

RESEARCH

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in review

Research News from the San Francisco VA Medical Center and
the Northern California Institute for Research and Education

Featured PI

Mary Whooley, MD

Mary Whooley, MD, recalls that when she began recruiting patients for the Heart and Soul Study, "I thought I would be lucky to have one paper published." Dr. Whooley, a staff physician in the medical service at SFVAMC, began the long-term prospective study in 2000 to investigate the apparent connection between depression and heart disease. She and her staff recruited 1,000 men and women with cardiovascular disease, conducted careful baseline measurements of physical and mental health, and have been following the subjects since then.

"We now have our preliminary results," she says. "It turns out that it's all about behavior. Patients with depression don't exercise, which makes them feel more depressed, which in turn leads to their exercising even less. It's a vicious cycle that leads directly to heart disease." Along the way, thanks to the meticulous patient data collected during the course of the study, the Heart and Soul group has had 50 peer-reviewed papers accepted for publication on different aspects of cardiovascular disease and mental health. "The nice thing is that almost all of the papers have been written by residents, fellows, and other young investigators who have been able to develop their careers by using these data," reports Dr. Whooley, who is also an associate

professor of medicine, epidemiology, and biostatistics at UCSF.

Dr. Whooley is being considered for promotion to full professor in July, 2008. "If you had to describe my interest broadly," she says, "it would be trying to understand the mind-body connection, and why psychological stress leads to disease." Her interest in the topic began in college, where her senior thesis was a 20-person study of depression and breast cancer. "Then, in medical school and residency, it was really obvious to me that the patients who were depressed had worse health," she says. "It was very difficult to help them when they were so unmotivated and had so little energy. So I thought, if I'm going to treat these people, I need to address their mental health issues or I'm never going to be able to improve their physical health."

The Heart and Soul Study is funded by the NIH through 2010, "and we hope to receive a grant to follow the patients for even longer," Dr. Whooley says. In the meantime, she and her team have begun a new study on post-traumatic stress disorder (PTSD) and heart disease. "We'll be working with Vietnam veterans with and without PTSD to try and figure out why people with PTSD are at increased risk of heart disease. These vets are now entering their sixties, which



Dr. Whooley enjoys spending time with her children, who are 6, 9, and 11. "This time is a magic window for being with your kids, and I'm making the most of it." She swims for exercise. "I have a waterproof MP3 player that attaches to my goggles, so now I have my tunes when I do laps!"

is a crucial time in terms of cardiovascular health. We hope that our findings will help prevent the current generation of Iraq and Afghanistan veterans from developing PTSD-associated heart disease."

In future research, Dr. Whooley hopes to pursue studies in genomic risk factors for disease: "We have DNA from all Heart and Soul Study participants, so we'd like to look at DNA as a predictor of cardiovascular disease." In addition, she would like to investigate methods of modifying and improving behavior in order to prevent heart disease. "Now that we know about the link between depression and lack of exercise, are there ways that we can change long-term behavior -- not over months, but years -- so that people have a better chance of staying healthy?"

Who is the VA/NCIRE Research Community?

Our research community at 4150 Clement is a mixture of VA, NCIRE, and UCSF investigators who work at our medical center. In most cases, researchers are associated with all three institutions, giving our community a broad and stable infrastructure. In this publication, we hope to introduce our brightest stars and many interesting areas of research that are carried out here on our campus.

Featured Junior PI

Michael Steinman, MD

In his research, SFVAMC geriatrics specialist Michael Steinman, MD, focuses which medications doctors choose to prescribe to older people, and whether that represents the optimal set of medications that are going to maximize health and minimize harm.

Dr. Steinman says, "Undertreatment is as big a danger as overmedication. It's a fine line. For example, if you have reasonably severe heart failure, there are probably five or six drugs that are recommended for your condition. But what happens if you have diabetes, high blood pressure, and dementia as well? Pretty soon, you're on 20 medications, the additive effects of which might be harmful."

One issue, he says, is that medications are usually tested on patients with relatively few diseases and conditions, so that the effects of multiple medications on individual patients often remain unknown and undocumented. "That's one of the qualities that makes geriatric medicine different," observes Dr. Steinman, who is also an Assistant Professor of Medicine at UCSF. "Treatment is much more individualized. Once a patient is old and frail with multiple medical problems, it becomes

even more necessary to learn about the individual characteristics of that patient."

Dr. Steinman is also interested in the relationship between physicians and pharmaceutical companies, in particular "the ethical grey areas that some doctors traverse when they prescribe certain drugs after receiving gifts and financial incentives from those drugs manufacturers." He and his research team have published studies demonstrating a link between sales calls from representatives of the manufacturer of the seizure drug gabapentin and physicians subsequently prescribing the drugs. "The good news is that these sorts of practices were not on people's radar screens before, and now they are, among doctors and government as well as the public," he observes. One offshoot of his research was the establishment of the online Drug Industry Document Archive at the UCSF Library, available at <http://dida.library.ucsf.edu>. "We're trying to expand the collection to include documents about other drugs," says Dr. Steinman.

Dr. Steinman is beginning a VA-funded study of the prescribing of guideline-recommended



Dr. Steinman enjoys "spending time with my two lovely children, ages 1 and 3. I also play in a San Francisco Ultimate Frisbee league. I'm tall, so I get asked to go long a lot."

medications for heart failure. "Certain institutional quality measures encourage doctors to treat patients according to specific care guidelines, and may implicitly penalize them if they do not. We are looking at reasons why patients are not prescribed guideline-recommended medications to better understand how much of non-prescribing really represents a quality problem, and how much it is the result of appropriate clinical decisions."

Upcoming Office of Research Oversight (ORO) Site Visit



The Office of Research Oversight (ORO), Western Region will soon be performing a routine comprehensive review of all aspects of research at SFVAMC. As directed by the VA Under Secretary for Health, the review will include comprehensive assessments of laboratories, human research, physical security, animal research, safety, and data security. The

reviews are intended to verify that research, biosafety, biosecurity, and research information security programs meet the highest VHA implementation and documentation standards. A site visit to SFVAMC is scheduled for the very near future.

The review and site visit mean a number of things for SFVAMC principal investigators. Investigators with web labs need to review and, if necessary, update their lab's toxic chemical and chemical hygiene plans;

make sure all laboratory staff are properly trained in lab work; and replace all cloth-covered chairs in biosafety labs with chairs covered in approved materials. In addition, wet labs can expect unannounced annual physical inspections by Rakita Singh, the newly appointed Research Safety Coordinator.

In dry labs and clinical research laboratories, the focus is on the human protection program and on compliance with annual data security, storage, and destruction requirements. Clinical research labs are expected to comply with all procedures and required documentation for human research.

In addition, all principal investigators are reminded to use only VA-approved encrypted thumb drives and laptop computers.

The Research Office sincerely appreciates the efforts of all PIs and compliance officers as we strive to maintain the San Francisco VA Medical Center, the largest research program in the VA, as the gold standard for VA research practices.

NCIRE Celebrates DoD Partnership



\$4 Million in New Funding

NCIRE has received \$4 million in continuing funding for the Neuroscience Center of Excellence, a research partnership between the Department of Defense (DoD), SFVAMC, and NCIRE. The Center has received over \$20 million in DoD funds since 2003. The money supports research projects focusing on neurological diseases and conditions suffered by veterans and active military personnel as well as the general public.

On October 29, NCIRE and the VA celebrated five years of research partnership with DoD when representatives from DoD, SFVAMC, NCIRE, and the offices of California Congressional members gathered at SFVAMC to review and discuss current and future research projects. It was the third annual meeting in recognition of the Neuroscience Center of Excellence investigators.



NCIRE Board Chair Raymond Swanson, MD, SFVAMC Chief of Staff Diana Nicoll, MD, PhD, MPA, SFVAMC Research Chief Lynn Pulliam, MS, PhD, and NCIRE Executive Director Robert E. Obana (L to R) share a light moment.

The program was opened by NCIRE Executive Director Robert E. Obana, SFVAMC Chief of Staff Diana Nicoll, MD, PhD, MPA, and SFVAMC Chief of Research Lynn Pulliam, MS, PhD, who welcomed special guest Colonel Karl E. Friedl, PhD, Director of the Army's Telemedicine & Advanced Technology Research Center (TATRC), which disburses the DoD funds. Dan Bernal, District Director for House Speaker Nancy Pelosi (D-Calif), presented greetings and congratulations from the Speaker.

Over the course of the day, investigators gave overviews and updates on a wide variety of clinical, translational, and basic research projects, including research on post-traumatic stress disorder, traumatic brain injury,

nerve damage to limbs following battlefield injury, and wound healing under conditions of psychological stress.



(L to R) SFVAMC neurosurgeon Grant Gauger, MD; U.S. Army Colonel Karl E. Friedl, PhD; Lynn Pulliam, MS, PhD

"In the short term, this research is about war injuries," observed Michael Weiner, MD, senior principal investigator of the Neuroscience Center of Excellence and director of the Center for Imaging of Neurodegenerative Diseases at SFVAMC. "In the longer term, however, we are laying the groundwork for studies aimed at diagnosing, treating, and eventually preventing neurological disease for everyone, civilian and military alike."

"I'm totally impressed," said Colonel Friedl at the conclusion of the event. "Every project makes sense, in basic as well as applied science. This place is becoming the nation's center for neuroimaging and neurocognitive research. It's really taking off."



(L to R) Executive Director, Community and Governmental Relations, Paul Takayama; SFVAMC physician Karen Seal, MD; SFVAMC brain researcher Valerie Cardenas-Nicolson, PhD

NCIRE

The Veterans Health Research Institute

News

by Robert Obana, Executive Director

NCIRE ended fiscal year 2007 with preliminary, unaudited expenditures of \$47 million. Currently, we are administering approximately \$100 million in approved research projects at SFVAMC, and rank 17th in the nation among independent research institutes in National Institutes of Health funding. With the NIH budget remaining flat, it is extremely important that NCIRE continues to receive support from the Department of Defense for the DoD/SFVAMC/NCIRE Neuroscience Center of Excellence. Our funding for fiscal 2008 is \$4 million, bringing the total that we have received from DoD to around \$20 million over the past five years. In the same vein, our third annual Department of Defense Investigators Day took place on October 29, and was judged a success by all participants. We look forward to the promise of continued support from DoD in the years ahead.

October 11, 2007 was a very special evening for NCIRE, marking the debut of "Above & Beyond," our annual fundraising gala. In terms of establishing NCIRE's public presence — in particular, our presence in the Bay Area philanthropic community — the gala was an important achievement. It has definitely kick-started our development and fundraising efforts, with both monetary donations and expressions of interest coming in from potential supporters after the event. I would like to thank all of our friends and supporters in the SFVAMC community for your dedication and support on behalf of what we hope will become a "must-attend" affair on the San Francisco fundraising calendar.

As part of our new, higher public profile, NCIRE unveiled a totally redesigned website during the last quarter. Besides simply looking better than the old site, the new site is much more dynamic, better reflects our mission and our goals, and provides easy links to those who wish to support us through donations. Many thanks to Susan Dugdale, NCIRE's Manager of Design & Creative Services, and the web team at dystrick design for their hard work and creativity.

We have also inaugurated a semiannual publication, *The Bridge*, which is designed to keep NCIRE's friends, supporters, and donors abreast of the latest developments in veterans health research at NCIRE. Please stop by Building 14 to pick up a copy. You can also read it on line at http://10.174.14.201/news_communications.htm.

On behalf of everyone at NCIRE, please let me wish you a happy and prosperous 2008.

NCIRE Board Member Co-Chairs NIH Panel

NCIRE Board of Directors member Keith R. Yamamoto, PhD, is co-chair of a working group established by the National Institutes of Health to explore ways of streamlining and improving the Institute's peer review and grant making process. On December 7, the group presented its findings to the advisory committee for NIH Director Elias A. Zerhouni.

The group suggested a series of reforms, including cutting the maximum length of grant applications from 25 pages to seven, giving more weight to potential scientific effects of research proposals, and providing more grant opportunities to young scientists. According to the Chronicle of Higher Education, the NIH is expected to decide in March whether to begin testing some of the proposed changes, which were suggested in part by more than 2,600 comments collected from scientists nationwide.

Dr. Yamamoto is Executive Vice Dean of the UCSF School of Medicine and Professor of Cellular/Molecular Pharmacology and Biochemistry/Biophysics at UCSF. "The biggest impact will come through a combination of multiple, decisive changes," he told the *Chronicle*.

News Bulletin

Veterans Affairs Clinic Looking for Troubled Soldiers

3,000 to 4,000 Bay Area veterans of Iraq, Afghan wars may be suffering mentally. The *Press Democrat* reports: "Thousands of Northern California veterans from Iraq and Afghanistan suffer from war-related psychological disorders, and the San Francisco Veterans Affairs Medical Center is launching a campaign to find them and get them enrolled in treatment."

Karen Seal, a staff physician at the San Francisco VA Medical Center, who is also an assistant professor of medicine at UC San Francisco, is interviewed.

For full story, see: *Press Democrat, Santa Rosa* Published September 21, 2007

Grants Funded

October 2007 – December 2007

Military Interdepartmental Request (MIPR) - DoD

LTC T. Sloane Guy

Live Transference of Surgical Subspecialty Skills Using Telerobotic Consultation to Remote General Surgeons
08/01/07 – 07/31/08

National Institutes of Health (NIH)

Valerie Cardenas-Nicolson, PhD

Free Tools for High Resolution Voxel-Wise Morphometric Analysis
09/24/07 – 8/31/08

Robert Raffai, PhD

Role of Apolipoprotein E4 in the Progression and Regression of Atherosclerosis
09/26/07 – 06/30/12

NIH - Subcontract from Yale

Judith Ford, PhD

Auditory Hallucinations in Schizophrenia
EPPS&fMRI
11/01/07 - 03/31/08

NIH - Subcontract from UC-Irvine

Judith Ford, PhD

Functional Imaging Research for Schizophrenia Testbed (FIRST) BIRN
12/01/07 – 11/30/08

VA Merit Review – Biological Laboratory Research and Development (BLR&D)

Conrad Alano, PhD

DNA Damage and Mitochondrial Failure in Ischemic Neuron Death
10/01/2007 – 09/30/10

Jialing Liu, PhD

Reducing Functional Deficits Following Traumatic Brain Injury
10/01/07 – 09/30/11

Robert Nissenson, PhD

Role of Cyclic AMP Signaling in Skeletal Anabolism
10/01/07 – 09/30/11

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