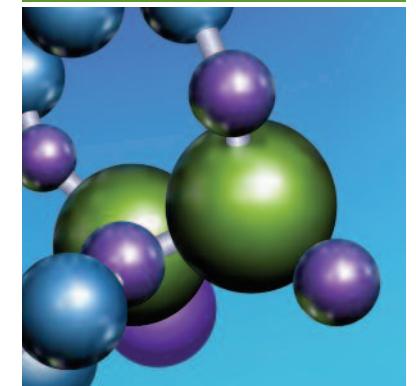


SOLVE CFS

The Chronicle of the CFIDS Association of America

Summer–Fall 2011



Putting Research First

Since its founding in 1987, the CFIDS Association of America has supported important research into the biological basis of CFS through direct grants to investigators, sponsorship of scientific symposia and meetings, fostering collaborations and, most recently, establishing the SolveCFS BioBank. As announced in the fall 2009 issue of *SolveCFS*, we have narrowed our focus to stimulate research aimed at the early detection, objective diagnosis and effective treatment of CFS through expanded public, private and commercial investment. We are transforming from a patient support and advocacy organization to one laser-focused on stimulating and supporting research. We are putting research first.

In this issue of *SolveCFS*, you'll read more about some of the early products of our last round of research grants (see pages 2–3). You'll also learn more about these activities:

Putting Research **FIRST**

SHARPER FOCUS.

DEEPER IMPACT.

ACCELERATED PROGRESS.

- We have formed a **Scientific Advisory Board** of top experts from many disciplines to advise our Board of Directors and staff on strategic research opportunities.
- We **issued a new funding opportunity** for projects that build on the most promising science to advance objective diagnosis and effective treatment for CFS. By September 30, we anticipate receiving 27 full proposals from researchers in six countries.
- We are expanding the **SolveCFS BioBank** and our collaborations with other research institutions to make the BioBank an even more valuable research resource.

We apologize for the long lapse since our last issue of this publication and hope you have been able to access our monthly enewsletter, *CFIDSLink*, and daily updates on Facebook and Twitter. We have recapped the most important news in this issue. On May 24, 2011, we expanded our web-based resources with the launch of a new website called **Research1st**, described on page 10. We've marked articles that appear on **Research1st** in expanded form with this icon: 1st.

The Association is fully committed to ending the life-altering disability, stigma and isolation of CFS. We are grateful for your loyal support and hope we can count on your continued generosity to make this vision a reality. ■

Newsworthy Highlights of 2011 (so far)

Two papers associating CFS with a family of gammaretroviruses (including XMRV) have generated lots of headlines and ample controversy over the past two years (see pages 8–9). Other events have also raised general and scientific awareness about CFS this year; here are several:

Jan. 26: The **Food and Drug Administration** announced that new applications for CFS treatments will be assigned to a single division. Previously, CFS applications were scattered to six different review divisions.

Feb. 4: Author **Laura Hillenbrand** educated *New York Times* readers about her 23-year battle with CFS and the resilience she shares with Louis Zamperini, hero of her latest bestseller, *Unbroken*.

Feb. 23: Researchers at the **University of Medicine and Dentistry of NJ** and **Pacific Northwest National Laboratory** reported on spinal fluid markers that distinguish CFS, non-recovered post-treatment Lyme disease and healthy controls. Katie Couric introduced the story that night on “The CBS Evening News.” 1st

Mar. 5: CFS was the subject of a major feature in the **Wall Street Journal**, “The Puzzle of CFS.” It spotlighted Dr. David Bell, some of his long-time patients in Lyndonville, NY, and the lengthy search for better diagnostics and treatment.

Mar. 12: The front page of the **Wall Street Journal** explored tensions between CFS patients and researchers in “Amid War on Mystery Disease, Patients Clash With Scientists.”

Apr. 7–8: The **National Institutes of Health** hosted the ME/CFS State of the Knowledge Workshop, its first in 10 years. 1st

May: For the first time, the **Department of Defense** included CFS as one of the eligible topics for its Congressionally Directed Medical Research Program.

May 10–11: The **Department of Health and Human Services** CFS Advisory Committee met to make recommendations to Secretary Kathleen Sebelius.

May 26: Researchers at the **University of Utah** reported results from an Association-funded study that shows potential biomarkers for CFS following a modest exercise challenge. 1st

June 29: The **Institute of Medicine** released its report, “Relieving Pain in America,” documenting that 116 million Americans experience chronic painful conditions (including CFS). 1st

July 20: An independent panel of 26 experts from 13 countries published new criteria for **myalgic encephalomyelitis** (M.E.) and recommended this term replace CFS. 1st

July 26: *Nature Reviews Neuroscience* published a six-page Q&A with four CFS researchers about their views on CFS, its causes and the future of research. 1st

Sept.: *Ladies’ Home Journal* covered the challenge of diagnosing, managing and living with CFS.

Sept. 5: Joanne Silberner took a look at CFS research on **National Public Radio’s “Morning Edition.”** ■

IN THIS ISSUE

Page 1 SOLVECFS

Putting Research First
Newsworthy Highlights of 2011 (so far)

Page 2 & 3 INNOVATECFS

Acceleration to Transformation
Returning On Your Investment

Page 4 & 5 INNOVATECFS

Expanding Research:
Looking to the Future
10 Ways
Scientific Advisory Board
Deepens Association’s Expertise

Page 6 & 7 VALIDATECFS

Journal Highlights Reflect Multiple Hypotheses and Body-Wide Dysfunctions
Hi-Fi Sci-Di: Dr. Suzanne Vernon Orchestrates High-Fidelity Research

Page 8 & 9 VALIDATECFS

The X Factor

Page 10 CONNECTCFS

Introducing Research1st
Federal Agency Updates

Page 11 CONNECTCFS

News Briefs
Board, Staff and Contact Info

Page 12 TRANSFORMCFS

The Catalyst Fund

Find links to online material in this issue at www.cfids.org/SolveCFS/smrfall2011.asp

Validate. Innovate. Eliminate.

Acceleration to Transformation

The CFIDS Association was founded in 1987 and our first dollar was invested in research. Over the first 20 years of service to the community, you helped us fund \$4.6 million in research grants, host three research symposia and support numerous conferences and meetings. Over those first two decades, our approach to research followed a traditional model and the studies we funded contributed to a knowledge base of 4,000 small studies.

In 2007, we carefully evaluated the gaps and opportunities. Three important themes emerged from this review:

- The literature was essentially a collection of “one and done” studies with few attempts to validate early observations or extend findings. These had limited benefit for improving patient care.
- Studies were hampered by the use of multiple case definitions and the lack of standardized ways of collecting data about patients or samples from them.
- Research priorities were driven by “in vogue” hypotheses, with few organized efforts to connect the dots or link findings from one study to another.

We knew there was a better way to approach research, and so did you.

In 2008, we added a full-time scientific director, Suzanne D. Vernon, Ph.D., to our staff and we asked you to help us:

- fund innovative studies;
- leverage existing data;
- strengthen international collaborations;
- recruit new talent to the field; and
- expand communication among scientists to share ideas, knowledge and data.

You came through and helped us accelerate the pace of CFS research.

Now we want to transform it.

Over the next four pages, we report on how we have delivered on the promises made in 2008 and what we propose to do next with your participation and support. It is an exciting and pivotal time, with many opportunities to seize. We hope you agree!



“All of this gives CFIDS Association funding a very special meaning. With every dollar being contributed by patients and their families, these projects represent a sacred trust if there ever were one. Looking back, the impact that these donations have had is nothing short of inspiring. They have changed the research landscape for CFS. Key preliminary findings were made possible as a direct result of the patients, their families and the governance of the Association. In turn, these findings have given us a solid scientific beachhead from which to apply for much larger grants. Indeed, results generated with Association-directed patient donations have allowed us to leverage \$125,000 in seed funding into three multi-year operating grants from the Department of Defense (DOD) and the National Institutes of Health (NIH) totaling over \$3.5 million. None of this would have been possible without preliminary research supported by patient donations administered under the stewardship of the Association.

“Also important is the role of this funding in training future clinicians in an area of practice sorely lacking in first-line care providers. Through its support of summer studentships in our laboratory, the Association has contributed to the research training of five undergraduate medical students and two post-doctoral research staff in the endocrine and immune abnormalities associated with CFS. The medical students alone went on to publish three papers in well-respected scientific journals, with two more currently in preparation. Finally, and perhaps most importantly, these patient-funded seed projects are promoting important changes in government research policy, the inclusion of CFS as a research topic in the recent U.S. Department of Defense funding mechanisms (see page 10) being only one example.”



Kathleen Light, PhD of University of Utah

Novel ion channel-based biomarkers in CFS

Objective: Evaluate post-exercise increases in acid-sensing and ion channel receptors on blood cells.

Preliminary Outcomes:

- Funding: Support from a pharmaceutical company to conduct a treatment trial of FDA-approved medications. Supplemental support from organizations supporting MS and fibromyalgia research to include additional comparison groups. Several NIH applications are under review, one pending an award notice.
- Publications:
 - >> Moderate exercise increases expression for sensory, adrenergic and immune genes in CFS but not in normal subjects. *Journal of Pain*. 2009.
 - >> Gene expression alterations at baseline following moderate exercise in patients with CFS and fibromyalgia syndrome. *Journal of Internal Medicine*. May 26, 2011.
 - >> Evidence for a heritable predisposition to CFS. *BMC Neurology*. May 27, 2011.
 - >> Additional manuscripts in preparation and under review.

“Support from the CFIDS Association for our research program on blood-based biomarkers of CFS/ME was vital in keeping this program alive. The data obtained using this support made it clear that we can use post-exertional gene expression for selected markers to differentiate patients with CFS from those with other disorders involving daily fatigue, like multiple sclerosis, as well as from healthy individuals. With this evidence in hand, we are also able to obtain a very strong review for our next grant application with NIH, which we expect to be funded in a few months;

Returning On Your Investment

The most recent research grants funded by the CFIDS Association of America have supported these six principal investigators and the projects that were evaluated to have the highest scientific and strategic merit among the 24 submitted during our 2008 cycle. Funding totaling \$647,940 was awarded to support these research studies, thanks to the generosity of our donors. This report builds on earlier progress updates and we'll continue to keep you informed about additional outcomes you made possible.



Gordon Broderick, PhD of University of Alberta

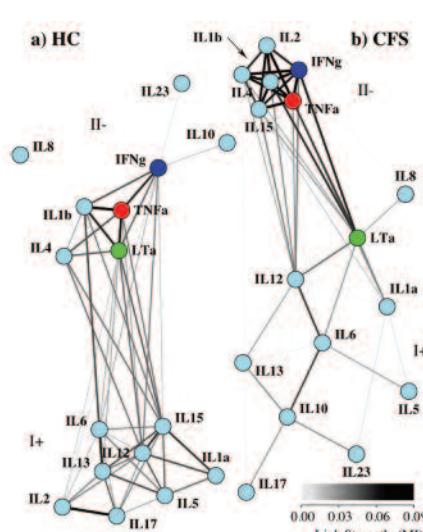
Molecular patterns of persistent immune activation in a post-infectious adolescent cohort

Objective: To use network analysis of gene

expression and endocrine measures to identify biomarkers that describe the events from infectious mononucleosis (IM) to post-infection CFS.

Preliminary Outcomes:

- Funding: Three new federal awards totaling more than \$3.5 million
- Publications:
 - >> A formal analysis of cytokine networks in chronic fatigue syndrome. *Brain, Behavior and Immunity*. 2010 Oct;24(7):1209–17.
 - >> Cytokine expression as a potential prognostic indicator in post-infectious fatigue. *Cytokine*. 2010; 52(1–2): SS11–7,81.
 - >> Plasma neuropeptide Y: a biomarker for symptom severity in CFS. *Behavioral and Brain Functions*. 2010 Dec 29;5:76.
 - >> A pilot study of immune network remodeling under challenge in Gulf War illness. *Brain, Behavior and Immunity*. 2011 Feb; 25(2): 302–13.



This figure shows the differences between “communication networks” of immune proteins in healthy controls (left) and CFS patients (right).

this new NIH R01 grant will assess whether our post-exertional biomarkers can differentiate CFS from clinical depression. Objective biomarkers for CFS will be valuable in diagnosis and to help individualize treatments for specific patients. Thank you to the CFIDS Association and its generous donors for this very important support.”



Marvin Medow, MD of New York Medical College

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

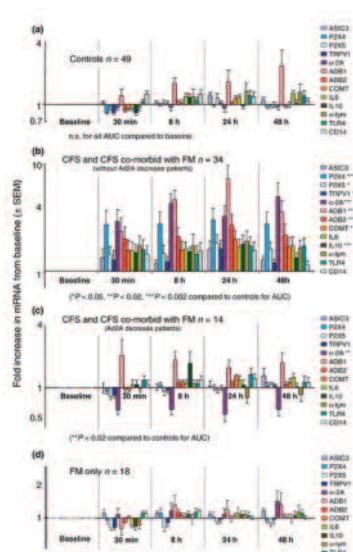
Objective: To determine if upright posture causes

neurocognitive deficits as a result of impaired cerebral blood flow and modulation of nitric oxide and reactive oxygen species.

Preliminary Outcomes:

- Funding: Application to NIH pending review.
- Publications (selected):
 - >> Decreased upright cerebral blood flow and cerebral autoregulation in normocapnic postural tachycardia syndrome. *AJP Heart and Circulatory Physiology*, 2009.
 - >> Respiration drives phase synchronization between blood pressure and RR interval following loss of cardiovagal baroreflex during vasovagal syncope. *AJP Heart and Circulatory Physiology*. Nov. 12, 2010.
 - >> Reactive oxygen species from NADPH and xanthine oxidase modulate the cutaneous local heating response in healthy humans. *Journal of Applied Physiology*. March 24, 2011.
 - >> Cutaneous constitutive nitric oxide synthase activation in POTS with splanchnic hyperemia. *AJP Heart and Circulatory Physiology*. June 3, 2011.
 - >> Increasing orthostatic stress impairs neurocognitive functioning in chronic fatigue and POTS and is not related to cerebral blood flow velocity. In preparation.
 - >> Additional data being analyzed; manuscripts in preparation.

“In addition to the obvious benefits of receiving financial support from the CFIDS Association that helps to defray the cost of conducting research on CFS, my research has allowed me to interact with many CFS subjects during these studies, which has put a ‘personal face’ on this syndrome. This has increased my appreciation for the need to provide answers to the many unanswered questions about the cause of and the mechanisms that underlie symptoms of CFS. I have also enjoyed providing information about CFS through our



This figure from the *Journal of Internal Medicine* compares gene expression increases following moderate exercise in patients with CFS and FM.

scientific publications, and the webinars and scientific meetings arranged by the Association. Lastly, the interactions that I have had with other health care professionals I have met through the Association have provided useful insights into CFS beyond the scope of my own investigations.”



Bud Mishra, PhD of New York University School of Medicine

Translate science to a cure for CFIDS

Objective: To build a knowledgebase for CFS that combines published literature with experimental data.

Preliminary Outcomes:

- Creation of a digital library of 250,000 full-text articles on CFS, 14 commonly co-occurring conditions of CFS and relevant biomedical literature to help decipher CFS pathophysiology.
- Publications:
 - >> Metamorphosis: the coming transformation of translational systems biology, *Queue*, 7(9):40–52, ACM, 2009.
 - >> Reverse engineering dynamic temporal models of biological processes and their relationships, *Proceedings of the National Academy of Science*, 107(28):12511–6, 2010.

“The main focus of this research program was to develop novel ‘systems biological’ tools focusing on understanding the causes of CFS. The NYU tools can be categorized into two groups: tools that generate novel hypotheses using data on how various genomics and related information vary over time and how they differ from patient and patient (the subject of a student’s PhD thesis); and tools that filter known hypotheses about the progression of the disease by data-mining the published literature. By using principled and rigorous approaches, such tools identify causal bases of CFS that go beyond anecdotal explanations of the syndrome. Since the results can be visualized on a computer, researchers thus have the ability to further examine the most significant hypotheses carefully and design new studies. In this way, the NYU team’s research has enabled the CFS community to move into the state-of-the-art genomics and systems biology arena, which would not have been possible without the Association’s funding.”



Sanjay Shukla, PhD of Marshfield Clinic Research Foundation

Metagenomics approach to study CFS patients

Objective: Determine if there is an altered ratio of gut commensal and pathogenic bacteria in CFS and if exercise increases microbe translocation to cause post-exertion symptoms.

Preliminary Outcomes:

- Secured supplementary funding of from Univ. of Wisconsin-Madison to expand sample size.
- Study data is currently being analyzed and prepared for publication.

“I am really excited to explore the potential role of the gut microbiome in explaining some aspects of CFS and I thank the CFIDS Association for funding this exciting project. Several recent research studies have suggested a role for the gut microbiome in modulating chronic diseases from diabetes to obesity to ulcerative colitis. With awareness of those findings, I am really excited to explore the potential role of the gut microbiome, especially gut permeability, in explaining at least some aspects of CFS.”



Dikoma Shungu, PhD of Weill Medical College of Cornell University

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

Objective: Use magnetic resonance spectroscopy

(MRS, an advanced MRI method) to measure specific brain chemicals. The investigators build upon preliminary evidence showing elevated lactate in CFS patients. Examine chemicals in blood and brain that are indicators of oxidative stress and mitochondrial dysfunction.

Preliminary Outcomes:

- Funding: NIH award in collaboration with Benjamin Natelson, M.D., with total funding of \$379,000. Another NIH application has been submitted.
- Publications:
 - >> Ventricular cerebrospinal fluid lactate is increased in chronic fatigue syndrome compared with generalized anxiety disorder: an in vivo 3.0 T (1)H MRS imaging study. *NMR in Biomedicine*. April 2009.
 - >> Increased ventricular lactate in chronic fatigue syndrome measured by H MRS imaging at 3.0 T. II: comparison with major depressive disorder. *NMR in Biomedicine*. July 2010.

“As is amply clear, the continuing skepticism that CFS is not a ‘real’ disease will not abate until there is foolproof scientific evidence that this debilitating illness is a distinct medical entity with biological or organic causes. To achieve this objective will require funding of high-quality, groundbreaking research, which is scarce and dwindling. The largest source of medical research funding is the National Institutes of Health (NIH). However, because research funds are limited, it is nearly impossible to compete for NIH funding without having strong preliminary data that support the validity of new research ideas or hypotheses about a disease that one wishes to investigate. This is even harder for CFS, which has no known causes. That is where small research funds that are provided by dedicated organizations like the CFIDS Association of America assume critical importance. With the support of the Association, my collaborators and I have been able to conduct small but high-quality and critically important pilot studies that have enabled us to test the validity of some of our ideas about the causes of CFS, and then to use the generated preliminary data to compete effectively for larger NIH grants to pursue those ideas. Case in point: using preliminary data obtained in a small pilot study supported by the Association, we submitted a grant application to the NIH to test ideas that could show that CFS was not a psychiatric disease, and were very recently informed that this application has been funded by the National Institute of Neurological Disorders and Stroke and the NIH Office of the Director, with total support of \$379,000 for the collaborative effort led jointly by Dr. Benjamin Natelson at Beth Israel Medical Center and Dr. Nora Weiduschat in my laboratory at Weill Cornell. In addition, we just submitted another NIH grant application, based on data generated with funding from the Association, to test a drug that we postulate could alleviate some of the disability associated with CFS. In short, without the type of funding that caring organizations such as the Association can provide, high-quality research into the biological causes of CFS by dedicated researchers would be virtually impossible due to lack of federal support. We and all those affected by this illness owe the contributors to the Association’s research funds a debt of gratitude.” ■

Expanding Research: Looking to the Future

The changes we've made over the past three years have transformed our organization and our approach to CFS research. The traditional model, marked by passive support of research grants, is appropriate for disease states for which there exist large government- and industry-supported research portfolios that can be augmented through private philanthropy. As you know, this is not the case for CFS.

To inform our transition beyond the traditional role, we have learned from other organizations that leverage their investment in research to get more from academia, government and industry. We have benefited tremendously from innovative research programs developed by the Myelin Repair Foundation (working on myelin repair therapies for M.S.), the Michael J. Fox Foundation (working for better therapies and a cure for Parkinson's disease), the Susan B. Love Army of Women (giving all women the opportunity to partner with researchers and take breast cancer beyond a cure), *FasterCures* (an "action tank" that works to improve the medical research system) and others.

Now, we look to the future and the opportunity to build on our dynamic program in four major areas by:

- Funding six to eight **new grants** from our 2011 Request for Applications;
- building a larger, **more valuable SolveCFS BioBank**;
- developing a **biomarker "hit list"** to drive future research priorities; and
- **expanding collaborations** and networks of investigators working in the field.

Learn more about each of these initiatives.

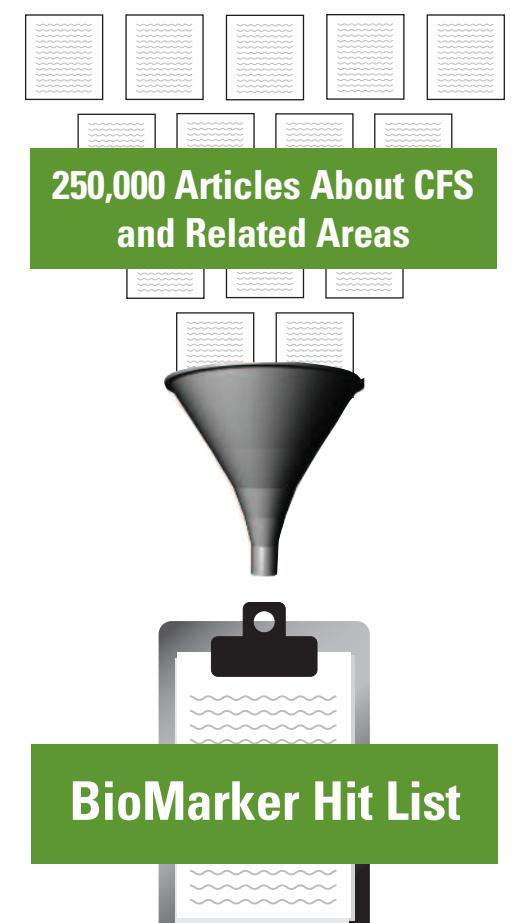
New Grants:

In April, we widely circulated a new Request for Applications that generated 36 letters of intent. Twenty-seven of the projects described were responsive to our emphasis on advancing

objective diagnosis and effective treatment. Full proposals were invited from those investigators and are due on Sept. 30, 2011. All applicants (and their institutions) have agreed to revised policies that strengthen the Association's data-sharing and intellectual property policies. Proposals will be reviewed on two levels: 10 measures of scientific merit by peers in related disciplines, and nine measures of strategic merit judged by reviewers familiar with the CFS literature and the field. The number of new projects awarded funding will depend on the rigor of applications submitted and the amount of funds available through the Catalyst Fund (see page 12).

More Valuable BioBank:

In March 2010, we announced the launch of the SolveCFS BioBank, the first combined patient registry and biorepository of its kind. In its first 18 months of operation, the BioBank has enrolled 449 participants (including well-characterized CFS patients and healthy controls) and we have completed our first collaborative study. Results from that study are being analyzed and prepared for publication. We are now ready to expand the BioBank and can engage participants anywhere in the world, matching subjects and samples to the needs of individual investigators. BioBank participants contribute to multiple studies and form the basis of study by various investigators focusing on different aspects of CFS, creating a "virtual center" in which we are partners in the design and conduct of research studies. Through the BioBank, we can deepen understanding of results obtained for individuals, subgroups and the population as a whole. It also helps provide continuity as individual investigators enter and exit the field.



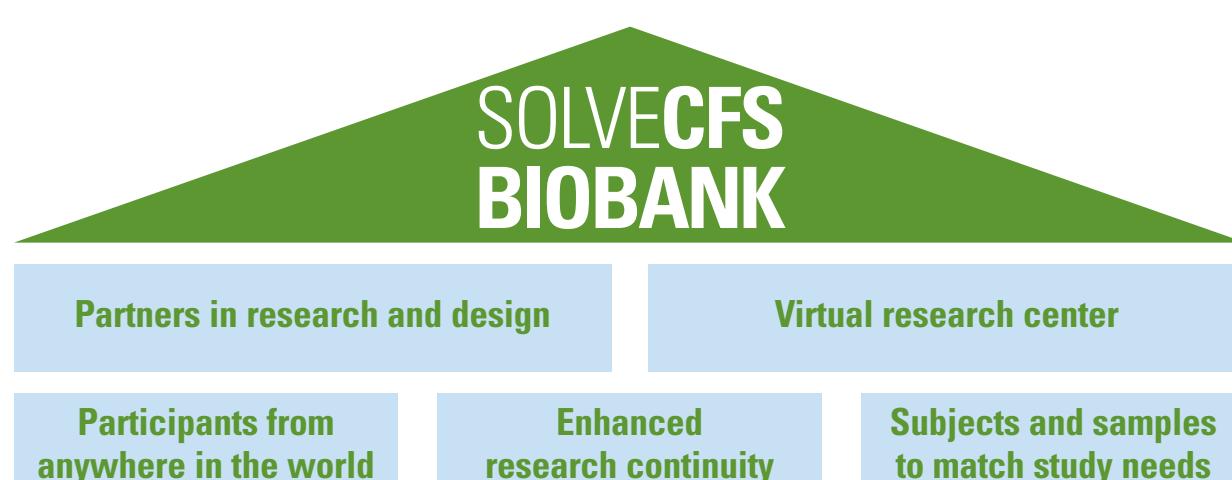
Biomarker Hit List:

One of the products of the projects funded in 2009–2010 is the knowledgebase generated from 250,000 articles about CFS and related areas of science (see page 3). Dr. Bud Mishra's team at New York University built this knowledgebase and the text mining tools that will enable us to use these assets to build a data-driven target list of biomarkers. We will then "shop" this list with academic centers and biotech companies to stimulate validation of these target biomarkers using samples from the BioBank or other clinical populations, accelerating the pace of moving from theoretical to practical applications for diagnostics and treatments.

Expanding Collaborations:

In 2009 we networked our funded investigators, bringing them together to discuss their study designs, data collection and subject recruitment — before their studies got started. The network was expanded to include NIH-funded investigators and has yielded new collaborations and greater sharing of resources, data and ideas. We are now working with NIH and several academic groups to establish a secure data-sharing platform and to standardize ways of defining cases and collecting and analyzing data to improve comparability of research across all settings and to provide a more formal infrastructure for collaboration and networking.

These new initiatives will truly transform the way that CFS research is conducted — not just for studies conducted with Association support, but for the field as a whole. This approach reflects an integrated strategy to overcome the barriers of the past and accelerate the pace of discovery and implementation for the future. ■



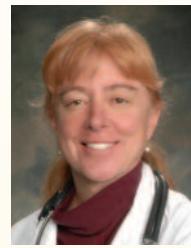
10 Ways the Association Has Readied to Transform Research

1. We narrowed our focus to execute the following strategy: "To stimulate research aimed at the early detection, objective diagnosis and effective treatment of CFS through expanded public, private and commercial investment."
2. We deepened our expertise with the addition of a Scientific Advisory Board. (More on page 5.)
3. We have learned from and collaborated with other innovative organizations working to end suffering caused by common and rare diseases.
4. We developed a rigorous review process to select the strongest research proposals based on scientific and strategic merit.
5. We networked our funded investigators and required them to work together.
6. We worked closely with our grantees to ensure their projects yielded results. (More on pages 2–3.)
7. We established a patient registry and biobank for clinical data and samples — the SolveCFS BioBank.
8. We conducted our first collaborative BioBank study and enrolled 449 active participants.
9. We engaged researchers, policy makers and patients around the world. (More on pages 6–7.)
10. We have become the leading resource for credible research information. (More on pages 10–11.)

Scientific Advisory Board Deepens Association's Expertise

The CFIDS Association has formed a Scientific Advisory Board to guide and shape its research program. We are honored to have the service of these esteemed experts representing diverse scientific and strategic disciplines. The formation of the Scientific Advisory Board is another important step in our transition to a research-focused mission and our commitment to "Put Research First" (see page 1).

Here are brief introductions to our scientific advisors. Learn more about them at Research1st. 



Lucinda Bateman, M.D.

Founder, Fatigue Consultation Clinic, Salt Lake City

Dr. Bateman's goal in establishing her clinic and the Organization for Fatigue and FM Education and Research is to encourage a more thoughtful evaluation process, sharing of information with patients and medical providers and cooperative research efforts aimed at understanding the cause(s) of CFS/ME and FM. Her focus on these conditions

is inspired by her sister, Shauna Bateman Horne, who had CFS for 15 years before she was diagnosed with non-Hodgkin's lymphoma and died a year later from complications of a stem-cell transplant.

Italo Biaggioni, M.D.

**Professor of Medicine, Professor of Pharmacology,
Vanderbilt University**

Dr. Biagioni leads a national referral center for the evaluation of patients with disorders of the autonomic nervous system (ANS). He sees patients with various forms of orthostatic hypotension, orthostatic intolerance, syncope and autonomic forms of hypertension. His clinical research focuses on the interaction between neural (autonomic) and metabolic (adenosine, nitric oxide) mechanisms that regulate blood pressure. The program's goal is to define the role of the ANS in blood pressure disorders to develop targeted therapies.



Gordon Broderick, Ph.D.

**Associate Professor, Pulmonary Medicine,
Department of Medicine, Faculty of Medicine and Dentistry,
University of Alberta**

An engineer by training, Dr. Broderick's current research efforts are focused on understanding immune dysfunction and autoimmunity from an integrated systems perspective.

In particular his group is investigating how subtle imbalances between the immune system's multiple components, as well as its interactions with the endocrine and nervous systems, may lead to complex disorders such as CFS and Gulf War Illness. His group is developing analytical approaches to map the communication network linking the nervous, endocrine and immune systems and to decipher its operation. (See page 2.)



Russell L. Bromley, B.A.

Principal, TRAC Consulting

Mr. Bromley formed TRAC Consulting to assist non-profit medical research organizations in Translational Research Acceleration via Collaboration. He specializes in designing and implementing strategic research plans and collaborative operational models that are aligned with an organization's mission and the unmet medical needs of patients. Prior to founding TRAC Consulting, he served as the chief operating officer of the Myelin Repair Foundation where he was instrumental in the creation, implementation and evolution of the MRF Accelerated Research Collaboration™ model.



Lin Chang, M.D.

**Professor of Medicine, UCLA Department of Medicine —
Division of Digestive Diseases, David Geffen School of
Medicine, UCLA; Co-Director, UCLA Center for Neurovisceral
Sciences and Women's Health**

Dr. Chang's main area of research is the pathophysiology of irritable bowel syndrome (IBS) with particular interests in the overlap of IBS with FM, as well as gender differences and neuroendocrine alterations. She is an NIH-funded investigator studying the central and peripheral mechanisms underlying IBS and she has conducted clinical trials for functional bowel disorders.



Paul R. DeStefano, J.D.

Partner, McDermott Will & Emery LLP

Mr. DeStefano is a member of the MWE's Health Industry group and the firm's Life Sciences & Medical Devices group. He specializes in strategic planning related to the formation, finance and operations of start-up companies in the biotech industry. Mr. DeStefano is a former chief legal officer of Genentech, Inc., and has served as an advisor to the Robert Wood Johnson Foundation and National Academy of Sciences on the commercialization of human gene therapy. He was also an advisor to the Institute of Medicine on vaccine liability issues.



Roger Dodd, Ph.D.

**Vice President, Research and Development and Director,
American Red Cross, Holland Laboratory**

Dr. Dodd's primary research interest is the epidemiology of transfusion-transmitted infections, with particular reference to emerging infections. He is responsible for the Red Cross research programs supporting its blood program and has more than 175 publications on transfusion-transmitted infections. He has been an advisor to the World Health Organization, serves on the editorial boards of *Transfusion*, *Transfusion Medicine* and *Transfusion Medicine Reviews*, and is a past president of the American Association of Blood Banks (AABB).



Nancy Klimas, M.D.

Professor, University of Miami, Miller School of Medicine

Dr. Klimas directs the Allergy and Immunology Clinic at the University of Miami and is director of research for the Clinical AIDS/HIV Research at the Miami Veterans Affairs Medical Center. A leader in the field of CFS research, Dr. Klimas is the past president of the International Association for CFS/ME. Dr. Klimas was the principal investigator of the National Institute of Health's Center for Multidisciplinary Studies of CFS Pathophysiology at the University of Miami.



Kelly Morren, B.S.

Vice President, Jones Lang LaSalle

Ms. Morren is vice president of Jones Lang LaSalle's Strategic Consulting organization. She is an engagement leader for the Workplace Solutions practice, with responsibility for client relationships, workplace strategy development, change management and product/service development. Her work focuses on the strategy, planning and management of complex transitions balancing strategic, financial and tactical perspectives.



Dimitris A. Papanicolaou, M.D.

Merck Research Laboratories

Before joining Merck's research and development program, Dr. Papanicolaou was a staff researcher of endocrinology at the NIH and Emory University. Dr. Papanicolaou's research interests focus on cytokines, particularly interleukin-6, in healthy and disease states. His interest in CFS research began with his work at Emory University; he has also studied sarcopenia, chronic insomnia and the effect of COX-2 selective inhibitors in acute and chronic pain conditions.



Vincent R. Racaniello, Ph.D.

**Higgins Professor, Department of Microbiology and
Immunology, Columbia University's College of Physicians
and Surgeons**

Dr. Racaniello has studied viruses including poliovirus, echovirus, enterovirus 70, rhinovirus and hepatitis C virus. He has served on the editorial boards of scientific journals, including the *Journal of Virology*, and is a community editor for the open access journal *PLoS Pathogens*. He is one of four authors of the textbook, *Principles of Animal Virology*. He hosts several popular science podcasts including "This Week in Virology" and writes Virology Blog.



Robert H. Silverman, Ph.D.

**Staff and Professor, Mal and Lea Bank Chair, Department of
Cancer Biology, Lerner Research Institute, Cleveland Clinic**

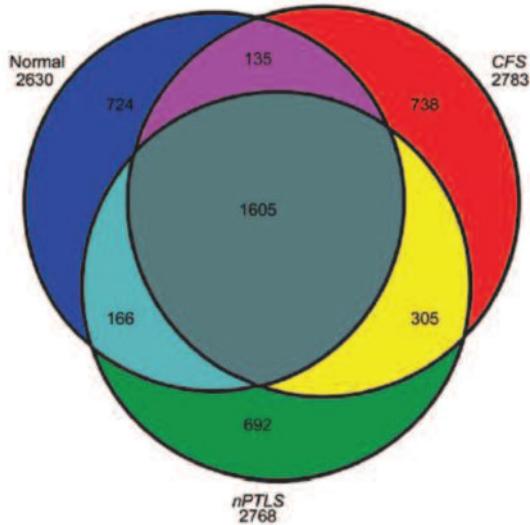
Dr. Silverman is dedicated to investigating antiviral innate immunity in health and disease. His studies are focused on RNase L, a key protein in the interferon response against many viral pathogens. Dr. Silverman also studies the role of viruses and human genetics in prostate cancer. Together with collaborators Joseph DeRisi and Don Ganem (UCSF) and Eric Klein (Cleveland Clinic), he discovered xenotropic murine leukemia virus-related virus (XMRV) during studies on prostate cancer. He is a fellow of the American Association of Microbiology. ■

Journal Highlights Reflect Multiple Hypotheses and Body-Wide Dysfunctions

On our new website, Research1st, we regularly update the progress being made in understanding CFS through engagement by researchers in a wide variety of medical and scientific disciplines and resulting publications in diverse journals. Here are some of 2011's top journal highlights. The  alerts you to more in-depth information about this study on Research1st.

Biomarkers

Spinal Fluid Proteins: Researchers at six institutions led by the University of Medicine and Dentistry of New Jersey and Pacific Northwest National Laboratory reported finding 738 unique protein markers in spinal fluid samples collected from 43 CFS patients and compared to samples from 25 neurologic post-treatment Lyme disease patients and 11 healthy control subjects. They were able to distinguish CFS from Lyme disease. Proteins identified in CFS patients only have been linked to Parkinson's disease and Alzheimer's. This study garnered attention from "The CBS Evening News" and other news agencies. (*PLoS One*, Feb. 23, 2011) 



Exercise Challenge Reveals Potential Biomarkers

Biomarkers: Forty-eight CFS patients were studied and two distinct subgroups were identified on the basis of changes to the α-2A receptor, a key regulator of neurotransmitters in the central nervous system. The larger group of CFS subjects (71 percent) could be identified with a combination of four biomarkers (P2XR, α-2A, β-2 and IL10) at any time point within 48 hours following the exercise challenge with high specificity and sensitivity. The smaller group showed a large decrease in α-2A, opposite of the larger group. This study was funded by the CFIDS Association; see page 2 for more information about it. (*Journal of Internal Medicine*, May 26, 2011) 

fibromyalgia (FM) criteria. They found that the chronic post-SARS syndrome shares clinical and sleep features with CFS and FM. (*BMC Neurology*, Mar. 24, 2011)

Brain & Autonomic Nervous System

Autonomic Function: Forty-four CFS patients and 52 healthy adolescents were recruited from a pediatric outpatient clinic in Norway. During night-time sleep, heart rate and mean blood pressure were significantly higher in CFS patients as compared with controls. During daytime, heart rate was significantly higher among CFS patients, whereas blood pressures were equal between the two groups. The findings supported other evidence of sympathetic predominance of cardiovascular control in adolescent CFS patients and suggested a possible target for therapeutic intervention. (*Acta paediatrica*, Feb. 2011)

Cerebral Blood Flow: Using an MRI technique called arterial spin labeling, this New Jersey group compared blood flow in the brains of 11 subjects with CFS and 10 age-matched healthy controls. The CFS patients as a group had significantly lower global cerebral blood flow (CBF) compared to controls. The reduction in CBF occurred across nearly every region assessed. Nine of the 11 patients showed these reductions compared to the average control data, while two patients showed actual increases relative to the controls. (*Journal of the Neurological Sciences*, Feb. 15, 2011)

Migraine Overlap: Headaches of a new type or severity is one of eight case-defining CFS symptoms. Two cohorts of Georgetown University CFS patients were evaluated using standard criteria for headache subtypes. 60 percent of CFS subjects had migraine without aura; 24 percent had migraine with aura; 12 percent had tension headaches only; only four percent had no

headaches. Co-occurring tension and migraine headaches were found in 67 percent of CFS subjects. Sumatriptan (Imitrex) was beneficial for 13 out of 14 newly diagnosed CFS migraine subjects. (*BMC Neurology*, Mar. 5, 2011)

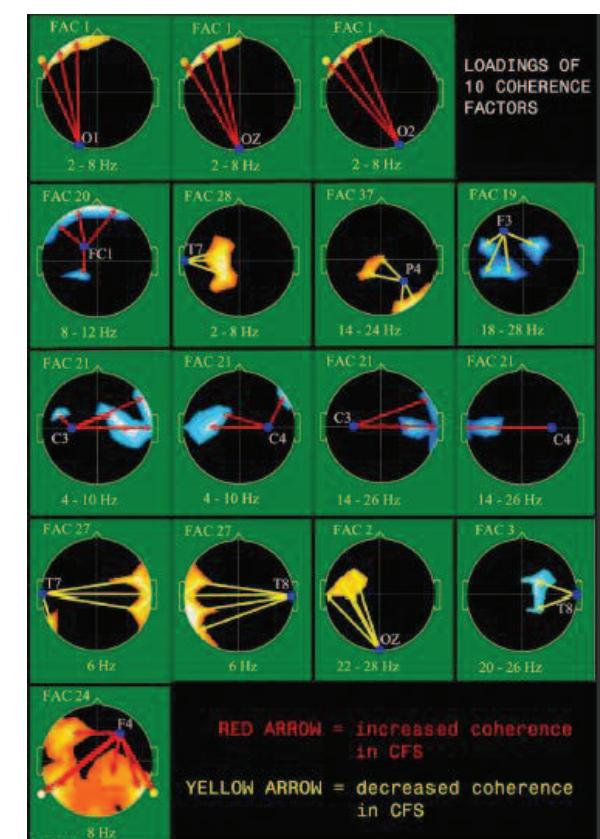
Impaired Cognition: A group in Belgium evaluated 25 subjects with CFS, 25 subjects with major depressive disorder (MDD) and 25 healthy subjects using standardized tests of attention, working memory and verbal and visual episodic memory. Patients with CFS had slower phasic alertness; they also had impaired working, visual and verbal episodic memory compared to controls. This study confirmed the presence of an objective impairment in attention and memory in patients with CFS. (*Clinical Neurology and Neurosurgery*, May 2011)

Brainstem Dysfunction and Altered Homeostasis

Homeostasis: Researchers in Australia used statistical parametric mapping of brain MR images and compared against clinical scores for 25 CFS subjects and 25 normal controls. Midbrain white matter volume was observed to decrease with increasing fatigue duration.

These results are consistent with an insult to the midbrain at fatigue onset that affects multiple feedback control loops to suppress cerebral motor and cognitive activity and disrupt local CNS homeostasis, including resetting of some elements of the autonomic nervous system. (*NMR in BioMedicine*, May 11, 2011)

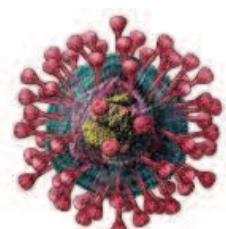
EEG Spectral Data Distinguishes CFS: A group at Harvard analyzed spectral data from electroencephalograms (EEGs) performed on 70 CFS patients, 390 healthy controls, 24 subjects with major depression and 148 patients with prolonged generalized fatigue, a total of 632 subjects. Ten factors distinguished CFS from healthy and depressed controls, with the highest rate of differentiation among unmedicated female CFS patients and female healthy controls, without misclassifying the subjects with major depression as CFS. "CFS patients manifest patterns of functional brain coupling that differ from those of normal controls. Such a difference of CFS brain physiology may help explain known differences in cognition, memory, sleep, and affect that afflict CFS patients." Chief among the distinguishing factors were those involved in the brain's temporal lobe function. (*BMC Neurology*, July 1, 2011)



Other

Gynecologic Problems Common: Researchers at the U.S. Centers for Disease Control & Prevention compared gynecological histories of 36 women with CFS to 48 nonfatigued controls. Women with CFS had more gynecological conditions, including non-menstrual pelvic pain, endometriosis and amenorrhea. CFS patients had a higher mean number of pregnancies. Seventy-six percent of the women with CFS reported hysterectomy compared to 55 percent of the healthy women. Fifty-six percent of the women with CFS had one or both ovaries removed, while only 34 percent of healthy controls had this surgery. (*Journal of Women's Health*, Jan. 2011)

Behavioral Therapies Compared: This large study compared four treatment approaches in



Post-SARS CFS-Like Syndrome: Moldofsky and Patcay studied 21 health care workers who had documented Severe Acute Respiratory Syndrome (SARS) and were not well enough to return to work one year to three years later and compared them to seven healthy females and 21 females who met

641 patients using Oxford, CDC and London criteria for CFS and ME. The study reported modest benefits following a six-month course of cognitive behavioral therapy (CBT) or graded exercise therapy (GET) compared to specialized medical care alone or adaptive pacing therapy, based on improvement in self-reported symptom scores. There were no biological measures taken during the study to correlate with the results and media reports greatly exaggerated the small gains made by some participants in self-report measures. This study sparked a firestorm within the patient community and at its boundary with the media, igniting tensions that sizzled in headlines through the summer months. A series of reports in the U.K. media alleged that Simon Wessely, one of the study authors, and

researchers who reported negative results in XMRV studies had received death threats from a small number of patient activists. (*Lancet*, Feb. 18, 2011) 

Heritable Predisposition: Utilizing the Utah Population Database, researchers searched linked medical records for the diagnostic code for CFS (780.71). They identified 941 persons with a CFS diagnosis for whom there was available genealogy data; 811 cases were included in the assessment. The analysis “shows clear evidence of significant excess familial clustering and significantly elevated risks for CFS among first, second, and third degree relatives of CFS cases. The results strongly support a genetic contribution to predisposition to CFS.” (*BMC Neurology*, May 27, 2011)

Impaired Cardiac Function: Julia Newton’s group at Newcastle University used a new method of assessing the shape, structure and function of the heart in this study of 12 CFS patients and 10 healthy controls. They found that compared to controls, “CFS patients have markedly reduced cardiac mass and blood pool volumes, particularly end diastolic volume: this results in significant impairments in stroke volume and cardiac output compared to controls.”



(*Journal of Internal Medicine*, July 27, 2011; accepted article approved for publication) ■

Case Definition

The name and definition have been debated for decades. Three papers published this summer in quick succession drew attention to both issues.

New M.E. Criteria: A panel of 26 physicians, researchers and teaching faculty led by Bruce Carruthers proposed new criteria for myalgic encephalomyelitis (M.E.) and recommended use of this term and criteria as a replacement for CFS. The criteria propose one compulsory feature – post-exertional neuroimmune exhaustion (PENE) – plus seven symptoms from three subdivided symptom clusters: neurological, immunological and energy production/transport impairments. The criteria are intended for clinical and research use and the paper states that the panel is developing Physicians’ Guidelines and an International Consensus Symptom Scale for use in these settings. There is sure to be more discussion about the change in both the name and criteria, for both have potentially far-reaching consequences for research, policy and education. (*Journal of Internal Medicine*, July 20, 2011; accepted article approved for publication) 

British Study Estimates Rates, Compares Case Definitions: The ME/CFS Observatory conducted a study of ME/CFS in three distinct areas of England to determine prevalence, incidence and the ability of different definitions to detect ME/CFS (CFS). The prevalence rate of cases meeting the 1994 (Fukuda) definition was 0.19 percent of the population and slightly lower (0.11 percent) for cases meeting the Canadian definition. Prevalence was higher in London (urban), among women and among white-British, compared to industrial or rural areas, men or non-white ethnic minorities. The group suggests combining the Fukuda and Canadian criteria for ascertainment of ME/CFS cases. (*BMC Medicine*, July 28, 2011)

Case Definition Face-Off: A group of researchers led by Leonard Jason used data-mining techniques to determine which questions were most effective for accurately identifying cases using two definitions: the Canadian ME/CFS clinical definition (Carruthers, 2003) and the “empiric” definition proposed by CDC in 2005. Their findings show that the Canadian definition selects cardinal features of the illness better than the empiric and is better at discriminating cases from noncases. (*Journal of Clinical Psychology*, Aug. 5, 2011)

Hi-Fi Sci-Di: Dr. Suzanne Vernon Orchestrates High-Fidelity Research



Our scientific director, Suzanne D. Vernon, PhD, has dedicated the majority of her professional career to studying CFS and bridging gaps in our scientific understanding of it. It's more than just an occupation for Suzanne, it's a personal passion. From the podium at scientific meetings to the steep and narrow trail at a 24-hour bike race organized to solve CFS, her leadership of the Association's research program is recognized and lauded by researcher-colleagues, patients and advocates alike. Here is a brief summary of some of ways in which Suzanne has been orchestrating transformation over the past year.

Sponsored Research Program

- Closely monitored grantees' performance milestones and outcomes. (See pages 2–3 for more information.)
- Developed and widely circulated new Request for Applications (RFA). (See pages 4–5 for more information about the next phase of funding.)
- Explored various data-sharing platforms and policies and other institutions' policies on intellectual property to foster discovery and development of promising findings.
- Reviewed Letters of Intent and issued invitations and declinations to investigators who submitted letters of intent.
- Distributed revised policies and addressed questions from invited applicants and their respective institutions.
- Recruited dozens of qualified reviewers to evaluate the scientific and strategic merit of proposals due Sept. 30.

SolveCFS BioBank

- Oversaw the conversion of the collection of extensive medical history and clinical data from BioBank participants from a paper-based system to a secure online system. (See page 4 for more information about the plans to expand the SolveCFS BioBank.)
- Completed the first collaborative study using BioBank resources, data for which is being analyzed and prepared for publication.
- Received two new applications to utilize BioBank resources; one has been approved and one is pending review by the Medical Research Advisory Committee.

Other Collaborations

- Served as a member of the NIH ME/CFS State of the Knowledge Workshop planning group. Participated in several group discussions as follow-up to the need for a centralized data-sharing platform.
- Participated in two XMRV-related working groups; CEO Kim McCleary participates in two other XMRV-related working groups.
- Consulted with a biotech company to develop a biomarker proposal in response to the Department of Defense Congressionally Directed Medical Research Program (CDMRP). (See page 10 for more information about the CDMRP.)
- Developed five research funding proposals submitted to other institutions, all of which are collaborations with other investigators and organizations.
- Helped identify clinical collaborators for a Phase II clinical trial of a promising therapy being planned by an academic center.

- Served as a peer-reviewer for several CFS-related grant applications and manuscripts.

Presentations and Meetings

- Participated in the meeting of collaborators for the study of XMRV being led by Dr. Ian Lipkin. (Dec. 20, 2010) (See page 9 for more info.)
- Provided an overall summary of research, existing gaps, areas of agreement and needed next steps at the ME/CFS State of the Knowledge Workshop. (April 7–8) (See page 10.) 
- Delivered public testimony at the DHHS CFS Advisory Committee meeting, along with CEO Kim McCleary and Board members Jennifer M. Spotila, J.D., and Amy Squires. (May 10–11) (See page 10 for more info.) 
- Gave a presentation on CFS and chaired a session at the 6th Annual TMJ Association Scientific Meeting on Co-Morbid Conditions. (June 5–7)
- Spoke to participants, volunteers, donors and sponsors about CFS at the second annual 24 Hours in the Enchanted Forest. (June 17–19) (See page 11 for more info.)
- Delivered three presentations on biobanking at the Genetic Alliance 25th Annual Conference. (June 23–26)
- Gave a series of presentations in Sweden, including a half-day seminar with other CFS experts at the Ministry of Health and a program for doctoral students at the University of Umeå. (Aug. 22–26) 
- Provided more than a dozen media interviews and authored numerous articles for Association publications. ■

The X Factor

Two years ago, a gammaretrovirus called xenotropic murine leukemia virus-like virus (XMRV) was linked to CFS with a high-profile study published in *Science* by a team of researchers from the Whittemore Peterson Institute (WPI), National Cancer Institute (NCI) and Cleveland Clinic. Today, this study by Vincent Lombardi et al. remains the only one to have shown an association between XMRV and CFS. Research groups in six countries have tested samples from CFS patients and published 15 papers that cast doubt on the original data. Through more than 170 publications about XMRV, researchers have documented a better understanding of its origins, life cycle and other properties, yet no links to human disease have been firmly established. 

Recent Studies

While several of the early follow-up studies involving samples from CFS patients were small, used broader criteria to define CFS or had other limitations, two major studies published in May 2011 addressed many of the criticisms. The first was from Clifford Shin et al., published May 4 in the *Journal of Virology*. Konnie Knox et al. published results in *Science* on May 31. Both groups tested samples from CFS patients who had tested positive at WPI, yet neither group found evidence of the virus in those samples or others they tested from well-characterized patients using multiple detection methods. Both studies attracted considerable media attention that kept CFS and XMRV in headlines for most of May and early June.

Another group at NCI led by Tobias Paprotka reported in the same issue of *Science* that XMRV originated through a laboratory recombination of two mouse viruses in the prostate cancer cell line CWR22Rv1. The recombination event occurred between 1993 and 1996. This evidence makes it unlikely that XMRV will be shown to be the sole cause of CFS, which certainly existed before these dates. The XMRV sequences submitted by WPI to the public DNA sequence database are 98–100 percent identical to VP62, an XMRV clone derived from 22Rv1 and used by WPI and the Cleveland Clinic.

The other piece of evidence weighing against XMRV as a human pathogen are multiple reports of contaminants with mouse DNA in laboratory reagents, supplies and equipment that can show falsely positive results in tests for XMRV and other murine leukemia virus-like viruses (MLVs). Four papers published on Dec. 20, 2010, in *Retrovirology* drew considerable attention to the

issue of contamination. The two CFS papers published in May (described above) reported specific sources of contaminants that were encountered in their studies. Information posted to NCI's website in early June states, "a sample of the XMRV viruses reported in the 2009 article has been cultivated from patient samples and was analyzed at NCI. In contrast to the original findings, the new data suggest it is unlikely that these XMRVs were derived from infected patients. Instead, like the other XMRVs that have been sequenced, they appear

to be laboratory contaminants." Robert Silverman of the Cleveland Clinic told the *Chicago Tribune* in March 2011 that he was "concerned about lab contamination, despite our best efforts to avoid it." His lab is conducting additional experiments to test for the possibility. WPI has stated repeatedly that its tests for contaminants have been negative.

By the end of May, doubts about the original report had grown so strong that the editor of *Science*, Bruce Alberts, requested the authors retract the original paper. They declined to do so, stating it was premature. On May 31, Alberts issued an "Editorial Expression of Concern" that is now tagged to the paper pending the outcome of two large multicenter studies being funded by the National Institutes of Health (NIH) (see below).

Supporting evidence for gammaretrovirus association with CFS has come from two groups who have reported finding sequences consistent with the larger family of gammaretroviruses, but not XMRV specifically. The first team, from the Food and Drug Administration (FDA), NIH and Harvard Medical School, published its findings in August 2010 in the *Proceedings of the National Academy of Sciences* (Shyh-Ching Lo et al.). Testing stored samples collected in 1993 for a study looking for mycoplasma, Dr. Lo found 32 of 37 samples from CFS patients positive for MLV sequences. Eight patients from that cohort provided fresh samples and seven of those tested positive again. None of the researchers involved in this study has reported any further data. However, two papers published this summer by groups working independently reported that the sequences obtained from the two time points were not consistent with evolutionary changes.

Blood Safety

At a Dec. 14, 2010, meeting of the FDA's Blood Products Advisory Committee (BPAC), the committee heard nine presentations on XMRV research and testimony from several public witnesses. The Committee was asked to vote on the following question: "Do the scientific data support asking donors about a medical history and/or diagnosis of as a basis for indefinite deferral?" Nine members voted "yes" while four voted "no." The 9–4 vote reflects opinion on the issue of whether asking a question of blood donors was better than using educational materials to elicit donor disclosure of past/present diagnosis, the process most blood centers had put in place in June 2010. All BPAC members indicated that they agree with the indefinite deferral of patients based on all evidence that it will promote donor and recipient safety. The FDA strongly considers guidance from its advisory committees when making policy. No date has been provided for a decision by the FDA.

In a special report published in the Apr. 2011 issue of *Future Microbiology*, Roger Dodd, Ph.D., vice president, research and development for the American Red Cross, addresses the issue of blood safety. He concludes,

"...the issue may perhaps best be analyzed by considering the safety issues relating to ME/CFS separately from those involving XMRV/MLV. It thus seems reasonable to accept that patients with a past or current diagnosis of ME/CFS should not give blood, both for their own protection and as a precautionary measure, given the potential associations of chronic viral infections with the disease."



The March 14, 2011 issue of *Nature*, one of the world's most prestigious science journals, covered XMRV in depth with Ewen Callaway's "Fighting for a Cause."

The other group, led by Cornell University researcher Maureen Hanson, has presented data at meetings, but its findings have not yet been reported in the literature. The WPI has presented positive data from a study of patients in the U.K., but that has not yet been published, either. News about other unpublished data has circulated through the community and some have charged that positive studies are being unfairly declined by journals, but no specific incidents have been made public.

Clarity Ahead?

To bring greater clarity to the issue, NIH is supporting two studies that involve some of the labs that have published conflicting data.

The first is being coordinated by the National Heart, Lung and Blood Institute and is known as the Blood XMRV Scientific Research Working Group study (SRWG). It is a four-phase study designed to evaluate XMRV detection assays in analytical and clinical samples and to make an initial estimate of XMRV prevalence in blood donors.

- Results from Phase I were reported in July 2010 at a meeting of the FDA's Blood Products Advisory Committee (BPAC). They showed that six participating labs (CDC, Gen-Probe, NCI-Drug Resistance Program, WPI and FDA-Lo and FDA-Hewlett) had comparable sensitivity in their testing methods using coded analytical samples spiked with XMRV.
- Phase II results were presented at a BPAC meeting in December 2010. The presentation was repeated days later during a webinar hosted by the CFIDS Association. (The recording is available on our YouTube channel for on-demand viewing.) In Phase II, samples were obtained from four subjects whom WPI indicated were positive for XMRV on multiple occasions and one pedigree negative control (tested in Phase I). Samples were collected in the same manner and then split into three groups for immediate processing and processing after two days and four days to compare results. Five labs (CDC, Gen-Probe, NCI-Drug Resistance Program, WPI and NCI-Ruscetti) tested the samples under blinded conditions using the assays from Phase I. Results from three labs (CDC, Gen-Probe and NCI-Drug Resistance Program) were all negative. WPI had at least one positive result for three of the four XMRV-positive subjects as well as the negative control. NCI-Ruscetti reported positive results for three of four XMRV-positive subjects, as well as the negative control. The results from WPI and NCI-Ruscetti agreed on two of the XMRV-positive subjects and differed on the other two. One of the aims of Phase II was to determine whether processing time affected testing results; the data indicated that it did not.

In spite of the other conflicting data, it was deemed that Phase III would proceed.

- This spring, samples were collected from 30 subjects who previously tested positive for either XMRV or MLV sequences, two pedigreed negative controls and 12 blood donor controls. Five analytical controls were included in the panel as well. Eight participating labs (CDC, Gen-Probe, NCI-Drug Resistance Program, WPI, NCI-Ruscetti, FDA-Lo, FDA-Hewlett and Abbott) tested blinded samples according to approved protocols and each has submitted its results to the Blood Systems Research Institute for decoding and analysis. Results will be presented at meetings this fall and submitted to a peer-reviewed journal.
- The need for Phase IV (focused on blood donors) will be based on the outcome of Phase III.

The second large study is being sponsored by the National Institute for Allergy and Infectious Diseases. W. Ian Lipkin, M.D., of Columbia's Center for Infection and Immunity, a renowned pathogen hunter, is coordinating the collection of samples from 100 well-characterized CFS patients and 100 matched controls from four sites around the country. Samples will be processed, blinded and sent to labs at the FDA (Lo), CDC and WPI. Dr. Lipkin will break the code and reconcile the results. Although the study was

expected to wrap up before year-end, delays in securing required institutional approvals may push the conclusion of the study into 2012.

Other studies continue as well:

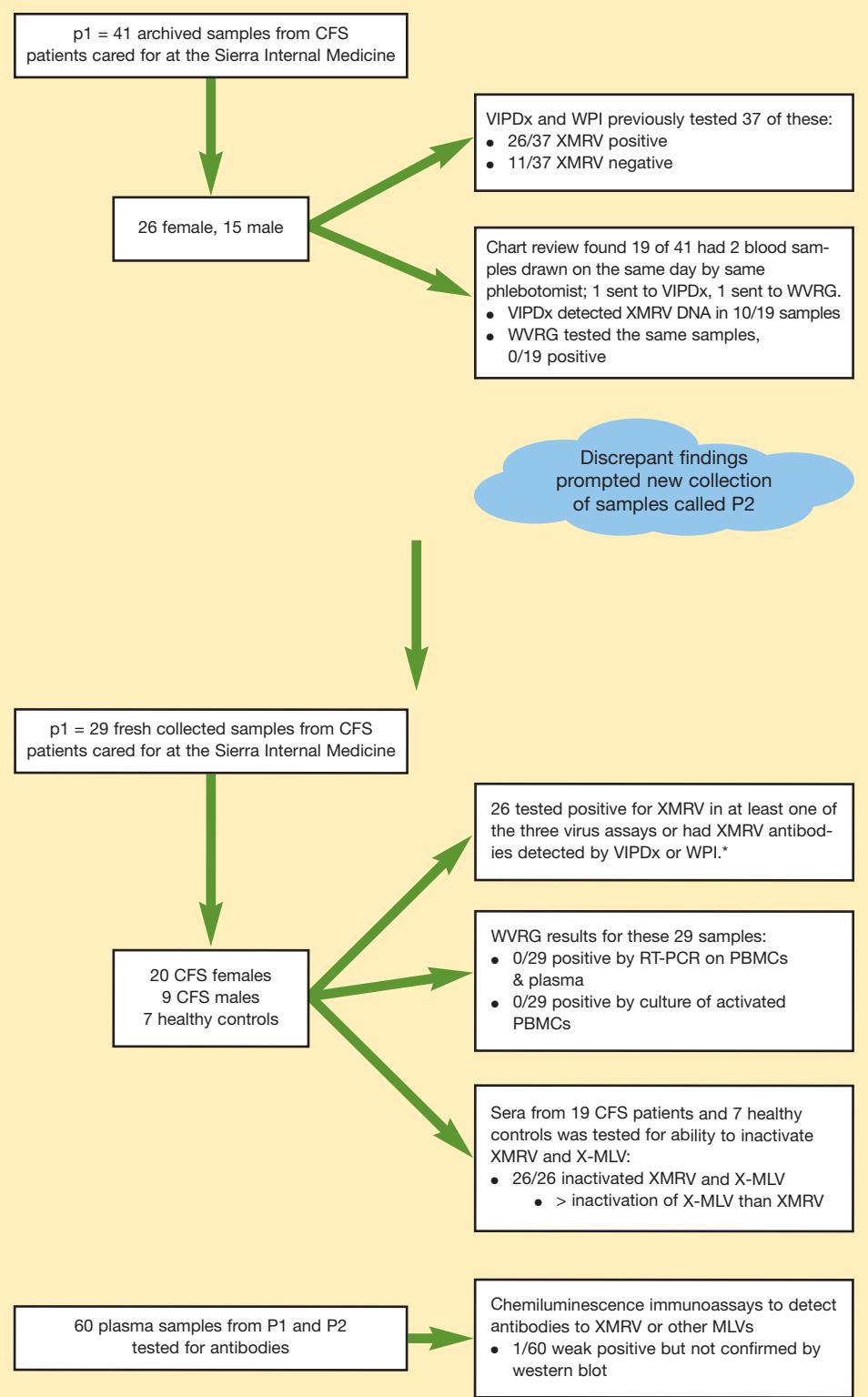
- The American Red Cross is collaborating with Gen-Probe and Abbott Laboratories to test samples from 10,000 healthy people in six geographic areas. They will also test samples from 120 recipients of blood donations from more than 4,000 donors. Both donors and recipients will be tested for evidence of XMRV and MLVs.
- The NCI has evaluated CFS patients who had been previously tested for XMRV at one of its clinics for a study of the different assays used to detect XMRV.
- The FDA's Center for Biologics Evaluation and Research has conducted a study of the transmission and infection processes of XMRV to address potential safety concerns in cells used to produce vaccines and blood products; results have been submitted for publication.
- Based on presentations made earlier this year at the 18th Conference on Retroviruses and Opportunistic Infections (March 2011) and the 15th Conference on Human Retrovirology, HTLV and Related Viruses (June 2011), there are other reports in the publication pipeline.

In testimony presented on May 10, 2011, to the federal CFS Advisory Committee, CFIDS Association president & CEO Kim McCleary made the following statement about XMRV:

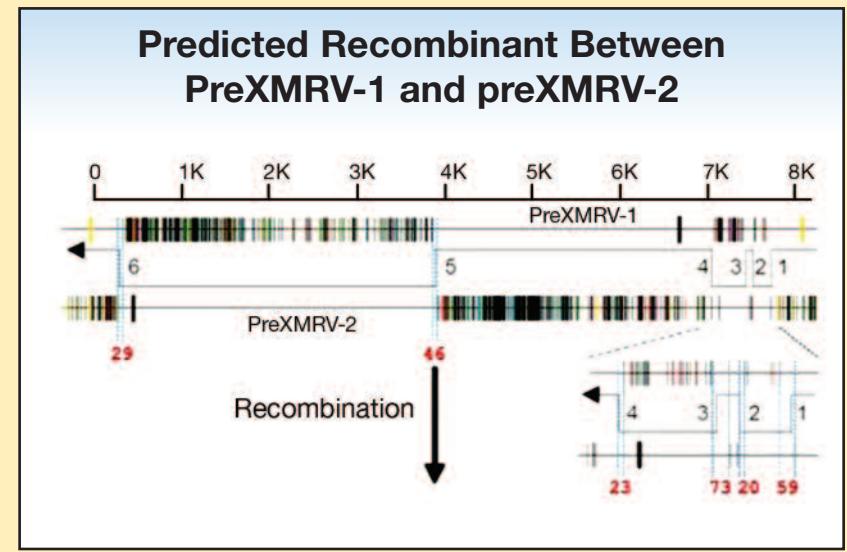
"The CFIDS Association stands for rigorous research that leads to better care for CFS patients. The results of NIH-supported research into XMRV will provide answers about whether XMRV is a route to better care. We will support the outcome of those studies, whichever way they lead. We will continue to foster the engagement of scientists interested in viral hypotheses and other well-reasoned approaches to improving diagnosis and treatment." 1ST

It remains to be seen whether XMRV will provide the answers to better methods of diagnosis and treatment that were heralded in October 2009. There is no question that the original report of an association has attracted remarkable scientific talent, increased engagement by health agencies and created unprecedented awareness of the devastating impact of CFS. No other report among the 5,000+ peer-reviewed articles about CFS has attracted this much attention or such sustained effort to investigate more thoroughly. The debate over XMRV has been polarizing at times, but there is no longer dispute about whether CFS is worthy of scientific endeavor; that, in itself, is progress. ■

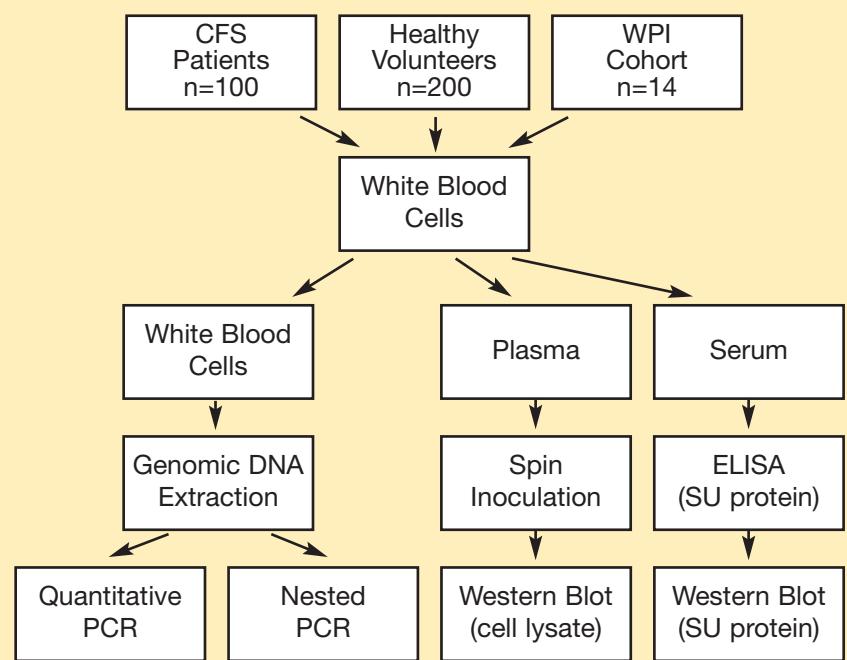
This diagram shows the testing of two CFS cohorts for XMRV by Knox et al. as reported in *Science*.



As reported by Paprotka et al., in *Science*, XMRV may have originated with a laboratory recombination of two mouse-derived viruses (left half and right half) in a prostate cancer cell line.



Shin et al., tested 100 CFS patients, 200 matched controls and 14 WPI patients for XMRV using multiple testing methods, as reported in the *Journal of Virology*.



Introducing Research1st: A New Internet Home for the Association

On May 24, we introduced Research1st.com, a new website and blog intended to become a one-stop shop for the most current and reliable information about CFS research. The site houses regularly updated information about current research initiatives and another section on findings from completed studies. A section on media coverage makes it easy to track how the press reports on studies and the evolving scientific understanding of CFS. Research1st.com also features a moderated blog with more than 100 posts by staff writers and guest contributors, where comments are welcomed. Posts provide in-depth analysis of new study results, conference reports, announcements and perspectives. The site has several search tools to aid in locating material. Research1st.com complements

our main website, Facebook page, Twitter feed, YouTube channel and our monthly e-newsletter, CFIDSLink.

We recognize that many *SolveCFS* readers don't have regular access to the Internet, so we'll point you to a few Research1st posts that you may want to prioritize:

"XMRV: Trials and Tribulations" |

Suzanne Vernon, Ph.D. and Kim McCleary | June 1, 2011

Analysis of two studies published in *Science* that led editor Bruce Alberts to request a retraction of the original study linking XMRV and CFS. (More info on pages 8–9.)

"Exercise Challenge Reveals Potential Biomarkers" | Kim McCleary |

June 2, 2011

Analysis of the exciting *Journal of Medicine* study from Dr. Kathleen Light and collaborators, funded by the Association (see pages 2 and 6).

"The Outs and Ins of OI" |

Kim McCleary | June 19, 2011

"Is it Anxiety or OI?" |

Kim McCleary | June 21, 2011

The first article provides a brief overview of OI, its diagnosis and management. Based on one of many excellent questions posed by readers, Kim followed up on the overlap of OI symptoms and anxiety.



Federal Agency Updates

NIH Convenes Experts

The National Institutes of Health (NIH) hosted the ME/CFS State of the Knowledge Workshop on April 7–8, 2011. Held on the NIH campus, the workshop brought together subject matter experts to discuss epidemiology, etiology, pathophysiology, diagnosis and treatment. Workshop panelists helped identify gaps in knowledge and opportunities for advancing biomedical research. NIH Director Francis Collins addressed the meeting and several other top Department of Health and Human Services and NIH staff attended all or part of the two-day session. Secretary of Health Kathleen Sebelius expressed her support in a letter sent to the 100+ workshop participants.

The meeting was webcast live and the recordings have been archived for on-demand viewing. Jennie M. Spotila, J.D., participated by webcast and prepared a summary posted to Research1st. Research1st The NIH issued a formal summary of the proceedings in August. You can find links to these and other meeting resources at www.cfids.org/SolveCFS/smrfall2011.asp

The Workshop was planned by the Trans-NIH ME/CFS Working Group under the leadership of Dennis Mangan, Ph.D., and a steering

committee comprised of the following volunteers appointed by NIH: Pat Fero; Ken Friedman, Ph.D.; Leonard Jason, Ph.D.; Nancy Klimas, M.D.; Mary Schweitzer, Ph.D.; and Suzanne Vernon, Ph.D.

CFS Advisory Committee Recommendations and Nominations

The CFS Advisory Committee (CFSAC) to the Department of Health and Human Services met May 10–11, 2011, to hear agency updates subcommittee reports and public testimony Research1st and to make policy recommendations. Three recommendations were made (excerpted from the official record):

1. The CFSAC considers CFS to be a multi-system disease and rejects any proposals to classify CFS as a psychiatric condition in US disease classification systems. (NOTE: no disease classification system under HHS' control proposes to move or to include CFS in or among psychiatric conditions.)
2. The April 2011 NIH State of Knowledge Workshop identified a number of gaps in what is known about the illness. CFSAC recommends that ME/CFS research receive funding commensurate with the magnitude of the problem and that the NIH (and/or other appropriate agencies) issue an RFA specifically for ME/CFS.
3. CFSAC asks that HHS organize a workshop to engage experts in disability assessment, the outcome being a document useful to patients and adjudicators which could contribute to a more efficient and fair disability process.

The terms of three CFSAC members will end in April 2012. In August, the Association responded to an open request for nominations

"From the CEO's Desk: What Can We Learn?" | Kim McCleary | July 8, 2011
Kim looks at the recent debate over Avastin and lessons from HIV/AIDS advocacy for messages about the often tense boundaries between patients, researchers, physicians and regulators.

"Oxidative Stress and Mitochondrial Dysfunction: Key Players in CFS?" |

Dikoma Shungu, Ph.D. | July 21, 2011

Dr. Shungu refers to two classic papers that point to clues.

"Shedding Light on Biomarkers" |

Alan Light, Ph.D. | Aug. 2, 2011

Dr. Light defines the term "biomarker" and describes how biomarkers are evaluated.

"I Can't Brain Today: I've Got the Dumb" | Katrina Berne, Ph.D. |

Aug. 9, 2011

Dr. Berne describes the cognitive dysfunction she experiences and offers tips for how to compensate.

"Doc Talk: Filling the Information Gap Between CFS Clinicians and Patients" |

Lucinda Bateman, M.D. | Aug. 22, 2011

Dr. Bateman offers insights and suggestions for how to bridge communication.

Throughout this issue of *SolveCFS*, look for the Research1st symbol; it signifies expanded information available on Research1st. ■



with the following recommendations: Roger Dodd, Ph.D. (Vice President for Research and Development, American Red Cross); Alan Pocinki, M.D. (Clinical Associate Professor, George Washington University Medical Center); Charles MacBrayer Sasser, J.D. (Founding Partner, Sasser Law Firm) and Suzanne D. Vernon, Ph.D. (Scientific Director, The CFIDS Association of America). Research1st

Department of Defense Recognizes CFS

The Department of Defense's Congressionally Directed Medical Research Program (CDMRP) included CFS in its priority topics for the first time in fiscal year 2011. The Association advocated for its inclusion during the FY11 federal funding cycle. This recognition enables researchers to compete for funding under this \$50 million program, although applications must successfully pass peer review. The Association is aware of several groups that submitted CFS-related applications to meet the July 5, 2011, deadline. ■



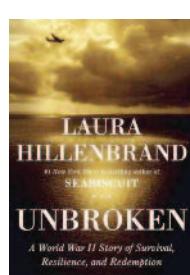
News Briefs

Building Awareness and Deepening Understanding

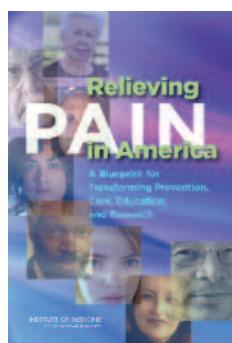
Award-winning author and CFS patient **Laura Hillenbrand** is again receiving rave reviews for her new book, titled *Unbroken*, released on Nov. 16, 2010, by Random House. She tells the true story of World War II bombardier Louis Zamperini in this “testament to the resilience of the human mind, body and spirit.” Since its release, the book has stayed at or near the top of multiple bestseller lists and has won or been nominated for several awards. It has also attracted international media coverage,



focusing attention on Laura’s own triumph of mind, body and spirit. “The Today Show,” *TIME* magazine, the *New York Times*, *USA Today*, the *Washington Post*, *ELLE* magazine and *Sports Illustrated* are just a few of the outlets that have helped inform the public about Laura’s courageous battle.



Pulitzer-Prize winning journalist **Amy Dockser-Marcus** was among the first to cover the research that connected CFS to XMRV. In the nearly two years that have passed, she has distinguished herself by sticking with the story and expanding the coverage to include other aspects of CFS research, writing more than 30 articles about CFS for the *Wall Street Journal* and its Health Blog. March 2011 was a big month. On March 5, CFS filled two pages of the *Journal’s* Review section with an article titled, “The Puzzle of Chronic Fatigue.” Amy traveled to Lyndonville, NY, to trace Dr. David Bell’s long journey caring for patients with CFS. On March 12, her article, “Amid War on a Mystery Disease, Patients Clash With Scientists,” shared the front page of the paper with news of the tsunami in Japan. It explores tensions that have deep roots going back to the name of the condition itself, a poorly funded federal research effort that has too often strayed to behavioral and psychosocial issues and decades of neglect by the medical community. “Unlocking Chronic Fatigue Syndrome,” ran in the paper on March 22. It featured an essay by patient Molly J. Billings about her life with CFS.



The **Institute of Medicine** (IOM) released a lengthy report, “Relieving Pain in America: A Blueprint for Transforming Prevention, Treatment, and Research,” on June 29, 2011. A press conference and a statement from 32 organizations (including the CFIDS Association of America) attracted considerable media attention to the 116 million Americans who experience chronic painful conditions, and its high economic toll, costing the nation up to \$635 billion annually. *TIME*, *US News & World Report*, Reuters and hundreds of other news outlets covered the story. The report includes several pages of policy recommendations. In particular, the IOM has recommended that “the Department of Health and Human Services develop a comprehensive plan with specific goals, actions, and timeframes...Given the burden of pain in human lives, dollars, and social consequences, relieving pain should be a national priority.” 

The CFIDS Association is pleased to announce that it has been approved to join **patientINFORM**, a collaboration of medical publishers, health organizations, medical societies and health information professionals. Through the unique **patientINFORM** partnership, participating publishers allow qualified nonprofit health organizations to provide access to the full text of journal articles without a subscription. The **patientINFORM** logo is like a seal of approval given to top websites that seek to link consumers with the most current, reliable information available about a particular condition. The CFIDS Association joins top-rated nonprofits including the American Heart Association, the American Diabetes Association and the Lupus Foundation plus publishers like Nature Publishing Group, AAAS (*Science*), Elsevier and Wiley-Blackwell. We are in the process of updating our Research1st site to add full-text links to research study summaries and analyses of articles published in participating journals. 



ACCESS + INTERPRETATION = UNDERSTANDING + EMPOWERMENT

Supporting the Cause

The Association welcomes to its **Board of Directors** Kevin Frick, co-founder and general partner of Serent Capital. Kevin is a graduate of Stanford University’s M.B.A. program and graduated summa cum laude with a B.S. in electrical engineering from University of Michigan. Before founding Serent Capital, Kevin was a partner in McKinsey & Company’s Palo Alto office. Kevin lives in San Carlos, CA, with his wife Michelle Thies. They have been actively pursuing a solution to her CFS symptoms for more than 10 years. We also extend tremendous gratitude to retiring directors Katrina Berne, Ph.D., and Dimitris Papanicolaou, M.D. Trina served from 2004 until early this year, most recently leading the Board’s Nominating Committee. Dr. Papanicolaou joined the Board in 2005 and now serves on the Scientific Advisory Board.



The CFIDS Association won \$25,000 by placing 23rd among the top 100 organizations competing in the **Chase Community Giving** contest on Facebook in May. Funds will support the Association’s research program.

The second annual “**24 Hours In the Enchanted Forest: A Race to SolveCFS**” was held June 18, 2011, in McGaffey, NM. The event raised more than \$10,000 for the Association’s research program. Claudia Goodell, who has had CFS since 1985, founded this endurance cycling event in 2010. This year’s event attracted about 40 percent more racers and next year’s event promises to be even larger. Thanks to Claudia, the SolveCFS Team (which included our scientific director Suzanne Vernon, Ph.D., and family members) and all the racers and volunteers who made it a success! Check out links on our website to an action-packed event video made by CFS patient Ken Holmes and a slideshow of photos taken by *Mountain Flyer Magazine* photographer Brian Leddy. ■



The CFIDS Association of America

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Web home for this issue of SolveCFS:
www.cfids.org/SolveCFS/smri-fall2011.asp

For 24 years, the CFIDS Association has steadfastly committed to making CFS widely understood, diagnosable, curable and preventable. We have evolved to meet new challenges and adapt to changing realities. Now, as the vast majority of our supporters have urged, we've narrowed our focus to research. The preceding pages of this issue of **SolveCFS** report on progress in advancing our new research-focused strategy and describe how we intend to transform the research landscape.

Your gifts have sustained this organization and we present a new opportunity to spur the next phase of vigorous growth and deepening impact.

THE Catalyst FUND

Become a Catalyst to transform research.

In science, catalysts are substances that change the rate of chemical reactions. "Positive" catalysts speed a particular reaction. We are seeking at least 200 individuals, families, foundations and corporations to help the Association transform CFS research by donating \$10,000 or more to a new fund that will speed discovery and transform the way that CFS research is conducted. This \$2,000,000 sum will allow us to immediately execute plans for the expanded research activities described on pages 4–5.

There are three ways you can join other Catalysts to make this goal a reality:

- 1** Make a gift or pledge of \$10,000 or more with special recognition and benefits at the Gold (\$10,000-\$24,999), Platinum (\$25,000-\$49,999), Palladium (\$50,000-\$99,999) and Rhodium (\$100,000+) levels of giving.
- 2** Engage family, friends, support group members and others to join with you in making a combined donation of \$10,000 or more. We can provide tools to help you prepare a fundraising letter to share with your contacts, set up a Facebook cause or host a local event in support of **THECatalystFUND**.
- 3** Help us secure a special matching grant. Two donor families (who wish to remain anonymous) have pledged up to \$75,000 to match a pool of smaller donations so that gifts of any size (up to \$10,000 each) help us build toward the \$2,000,000 goal and engage as many supporters as possible in **THECatalystFUND**. This challenge grant has a Dec. 31, 2011 deadline.

Catalysts at all donation levels will be provided exclusive updates from Association leaders, members of the Association's Scientific Advisory Board and funded investigators. Web-based programs offered only to Catalysts will help keep you personally informed about progress being made across the research field. In addition, Catalysts will receive special recognition in Association publications and events. (Anyone who wishes to remain anonymous is welcome to do so.)

In 2012, we will host a special event marking the Association's 25th year of service where we will honor Catalysts and members of the President's Circle, a group of extraordinary individuals whose lifetime gifts to the organization exceed \$50,000. Further details about this gathering will be provided early in the new year.

We invite **you** to become a Catalyst. Gifts of every size are needed to reach our \$2 million goal and will be gratefully recognized as part of **THECatalystFUND**.

We are delighted to announce that within days of sharing the news of the creation of **THECatalystFUND** with just a few of our most enthusiastic supporters, a rapid reaction was generated and gifts totaling \$192,000 were provided to speed the Fund's growth. That's the power of catalytic action! We'll share Catalyst profiles and updates on the \$2,000,000 goal through the fall and into winter.

We invite you to become a Catalyst. Gifts of every size are needed and will be gratefully recognized as part of **THECatalystFUND**. Please use the enclosed envelope to make your gift today, call Ashley Comstock at 704-364-0016 ext. 101, or make a secure gift online at www.cfids.org.

Thank you for your generous support and for considering this unique opportunity to help us transform CFS research!

Did You Know?

Gold, platinum, palladium and rhodium are metals required in many catalytic reactions. Rhodium is one of the rarest precious metals and is the most costly on earth.

THE Catalyst FUND



THE CFIDS ASSOCIATION OF AMERICA

Our Mission:

For CFS to be widely understood, diagnosable, curable and preventable.

Our Strategy:

To stimulate research aimed at the early detection, objective diagnosis and effective treatment of CFS through expanded public, private and commercial investment.

Our Core Values:

To lead with integrity, innovation and purpose.