for their work in making this happen.*

The letter, signed by N.O.W. president Toni Van Pelt, urged congress "to seize this opportunity to quickly advance diagnosis, treatment, and a cure for ME/CFS, by restoring and expanding funding in research and education programs at a level commensurate with other similarly burdensome diseases unaffected by stigma or gender bias. Doing so will spur research at a time when many scientists believe that major discoveries are imminent, as well as bring new investigators into the field."

SMCI welcomes N.O.W. as an ally and eagerly looks forward to more joint actions in the future for the millions of men AND women suffering with ME/CFS. ■

# PATIENT VOICES

In this recurring section of *The Solve ME/CFS Chronicle*, SMCI features the creativity and talent of the ME/CFS community. In every issue you can find the art, writing, or other creations of ME/CFS patients here.

In the summer of 1996, when Hal Kahn picked up his many prescriptions at his local pharmacy his eyes lingered on a tin of watercolors. He wanted to buy one but didn't know why. By 1997, Hal had to stop working due to ME/CFS and he gave in and purchased the paints. He could no longer hike or go birdwatching and found that painting lifted his spirits in an unexpected way.

A new passion seized him, helping him deal with the frustrations of ME/CFS: photography. He started with flowers, then a long series of models and finally what became his true calling—faces of the elderly.

“I found meaning in the deeply weathered faces that mirrored my own physical and emotional exhaustion,” Hal shared.

Hal found that photography supplied three key ingredients for dealing with his ME/CFS. It gave him learning, short-term visitors who didn't stay long enough to tire him out, and personal growth that allowed him to find a new identity.

“In my photographs, I strive for meaning rather than beauty... Today, art is the most enriching part of my day. And in the struggle against this illness that brings so



many negatives, it is important to find the positives.” ■

To submit an item to Patient Voices, please email Emily Taylor at [ETaylor@SolveCFS.org](mailto:ETaylor@SolveCFS.org).



# SMCI Answers Reader Questions

SMCI addresses common questions we receive from those in the ME/CFS community.

**Q:** I was looking for specific information on prevalence of ME/CFS, but I could not find it anywhere. I have heard it said that ME/CFS is more prevalent than AIDS and MS. I was unable to find any prevalence figures today anywhere on the Internet, despite about half an hour of looking. Can you please direct me to prevalence figures for ME/CFS compared to other diseases?

**A:** According to the Institute of Medicine report published in 2015, “between 836,000 and 2.5 million Americans suffer from ME/CFS” or between 0.3% – 0.8% of the US population. But, as the report clarifies, the estimate varies because different prevalence studies utilize different definitions of ME/CFS and because between 84%–91% of patients are undiagnosed. By way of comparison, multiple sclerosis (MS) is estimated to afflict 400,000 Americans and 1.1 million Americans are estimated to have HIV/AIDS. ME/CFS also afflicts more patients than Parkinson’s (about 1 million Americans), amyotrophic lateral sclerosis or ALS (about 30,000 Americans), and breast cancer (about 250,000 cases a year).

The most recent Canadian prevalence study was released in March 2017 by Statistics Canada and found that 560,000 Canadians (1.6% of the Canadian population) report being diagnosed with ME/CFS by a doctor, a 37% increase from previous estimates. If that same percentage were applied to the US population, it would mean that about 5.2 million

Americans have the disease.

It has been nearly a decade since the last CDC prevalence study in the United States so new research using an appropriate criteria is desperately needed to determine an accurate prevalence rate in the United States. Currently, the CDC has no plans to do an ME/CFS prevalence study, despite our many inquiries regarding this issue.

**Q:** Today was Severe ME/CFS day but no one in my town is aware of that. Where are you putting the word out? Most people still don’t believe I’m really sick. I’ve been sick for 45 years. I know social media is considered the best way to capture an audience. But, what about TV? What about using some PSAs? Companies continue their TV advertising, they must be hitting a huge target audience. So, why not try this avenue of outreach?

**A:** The simple answer is that it is very, very expensive to do this kind of outreach, particularly on television. Neither our organization, nor any other in the ME/CFS space, has anywhere near the financial resources to mount a meaningful campaign.

And at the same time, we make many efforts to get into ME/CFS into the spotlight. When we find low-cost, high-reward media opportunities, we jump on them. Last year, with the support a dedicated and generous donor, we were able to purchase a Times Square billboard advertisement for 3 months



reaching an estimated 185 million viewers with information about ME/CFS. In the next Chronicle issue, we will share the details of our work on a two-part series on ME/CFS with a nationally syndicated TV show on PBS. Additionally, we are proud to have instigated a feature story regarding ME/CFS that will publish in the December issues of Ms. Magazine, reaching 110,000 paid print subscribers, in addition to online readers.

So while television advertising is prohibitively expensive for an organization our size, we believe that our donors’ precious dollars are best invested in research and scientific discovery. ■

## CHRONICLE READER SURVEY

Thank you to everyone who completed the reader survey in the spring 2017 issue of our Chronicle, to help us improve *The Chronicle* and our other publications. We think about the accessibility of our communications and publications.

Font # 3 received the most votes and we will utilize it in our future publications.

# Make A Lasting Gift to Solve ME/CFS Initiative

Solve ME/CFS Initiative (SMCI) is the leading disease organization solely dedicated to solving the devastating disease Myalgic Encephalomyelitis (ME), commonly known as Chronic Fatigue Syndrome (CFS).

Science and discovery are the core of our work supported by strategic policy advocacy, community building, and targeted education initiatives. We believe that the best way to serve patients is to defeat this debilitating disease by investing in promising research, fostering an environment for scientific collaboration, providing information to patients based on credible research, and by advocating for increased federal funding to support scientific discovery. At SMCI, we are committed to making ME/CFS *understood*, *diagnosable*, and *treatable*.

You can support our work and help us defeat this disease by making a provision for SMCI in your will.

We all think about the legacy we will leave behind. By making a provision for SMCI in your will, you can help support those who suffer from ME/CFS well into the future. You may also be able to make a larger gift than otherwise possible, and your heirs may save on estate taxes. These kinds of planned gifts can also be revoked, allowing for changes as needed. You may designate a bequest for a specific purpose or leave it unrestricted. An unrestricted bequest provides general support for SMCI and will allow us to use the gift where it is most needed at the time. You can make a bequest to SMCI by preparing a new will or revising an existing one.

## You can provide for SMCI in your will in several ways by:

- Making a specific bequest of cash, securities, or other property by designating an exact dollar amount, an asset, or a fixed percentage of your estate, or
- Making a bequest of all or a portion of your estate, after it has provided for all other beneficiaries, or
- Making SMCI a contingent beneficiary of your estate by specifying that SMCI will receive all or a portion of the estate if named beneficiaries do not survive you.



For more information about SMCI's planned giving program, please contact Carolyn Mayo, Director of Development at [CMayo@SolveCFS.org](mailto:CMayo@SolveCFS.org) or (704) 364-0016 ext. 207.

**You can also help by making a direct contribution to Solve ME/CFS Initiative to defeat myalgic encephalomyelitis/chronic fatigue syndrome by using the envelope enclosed inside this issue.**

# Parting Thoughts from our President Carol Head

Dear Friends,

I spend virtually all my energy thinking about the awful, misunderstood disease that we know all too well. This intense focus is, indeed, my job, but more importantly my deeply felt passion.

I remember all too well my own anger, frustration and sense of injustice from those years when I lived in constant pain. I felt that my life as I had wanted it to be was over. I'm aware that I somehow got lucky and dodged a bullet with my significant (though far from complete) recovery. But those memories of despair run deep.

I often force myself to sit back and ask myself how our grand struggle against this disease that we each experience alone, but also collectively, is going. In other words: are we on the path toward genuine reason for hope in solving this disease?

First, I think about the areas in which *real frustration* continues:

- There are a smattering of studies with interesting findings, but they are limited—and there is no research funding for replicating them, so that they can be acted upon to move forward toward treatments.
- The vast majority of doctors still have no capability—and many have no interest—to treat the hundreds of thousands of people with ME/CFS who show up in their offices expecting medical care.
- There are no FDA-approved therapies or drugs.
- And while there are exceptions, many families and friends are still bewildered by our illness and fall short in their care and compassion for their loved ones. That can be deeply painful.

Then, I focus on the areas in which *genuine progress* is being made. And there are many. Here are just a few:

- Although there are not nearly enough studies, and those that exist are small, more and more are being done around the world. There is a slowly evolving therapy of the disease, with an increased focus on specific

areas of dysfunction. While there have been no breakthroughs, there is real movement. Let me repeat that: There is real movement.

- The NIH has begun a comprehensive, deep, rigorous study of this disease. Reports from participating patients are quite positive about the NIH's sensitivity and commitment.
- The NIH will soon announce the first-ever funding of two or three new research centers for ME/CFS.
- The CDC has updated its website so that doctors, patients or loved ones who go there seeking understanding will find much improved information.
- A rigorous, comprehensive new guide for the treatment of children and adolescents with ME/CFS has been written.
- The powerful documentary film about ME called "Unrest" recently premiered in the United States. Conservative estimates are that at least a million people will see it in the coming year and gain a deeply felt, new understanding of the severity of this disease.

So, yes, I am more hopeful with each passing month. We are all in this together. Those of us at SMCI continue to give it all we've got. We are obsessed and find deep gratification in working on behalf of those of you who are so burdened by this disease.

I wish you more good days than bad. I wish you peace as we move together along this too-long road to toward understanding this disease. And I wish *hope* to all, that one day you will be restored to the life you were born to lead.

Onward!



Carol Head  
President and CEO, Solve ME/CFS Initiative



Carol Head, CEO and President

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## SUMMER 2017

The Solve ME/CFS Chronicle is a quarterly publication about Myalgic Encephalomyelitis (ME), also known as chronic fatigue syndrome (CFS) or ME/CFS. This publication focuses primarily on scientific research, patient, and advocacy features and is provided free of charge by US mail and electronically by the Solve ME/CFS Initiative.

**Solve ME/CFS Initiative (SMCI) is the leading disease organization solely dedicated to solving the devastating disease Myalgic Encephalomyelitis (ME). SMCI is committed to making ME/CFS understood, diagnosable, and treatable.**

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