



Propelling CFS Science Forward

Together the CFIDS Association of America and the CFS community raised \$1 million dollars for CFS research in 2008! Here's a look at what that money will fund in 2009 and the reasons we all have to feel hopeful about finding scientific answers to this illness. Read on . . .



From the Desk of K. Kimberly McCleary, President & CEO

In November 2007, we announced the ambitious Campaign to Accelerate CFS Research with its one-year fundraising goal of \$1 million. By August, our supporters had enabled us to exceed that goal. And in November 2008, following an exhaustive review process, we announced funding for the six innovative research projects described in the following pages. In January 2009, the six teams of funded investigators met to synchronize their studies and launch the first formal CFS research network. A midterm investigators meeting at the prestigious Cold Spring Harbor Laboratories promises to further maximize the synergy of these gifted scientists. We are actively leading this network and connecting the dots to other research. I have never been more hopeful about a specific CFS research initiative than I am today.

We've also looked to the change in Washington, D.C., as a positive force in our mission to conquer CFS. Throughout the upcoming year, Dr. Suzanne Vernon and I will be active on Capitol Hill, providing updates to staff of key members of Congress. In early 2009, we briefed Dr. Wanda Jones, a senior Department of Health and Human Services leader given responsibility for CFS, about CFS research and the community's needs. With all the challenges our nation currently faces, an era of "tough love" is being ushered in by those who propose funding laws. But the status quo is simply not good enough and we're challenging Congress and the health agencies to do much more.

To position these programs as top priorities, we have had to give up some other activities. The world changed literally and figuratively in 2008, on every front including the CFS horizon. The weak economy took a toll on the Association's donors and we've had to make some difficult choices to conserve precious resources and protect vital programs that don't exist elsewhere. But we're energized by the opportunity to focus more intensely on a limited number of programs. It's actually the one thing we haven't tried in 22 years, as each year we've taken on greater responsibility for filling the wide spectrum of needs that exist. We believe these changes will make the Association stronger and more potent in its work looking ahead, and you have clearly told us you want to see accelerated progress.

The *CFIDS Chronicle*, our quarterly magazine for patients distributed as a membership benefit, is one of the things that will change to accommodate the tighter focus and present fiscal realities. To reduce printing and postage expenses, we are refocusing the content, size and frequency of future issues. You'll continue to hear from us in print and through electronic and digital means, both as a way of curbing costs and adapting to the growing popularity of other communication channels.

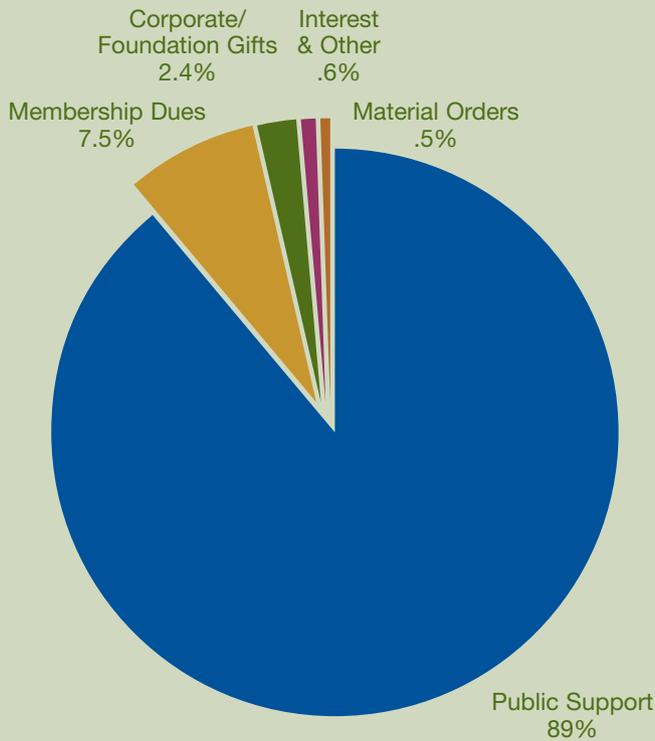
We are confident that our new focused purpose adapted by our Board of Directors last November and other changes will yield inspiring progress. We hope we can count on your continued interest and support.

With warmest regards,

K. Kimberly McCleary
President & CEO, the CFIDS Association of America

“To accelerate progress toward accurate diagnosis and effective treatment of CFS by directly supporting research studies; facilitating collaboration among investigators; and advocating for increased investment in CFS research by public, private and commercial institutions.”

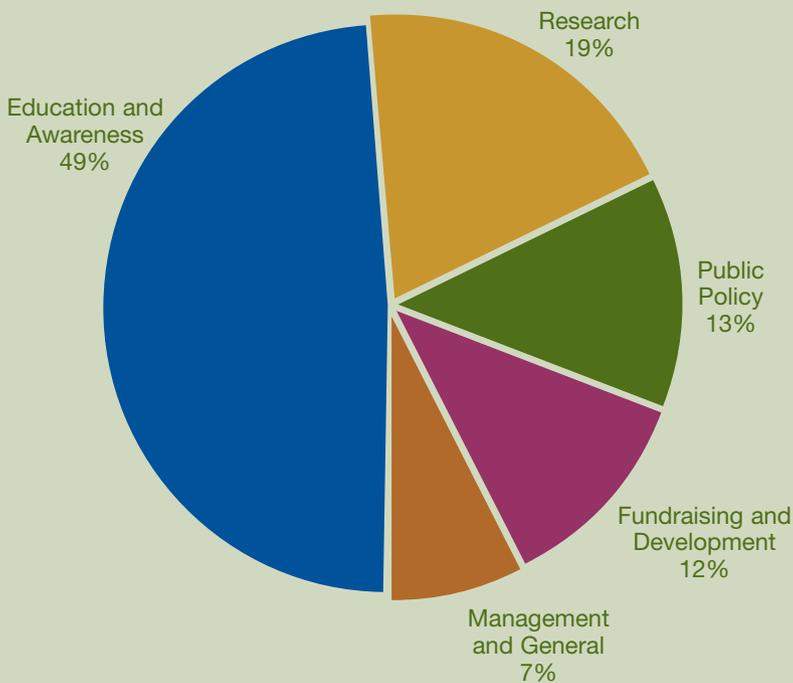
Purpose statement of the CFIDS Association of America as adopted by the Board of Directors, November 5, 2008



2008 Sources of Revenue

Excluding government grants for specific projects

Public Support	\$1,407,911
Membership Dues	118,672
Corporate/Foundation Gifts	37,702
Interest & Other	10,360
Material Orders	7,338
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	\$1,581,983



2008 Use of Funds

Education and Awareness	\$ 890,608
Research	350,186
Public Policy	235,845
Fundraising and Development	213,084
Management and General	136,675
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	\$1,826,398

Statement of Activities

Year Ended December 31, 2008

(with comparative totals for year ended December 31, 2007)

	Year Ended December 31, 2008			Totals	Year Ended December 31, 2007
	Unrestricted	Temporarily Restricted	Permanently Restricted		
Support and revenues					
Public support:					
Contributions and grants	\$ 727,090	\$ 718,523	–	\$ 1,445,613	\$ 1,281,030
Federal funds:					
Government grants	336,119	–	–	336,119	1,881,388
Revenues:					
Membership dues	118,672	–	–	118,672	145,252
Educational material sales	7,338	–	–	7,338	11,631
Interest and other	10,360	–	–	10,360	34,976
	136,370	–	–	136,370	191,859
Assets released from restrictions					
Satisfaction of donor restrictions	280,941	(280,941)	–	–	–
Total support and revenues	1,480,520	437,582	–	1,918,102	3,354,277
Expenses and losses					
Program services:					
Research	350,186	–	–	350,186	265,388
Public Policy	235,845	–	–	235,845	227,188
Education	890,608	–	–	890,608	2,545,543
Supporting services:					
Management and general	136,675	–	–	136,675	135,042
Fund raising and development	213,084	–	–	213,084	236,325
	1,826,398	–	–	1,826,398	3,409,486
Gain on assets disposed					(5,437)
Total expenses and losses	1,826,39	–	–	1,826,398	3,404,049
Change in net assets	(345,878)	437,582	–	91,704	(49,772)
Net assets					
Beginning of year	1,030,539	539,964	5,400	1,575,903	1,625,675
End of year	\$ 684,661	\$ 977,546	\$ 5,400	\$ 1,667,607	\$ 1,575,903

Research Matters

From its earliest days, the CFIDS Association of America has funded research and sought the ways most likely to accelerate scientific progress. We've provided seed money to the earliest clinicians who treated CFS patients while gathering information about the illness. We've funded more than 70 studies to date, exploring nearly every facet of this complex illness, and we've sponsored symposia and conferences to help grow the field of CFS research and increase the number of researchers investigating it. During this time, we've also worked diligently to underscore the need for more CFS research by lobbying the federal government and keeping CFS in the public spotlight.

Now with greater public awareness and advances in technology giving us better tools, the CFIDS Association, with your support, has taken its next major step in building the capacity of the scientific community to transform CFS into a condition that's treatable, preventable and curable.

Intent on seizing critical opportunities to propel the field forward and to speed progress, we launched an ambitious *Campaign to Accelerate CFS Research*, with the unprecedented goal of raising \$1 million to expand our research program. And with the help of people like you from the CFS community, the Association reached that \$1 million milestone goal in October of 2008!

This marks a bold advance in the work to conquer this illness—sending the signal that people with CFS, their loved ones and the Association have united to resolve the scientific challenges facing us. The success of this campaign can now be directed at key leverage points to move CFS science forward. In fact, that has already begun.

In November of 2007, as the million-dollar campaign was getting under way, the CFIDS Association hired Suzanne Vernon, PhD, as scientific director—the first scientist the CFS community has had working fulltime with the sole focus of accelerating research. She's hit the ground running, already participating in more than six scientific conferences, facilitating strategic collaborations between researchers, encouraging better CFS public policy and efforts by health agencies, and updating the CFS community in three online sessions. She's also coauthored a noteworthy eight CFS-related papers published in scientific journals over the past year.

In addition to this force of work out in the field, Vernon applied her scientific prowess and professional experience to enhancing the Association's grant-making program, adding more rigor to the grant application process and involving 44 independent scientific experts in the review process.

As a result of the funds raised and the robust grant process employed, the CFIDS Association awarded six grants in this cycle, totaling \$647,940, to research teams with broad expertise covering a wide range of fields including bioinformatics, microbiology, immunology and physics. Most of the grant recipients, while experts in their own respective fields, are new to CFS research, offering exciting possibilities and suggesting a heightened level of interest in studying this illness.

Selected from among 33 initial grant applications, these six research teams will also share data and expertise with each other in a collaborative element that's new to the program and holds great promise for advancing both the science and the results.

The grant recipients are:

- Gordon Broderick, PhD, associate professor, Department of Medicine, University of Alberta, Canada
- Kathleen Light, PhD, research professor, University of Utah Health Sciences Center
- Marvin Medow, PhD, associate professor, Department of Pediatrics, New York Medical College
- Bud (Bhubaneswar) Mishra, PhD, professor, Courant Institute of Mathematical Sciences, New York University
- Sanjay Shukla, PhD, research scientist, Marshfield Clinic Research Foundation
- Dikoma Shungu, PhD, professor, Weill Medical College of Cornell University

In the next six pages you will be introduced to these six researchers and the investigations they'll be conducting to help identify biomarkers that will lead to improved diagnosis and treatment of CFS.

Recipe for Discovery

What do you get when you take an energetic chemical engineer who thinks no challenge is too big and a unique “systems biology” approach to science and apply them to studying patients who developed CFS after infectious mononucleosis? You get the work **Gordon Broderick, PhD**, will be doing with the grant he received from the CFIDS Association. You also get a great deal of promise for uncovering biomarkers for postinfectious CFS.

Broderick, an emerging leader in the field of computational biology, will direct a cross-disciplinary team from four institutions to study adolescents who became ill with CFS after contracting infectious mononucleosis, which is caused by Epstein-Barr virus (EBV).

Earlier studies suggest that infection with certain agents such as EBV can trigger CFS, and that the severity of the initial infection is a key predictor of who will develop CFS (see “The Viruses We Live With” on page 14).

Broderick’s study is unique in several ways. First, he’ll look at CFS in a very specific and well-defined group of patients, hoping to reduce some of the confounding variables that age and illness duration can impose. Adolescent patients will be studied through a collaboration with Renee Taylor, PhD, of the University of Illinois at Chicago. Taylor has studied CFS with support from the National Institutes for Health (NIH).

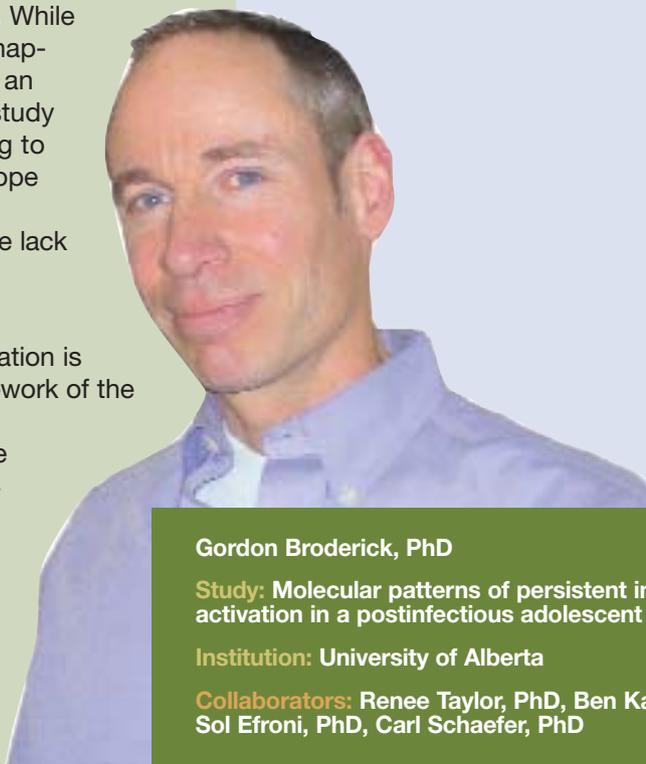
Second, Broderick will investigate the immune and endocrine responses of the study subjects from initial infection through the first 24 months after becoming ill. While most CFS studies look at a single-point-in-time snapshot of the illness, this longer term look provides an exciting opportunity to track the changes in the study subjects as the illness process unfolds. According to Broderick, “By studying patients over time, we hope to identify the series of events that precede disease and the factors responsible for the lack of recovery in the people who develop CFS after mononucleosis.”

Another unique feature of Broderick’s investigation is the approach he’ll employ to “engineer” the framework of the illness through the data he collects. By applying advanced mathematics, he will “map out” how the body’s different systems talk to each other in CFS and how this conversation might differ from the one found in healthy people.

Add to all that Broderick’s striking enthusiasm and energy to tackle any challenge, and you have a potent mix of possibility indeed.

Perspective
from our scientific director
Suzanne Vernon, PhD

“What makes this study exciting is not only the topic of postviral CFS but also the principal investigator. Broderick is adept at using mathematics to analyze chemical and physical processes and using that data to construct the underlying system of an illness. He’s applying that unique expertise to CFS, and the skills and tools he’ll use in this study hold great promise for identifying subtle disruptions in immune and endocrine function that might otherwise go undetected.”



Gordon Broderick, PhD

Study: Molecular patterns of persistent immune activation in a postinfectious adolescent cohort

Institution: University of Alberta

Collaborators: Renee Taylor, PhD, Ben Katz, MD, Sol Efroni, PhD, Carl Schaefer, PhD

Shedding Light on Fatigue and Pain

Until recently fatigue and pain have been thought of primarily as symptoms rather than physiology. But what if the biochemistry of fatigue and pain could actually be detected and quantified in the blood? **Kathleen Light, PhD**, made that preliminary finding in her recent NIH-funded research of CFS, and now the CFIDS Association is enabling her group to expand its work.

Light is an established scientist in pain research. In the NIH-funded study, she and her research partner and husband Alan Light, PhD, found preliminary evidence of increased expression of pain receptors (called acid-sensing and ion-channel receptors) in the blood of CFS patients after an exercise challenge designed to replicate normal daily activity. The increase in these fatigue- and pain- sensing receptors lasted for two days following the 30-minute exercise, corresponding with the CFS patient's reports of more intense fatigue and pain.

With the new grant from the CFIDS Association, Light and her team will expand their observations from the earlier study by examining a larger group of CFS patients.

The investigation could also have diagnostic significance. According to Light, "We can explore whether increased expression of specific receptors following exercise could be blood-based biomarkers for CFS that would help identify patients with this disorder through a safe and unbiased medical test."

The study also has treatment implications since it will explore whether CFS patients who exercise more or use certain medications show closer to normal levels of these post-exercise blood biomarkers, and if they experience less fatigue and pain. That could prove helpful in determining whether specific treatment regimens are likely to be effective or not.

Another interesting feature of this study is Light's collaboration with well-known CFS clinician Lucinda Bateman, MD, who'll be providing subjects for the investigation. Bateman's clinical expertise will ensure that the patients are well-characterized for the study, and she'll lend additional clinical insight to the analysis of study data.

With Bateman and both Lights working on this investigation, the potential to illuminate the postexertional fatigue and pain of CFS is high.



Perspective
from our scientific director
Suzanne Vernon, PhD

"Light's preliminary findings of blood-based biomarkers for postexertional fatigue and pain in CFS is groundbreaking, putting these elements of CFS on physiologic footing. Because postexertional symptoms are a hallmark of CFS, this study could lead to a specific CFS blood test."

Kathleen Light, PhD

Study: Novel ion channel-based biomarkers in CFS

Institution: University of Utah Health Sciences Center

Collaborators: Alan Light, PhD, Lucinda Bateman, MD

Exploring the Frontier Within

Microbes are minute one-cell life forms, millions of which live within our bodies in what science has termed the “microbiome.” As science uncovers more about this microbial world within us, those who study it are finding that the composition and balance of microbes in the gastrointestinal tract, or gut, influences health, affects drug metabolism and may even be associated with disease. So the CFIDS Association is optimistic about exploring this frontier of science through its grant to research microbiologist **Sanjay Shukla, PhD**, to investigate microbial markers in CFS following an exercise challenge.

By studying the gastrointestinal microbiome, Shukla’s work will determine if the ratio of normal to pathogenic (illness-causing) bacteria is off-kilter in CFS patients and if exercise causes harmful bacteria to travel into the body from the gut, creating the postexertional symptoms that are such a prominent feature of the illness. To do this, Shukla’s team will use metagenomics—a novel technique that involves sampling the genome sequence of a community of organisms inhabiting a common environment. The results have the potential to yield microbial biomarkers for CFS as well as targeted treatments aimed at rebalancing the ratio of bacteria.

As with many of the other studies the Association is funding in this cycle of grants, Shukla’s study is unique in several ways. It’ll be the first to use metagenomics for microbial investigation in CFS. It also applies cutting-edge science to synthesize several common characteristics of the illness—specifically, postexertional relapse, gut disturbance and chronic inflammation.



Sanjay Shukla, PhD

Study: Metagenomics approach to study chronic fatigue syndrome patients

Institution: Marshfield Clinic Research Foundation

Collaborators: Dane Cook, PhD, Dan Frank, PhD, Steve Yale, MD

Perspective
from our scientific director
Suzanne Vernon, PhD

“This study is exciting not only because it will be the first to carefully examine the gastrointestinal microbiome in CFS but also because of the remarkable team Shukla has assembled. Because the study explores microbes, exercise-induced reactions and gut disturbances, Shukla will conduct the study with the help of a clinical researcher, an exercise physiologist and a microbial ecologist—all of whom are highly skilled in their respective fields. This multidisciplinary strength will bring enormous rigor and insight to the investigation.”

Brain Power

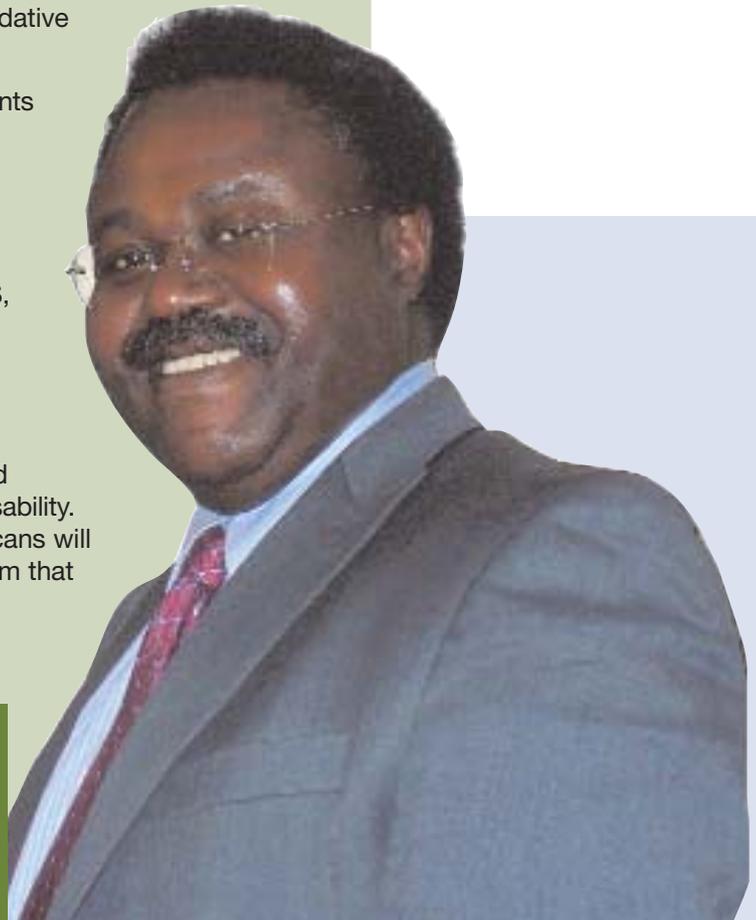
Dikoma Shungu, PhD, an established scientist in neuroimaging and neurometabolism, has been training his sights on the brain metabolism of CFS patients since he received a grant from the CFIDS Association in 2006. And what he's found has been remarkable.

In that initial study Shungu and his team used a brain scanning technique called magnetic resonance spectroscopy (MRS)—which not only provides a picture of the brain but also detects levels of various brain chemicals important to metabolism (energy transformation), including creatine, N-acetylaspartate, choline and lactate. Astoundingly, the results indicated as much as 348% higher lactate levels in the brain fluid of CFS patients than in that of the healthy control subjects. These findings were published in October 2008 in the journal *NMR in Biomedicine*.

The new award from the Association will allow Shungu's team to verify the results of the earlier study by examining a larger group of CFS patients and comparing results to a disease control group of depressed study subjects. It'll also enable the scientists to explore the reason for the elevated lactate levels. According to Shungu, "We want to determine whether lactate levels are higher in the CFS patients because their brains contain high levels of toxic compounds that cause oxidative stress, which could implicate chronic inflammation, or because mitochondrial dysfunction is causing a malfunction in their brain energy production." (See the feature on oxidative stress on page 10.)

This research is significant because it represents the first comprehensive attempt to establish the brain mechanisms that might be going wrong in CFS. According to one leading brain imaging expert who reviewed Shungu's grant application, if this subsequent study finds such high elevations of lactate in another set of people with CFS, then it would be very hard for science or the medical establishment to ignore that something is very physiologically wrong with these patients.

The objectivity of the brain scan results could also be important in establishing occupational disability. If Shungu's earlier results are confirmed, these scans will provide objective evidence of a metabolic problem that indicates an incapacitating level of fatigue.



Dikoma Shungu, PhD

Study: MR neuroimaging assessment of cerebral metabolic substrates and regional blood flow in CFS

Institution: Weill Medical College of Cornell University

Collaborators: Sanjay Mathew, MD, Benjamin Natelson, MD

Going with the Flow

It's long been established that many people with CFS experience symptoms like light-headedness associated with upright posture, broadly called orthostatic intolerance. Is it possible that these symptoms could be connected to blood flow, ultimately reducing the amount of blood that flows to the brain? That's what researcher **Marvin Medow, PhD**, and his team will be investigating with their grant from the CFIDS Association.

Medow is a physiologist and associate director of the Center for Hypotension at New York Medical College where he works with Julian Stewart, MD, a longtime CFS researcher with NIH funding.

This grant will allow Medow's team to examine if CFS patients have increased pooling of blood in the abdomen, resulting in decreased blood flow to the brain when patients are in an upright position, and whether this causes changes in blood chemistry including increased oxidative stress.

Says Medow, "These blood flow and chemical changes could explain many of the symptoms experienced by CFS patients."

Medow's work also has the potential to more clearly characterize the large subset of CFS patients who have autonomic problems. Understanding more about individual subtypes of CFS is the first step to developing effective targeted treatments that can improve function and quality of life.

Another defining feature of this study is the extensive testing Medow's team will employ, including tilt table testing, transcranial Doppler and microdialysis. Medow is also collaborating with CFIDS Association grant recipients Dikoma Shungu, PhD, (see profile at left) and Bud Mishra, PhD, (see profile on page 26) to run brain scans on the same group of patients and to analyze the resulting combined data using cutting-edge bioinformatic techniques.

The combination of Medow's significant expertise, the use of his top-notch hypotension facility and the scope of sophisticated tools and collaboration he'll employ, marks the most intensive exploration of blood flow in CFS and what implications and consequences impairments in these circulatory functions may have for people living with the illness.



Marvin Medow, PhD

Study: Splanchnic vasoconstriction is impaired by microbiomic nitric oxide production reducing cerebral blood flow in CFS

Institution: New York Medical College

Collaborators: Benjamin Natelson, MD, Julian Stewart, MD

Perspective
from our scientific director
Suzanne Vernon, PhD

"An exciting aspect of the awards to Shungu and Medow is that they'll be able to share study subjects to see if the blood flow disturbances Medow finds could help explain the elevated brain lactate levels that Shungu has reported. Each independent study is full of investigative potential, but the collaborative approach marks an exciting advance in the field of CFS science."

The Software Generation

Powerful computational tools are being used on everything from predicting pandemics to personalizing medicine. Now, in perhaps the most “out-of-the-box” project funded in this cycle of CFIDS Association research grants, renowned computer scientist **Bud Mishra, PhD**, will focus his expertise on CFS, building a large-scale software program with the potential to explain mechanisms and identify possible causes of the illness.

Two decades of biologic and biomedical information on CFS exists, but it’s scattered among many sources and not coordinated or organized in any universal way. For years, many people in the CFS community have wished for a way to bring all these studies together to see what patterns emerge. Mishra, with the help of research associate Eric Aslakson, will tackle that challenge.

“There are multiple hypotheses about the etiology of CFS,” says Mishra. “Sophisticated new computational approaches not only can be useful to analyze massive datasets that have accumulated over decades, they can also present a global view of this illness for the first time.” Mishra believes this universal software platform will be able to help characterize CFS and its effects on the body.

It’s a huge undertaking—one that might normally require massive funding to support the required computer infrastructure alone—but Mishra has become so intrigued with the complexities and information challenges of CFS that he’s interested in doing the work for a fraction of what it might otherwise cost. And as one of the scientific reviewers of Mishra’s grant application put it, “If there’s one guy on the planet who can do this, it’s Bud Mishra.”

Once the software tools Mishra and Aslakson create are complete, they will be made available to other CFS researchers. In this way, they hold great potential for encouraging data-sharing and collaboration among researchers worldwide. In fact, the collaborative element will begin right away by using data gathered from other grant recipients to feed into the system for analysis as it’s being developed.

With this grant, the CFS community gains an extraordinary opportunity to reap the benefits of sophisticated computational biology and the millions of dollars spent on research conducted over the past 20+ years.

Bud Mishra, PhD

Study: Translate science to a cure for CFS

Institution: New York University School of Medicine

Collaborators: Eric Aslakson, MS

Perspective
from our scientific director
Suzanne Vernon, PhD

“There’s a wealth of information that can be harnessed and transformed into knowledge about CFS by experts like Mishra and Aslakson, who see computers as their laboratory tool of choice.

This study also serves to weave other grant recipients’ study findings together, connecting the data gained from individual studies and mining it for greater implications. That’s a big first in the area of CFS science.”



Scientifically Speaking

Perspective from our scientific director
Suzanne Vernon, PhD



You've just been introduced to the principal investigators who'll lead six studies aimed at bridging the gap between basic and clinical research and creating a pipeline for objective diagnosis and improved treatment for CFS.

Each investigator brings a unique expertise to what will be the first formally coordinated CFS research network. Additionally, each investigator has assembled an impressive team to tackle the various aspects of clinical evaluation, study coordination and laboratory testing. Altogether, 29 investigators will contribute to this research. And taken as a whole, these studies represent a blend of cutting-edge scientific technology, deeper exploration into proven areas of CFS interest and novel areas of investigation that are receiving attention in the greater scientific community. Yet another first.

All of these firsts make this set of researchers and this research stand out. There's little doubt in my mind that we will, in fact, accelerate the pace of CFS research through these grants and this coordinated approach.

In January of 2008 the Association made the very strategic decision to issue a broad request for research grant applications, hoping to receive an abundance of promising proposals to study CFS diagnosis and treatment. Of the 33 initial proposals we received, these six studies represent the cream of the crop both scientifically and strategically.

Scientifically speaking, these studies will research pertinent CFS subtypes such as postinfection CFS, orthostatic instability, pain and postexertional relapse. Strategically speaking, the investigators will be collecting standardized data on all study subjects, sharing study design information and communicating progress in an effort to boost the real-world implications of their work. By doing so, we believe it's possible to generate sound results that will lead the way to diagnostic and treatment breakthroughs and garner funding from sources like the NIH and industry.

The Association announced its grant-funding decisions in November, and by the time you read this article, we'll have had our first investigators meeting, begun coordinating the research network and started sharing ideas and study data. We've come out of the gate at a sprint because the Association understands the urgency of research to find objective means to diagnose and treat CFS.

The year 2008 was significant for CFS science because people like you from within the CFS community made this first-ever research network a reality. This year promises to be even better because of the coordinated work these six teams will do. You've made this research possible with your investment in us, and we promise to work hard, passionately and around the clock to bring you the best return possible. ■■

NETWORK LAUNCHED

On January 19-20, 2009, all principal investigators and key collaborators met in Charlotte, NC, to exchange ideas, discuss study design and begin the process of sharing study data under the coordination of the Association's scientific director Suzanne Vernon, PhD. Kim McCleary explained the Association's funding strategy and expectations.



Front row (L to R): Ben Katz, Kathleen Light, Dikoma Shungu, Lucinda Bateman, Bud Mishra. Back row (L to R): Suzanne Vernon, Steve Yale, Sanjay Mathew, Gordon Broderick, Julian Stewart, Sanjay Shukla, Marvin Medow, Eric Aslakson, Satish Raj

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