

# RESEARCH

Volume 20 • Winter 2010

# in review

Research News from the San Francisco VA Medical Center  
and NCIRE – The Veterans Health Research Institute

## Featured PI

### Kenneth Covinsky, MD, MPH



*Dr. Covinsky is an avid bridge player who sometimes plays competitively. "Every bridge hand is different from every hand you've had before. How you work with your teammate makes all the difference."*

SFVAMC clinician and researcher Kenneth Covinsky, MD, MPH, put his focus on geriatrics, which he defines very simply as "the care of older persons." Dr. Covinsky is part of the SFVAMC Geriatrics Division, "a group of clinicians, educators, and researchers whose work stems out of a devotion to, and respect for, the elderly."

He recounts that in medical school and as a resident, "I found myself trying to understand the impact of what we do as physicians, what works and what doesn't, why patients do well and why they don't. So that led me into clinical research."

In his research, Dr. Covinsky pursues the question of "why older people become disabled, by which I mean the loss of the ability to do basic tasks of daily living – walk short distances, bathe, dress – without relying on caregivers."

One insight of Dr. Covinsky's research has been the realization that day-to-day functioning is essential in predicting the health and longevity of older people. "You can know a lot more about the health of an older person by understanding their functional status than by understanding what diseases they might have," he says. "It's possible to be an older person with a lot of illnesses but, functionally, do very well. Conversely, you can be free of illness, per se, but not function very well at all."

Dr. Covinsky has found that hospital stays are a major contributor to disability among the elderly. He notes that as an attending physician on the medical service, "I directly see the impact of hospital-associated disability on our older Veteran patients."

The risk of hospital-associated disability goes up dramatically with age, he explains. "Our work has shown that once you're past the age of 85, there's a greater than 50 percent risk that you are going to go home from the hospital with a major new disability that you didn't have before you were sick." Dr. Covinsky emphasizes that such a disability usually has little or nothing to do with the illness that led to hospitalization in the first place. In fact, "We've found that one of the biggest risk factors for hospital-acquired disability, besides age itself, is depression, which more than doubles the risk that an older person will become disabled."

He points out that because many older people are frail, "it takes just a very minor health insult to move them into disability." Dr. Covinsky and his colleagues are "working to get doctors to recognize that you may see a patient for a medical illness – pneumonia, for example – and you'll treat them with antibiotics, and if you're not looking carefully, you'll think they're better. But if you look at functioning, you will realize that they are now disabled. It's a matter of looking at the

whole patient rather than this organ system or that organ system."

Dr. Covinsky, who is also a Professor of Medicine at UCSF, mentors young clinical researchers in geriatrics. The challenge for the field, he says, is that there are "very few clinicians who have had specialized training either in the clinical approach to the older patient or how to do effective clinical research. So a lot of my focus has been on training and developing researchers in gerontology, and developing our capacity to do research in this area." One bonus has been "seeing some of the physician researchers on the Geriatrics Service that I've mentored along the way – Dr. Louise Walter, for example, or Dr. Sei Lee – take these ideas in novel directions that I would never have thought of. It's been both inspiring and gratifying."

## Who is the VA/NCIRE Research Community?

Our research community at SFVAMC is a mixture of VA, NCIRE, and UCSF investigators. 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 you to our brightest scientists and the many interesting areas of research that are carried out here on our campus.

## Featured Junior PI Shira Maguen, PhD

"My clinical work informs my research," says Shira Maguen, PhD, a staff psychologist in the Mental Health Service at SFVAMC and an Assistant Clinical Professor of Psychiatry at UCSF. Dr. Maguen works with Veterans in individual practice, group therapy, and in the SFVAMC Operation Enduring Freedom/Operation Iraqi Freedom Integrated Care Clinic. Her clinical focus is the treatment of post-traumatic stress disorder. Her research spans a wide range of Veterans' health interests.

One is "the mental health impact of killing in war, and how people are impaired functionally in their lives by killing." The challenge, she says, is "to ask about these questions in ways that leave Veterans feeling supported, where they can respond honestly and talk comfortably about a very, very difficult topic."

Dr. Maguen notes that "it's not clear whether current treatments for PTSD are always appropriate" for treating the psychological and emotional effects of killing. "We need to better understand how to treat people who have struggled with these issues," she says.

Another research project, funded by the Department of Defense, involves mental health and

readjustment among female Veterans of the wars in Iraq and Afghanistan. "We're looking at multiple questions," she says. "One is, are there gender differences in mental health diagnoses after military personnel get back from war, and when they come to the VA?"

Beyond that, says Dr. Maguen, "I want to look at military sexual trauma and how that factors into the picture, for men as well as women. Nationally, we're looking at a sample of Veterans with PTSD and separating them into those who have experienced military sexual trauma and those who have not, and looking at whether there are differences in mental health disorders between the two groups."

Another question is gender differences in service utilization at VA hospitals and clinics. "If you have a military sexual trauma incident and PTSD, does that impact the frequency and type of VA service utilization?"

The third research project, also funded by the Department of Defense, is "trying to understand the unique symptoms that distinguish traumatic brain injury from the symptoms of PTSD and other mental health disorders" among Iraq and Afghanistan Veterans. "If you



Dr. Maguen loves to travel. At home in San Francisco, "I bicycle to work every day through Golden Gate Park, which is a really nice start to the day. And yoga helps keep me grounded."

have PTSD, how is TBI going to affect your treatment? What are the treatments that might help both at the same time?"

Before she became a psychologist, Dr. Maguen was a journalist. "There are similarities between that field and what I do now," she says. "I've always been interested in understanding people's stories and lives, and putting it all together into a cohesive whole."

## Alzheimer's Disease Neuroimaging Initiative Expands, Seeks New Volunteers



Michael Weiner, MD

The National Institutes of Health (NIH) is expanding the Alzheimer's Disease Neuroimaging Initiative (ADNI), a groundbreaking study that will recruit hundreds of new volunteers to help define the subtle changes that may take place in the brains of older people many years before overt symptoms of Alzheimer's disease appear.

Michael Weiner, MD, Director of the Center for Imaging of Neurodegenerative Diseases at SFVAMC, is principal investigator for the study. "By determining how brain scans, biomarker measures, and cognitive testing results relate to each other and the symptoms a person is having, we are getting a much clearer picture about the onset and progression of this devastating neurodegenerative disorder," said Dr. Weiner, who is also a Professor of Radiology, Medicine, Psychiatry, and Neurology at the University of California, San Francisco.

ADNI is led by the National Institute on Aging at NIH through a \$69 million grant to NCIRE-The Veterans Health Research Institute, with private sector support provided through the Foundation for the National Institutes of Health. NIH anticipates providing \$40 million to the project over the next five years; \$8

million was awarded in fiscal year 2010, with a further \$32 million committed, subject to funds availability. Another \$29 million will be contributed by private industry and the Canadian government.

Researchers are seeking 550 new volunteers to join those already participating in the study as it enters a second phase, called ADNI2. Over the next five years, a total of approximately 1,000 people aged 55 to 90 will be enrolled at approximately 55 sites in the United States and Canada.

ADNI researchers have published over 170 papers. The study has resulted in new findings about how changes in the structure of the hippocampus, a brain area important to learning and memory, may help detect disease progression and effectiveness of potential treatments. It has also established biomarker and imaging measures that predict risk for cognitive decline and conversion to dementia.

## Research Program in Neuroscience



### DoD Investigators Day 2010

On November 16, NCIRE welcomed researchers and clinicians to the seventh annual Neuroscience Center of Excellence Investigators Day. The Department of Defense-sponsored conference provides an opportunity for presentation and discussion of research projects on traumatic brain injury, post-traumatic stress, and other neurological injuries and conditions of military relevance. The US Army Telemedicine and Advanced Technology Research Center (TATRC) partners with NCIRE and SFVAMC on this program.

The day began with a welcome from TATRC Director Colonel Karl Friedl, PhD, and Psychological Health Portfolio Manager Jay Shore, MD, MPH. US Air Force Major Jennifer Hatzfeld, RN, PhD of David Grant Medical Center spoke about the challenges of implementing Deployment Anxiety Reduction Training, a one-hour evidence-based mental health and trauma recovery protocol for combat troops, in Afghanistan.



Maj. Jennifer Hatzfeld, RN, PhD, US Air Force

Health Clinical Center. Colonel Engel spoke about the creation and implementation of RESPECT-Mil (Re-Engineering Systems for the Primary Care Treatment of Depression and PTSD in the Military), a program to provide systematic evidence-based care in a primary care setting to soldiers with symptoms of depression and PTSD.

In the afternoon, Thomas Neylan, MD, Director of the Posttraumatic Stress Disorders Program at SFVAMC, led a review of psychological health research, ranging from basic research on biomarkers for PTSD to the challenges of providing care for combat-related psychological conditions in a primary care setting. To wrap up the day, Neuroscience Center of Excellence Principal Investigator Michael Weiner, MD, conducted a review of militarily-relevant neuroimaging research at the SFVAMC Center for Imaging of Neurodegenerative Diseases, which he directs.



Col. Karl Friedl, PhD, Director of TATRC; Thomas Neylan, MD, Director of the PTSD Program at SFVAMC; Col. Charles Engel, MD, MPH, Director of the Deployment Health Clinical Center; and Robert Nissenson, PhD, Deputy ACOS for Basic Research at SFVAMC (L to R)

Geoffrey T. Manley, MD, PhD, Chief of Neurosurgery at San Francisco General Hospital and Professor and Vice Chair of Neurosurgery at UCSF, provided an alternate view of traumatic brain injury in his talk on "redefining TBI." Members of the SFVAMC musculoskeletal research group - Robert A. Nissenson, PhD, Bernard Halloran, PhD, and Hubert Kim, MD, PhD - reviewed their work on the neurological aspects of combat-related bone and muscle injury.

The mid-day presentation was conducted by Colonel Charles Engel, MPH, MD, Director of the US Department of Defense Deployment



NCIRE Board of Directors Member Walter S. Newman, US Army (Ret.), TATRC Senior Scientist and Clinical Consultant John M. Carney, PhD, and TATRC Psychological Health Portfolio Manager Jay H. Shore, MD, MPH (L to R)

# NCIRE

## The Veterans Health Research Institute

### News

by Robert Obana, Executive Director

2010 was a remarkable year for NCIRE - The Veterans Health Research Institute. Thanks in large part to our mission of supporting and facilitating Veterans health research, SFVAMC continues to maintain its position as the VA's leading academic medical research program.

While we enjoy continued progress, cautious optimism is the watchword going forward. The state of the economy plus recent political changes mean that research funding will likely remain essentially flat for at least the next several years.

Regardless of these uncertainties, we have been able to develop and expand partnerships with the Department of Defense (DoD), private philanthropists, and private enterprise. These alliances underscore NCIRE's role as a model of the patient-centered health research institute, self-contained yet bridging many communities of interest.

Here at Fort Miley, Dr. Michael Weiner's Center for Imaging of Neurodegenerative Diseases (CIND) serves as the nucleus of several initiatives. One is the Neuroscience Center of Excellence, with over 50 projects funded by DoD. Another is a proposed SFVAMC Neuroimaging Core, built around the new 7.0 and 3.0 Tesla MRI units due to be installed at CIND over the next year. This Core would serve not only CIND investigators but researchers from across SFVAMC and its extended community.

One very promising pilot project facilitated by NCIRE is the creation of a transparent, interoperable electronic records system that can be shared by the VA, DOD, academic medical centers, and private industry. Partners include NCIRE, SFVAMC, UCSF, DoD, and Kaiser Permanente Northern California. This project is in its formative stages, and we look forward to reporting on its progress in future communications.

NCIRE congratulates Carl Grunfeld, MD, PhD, SFVAMC Chief of Endocrinology and UCSF Professor of Medicine, on his selection as Associate Chief of Staff for Research and Development at SFVAMC. In that capacity, Dr. Grunfeld joins the NCIRE Board of Directors as an ex-officio member. We look forward to working with him to bring the highest level of dedication and creativity to Veterans health research at Fort Miley.

### Department of the Army/DoD

#### Steven Batki, MD

Topiramate Treatment of Alcohol Use Disorders in Veterans w/PTSD: A Pilot Controlled Trial of Augmentation Therapy  
4/1/2010 – 3/31/2012

#### Hubert Kim, MD, PhD

Diagnosis of Compartment Syndrome Based on Tissue Oxygenation  
9/30/2010 – 9/29/2013

#### Alfred Kuo, MD, PhD

Peripheral Nerve Repair With Hydrogel-Mediated Delivery of Growth Factors in Aligned Nanofiber Scaffolds  
8/1/2010 – 7/31/2012

#### Shannon E. McCaslin-Rodrigo, PhD

Functional Brain Mechanisms of Mutual Maintenance of PTSD and Chronic Pain: A Pilot fMRI Study: 5/1/2010 – 4/30/2012

#### Thomas Neylan, MD

Mental Health Core: 5/1/2010 – 4/30/2012

### National Institutes of Health

#### Daniel Bikle, MD, PhD

Vitamin D Receptor Co-Activators in Keratinocytes: 9/28/2010 – 5/31/2011

#### Ruby Ghadially, MBCHB, FRCP

Reversing Epidermal Stem Cell Aging: Role of BMI-1 and the Stem Cell Niche  
9/10/2010 – 5/31/2012

#### J. McLeod Griffiss, MD

Risk Factors and Susceptibility to Gonococcal Infection: 4/5/2010 – 3/31/2011

#### Millie Hughes-Fulford, PhD

Suppression of the Immune Response in Spaceflight and Aging  
9/1/2010 – 8/31/2012

#### Chris Lau, PhD

Sex Chromosomes and Gender Disparity in HBV-Related Hepatocellular Carcinoma  
7/23/2010 – 6/30/2012

#### Robert Nissenson, PhD

G Protein Signaling in Osteoblasts  
4/12/2010 – 3/31/2011

#### Michael Shlipak, MD, MPH

The Aging Kidney in HIV Infection: Biomarkers for Early Detection of Injury  
5/1/2010 – 4/30/2015

#### Raymond Swanson, MD

Mechanisms of PARP and PARG Mediated Cell Death: 6/1/2010 – 5/31/2015

#### Phyllis Tien, MD

Visceral Adiposity, HIV, and HCV Biologic Mediators of Hepatic Steatosis  
7/1/2010 – 6/30/2014

#### Chai Ling Tu, PhD

Calcium-sensing Receptor and Keratinocyte Differentiation: 5/1/2010 – 2/28/2015

#### Michael Weiner, MD

Alzheimer's Disease Neuroimaging Initiative II: 9/30/2010 – 8/31/2015

#### Kristine Yaffe, MD

Long Term Depressive Symptom Course & Adverse Health Outcomes Among Older Women: 3/4/2010 – 2/28/2013

#### Midori Yenari, MD

Inflammatory Mechanisms in Cerebral Ischemia: 6/1/2010 – 5/31/2015

### VA Grants

#### Lilly Bourguignon, PhD

CD44 & Stem Cell Marker (Nanog) in Head and Neck Cancer: 10/1/2010 – 9/30/2014

#### Peter M. Elias, MD

Regulation/Role of AcylCer in Normal Epidermis and Atopic Dermatitis  
10/1/2010 – 9/30/2014

#### Ruby Ghadially, MBCHB, FRCP

Characterization of Human Epidermal Stem Cells: 10/1/2010 – 9/30/2014

#### Hubert Kim, MD, PhD

ECM and MMPs in Muscle Atrophy and Rehabilitation: 10/1/2010 – 9/30/2014

#### Sara J. Knight, PhD

Incorporating Genomics into Routine Clinical Care for Veterans with Colon Cancer  
4/1/2010 – 3/31/2013

#### Chris Lau, PhD

Role of the Y-Located TSPY Gene in Human Oncogenesis: 10/1/2010 – 9/30/2014

#### David Lovett, MD

Mitochondrial Matrix Metalloproteinase-2 and Cardiac Injury: 10/1/2010 – 9/30/2014

#### Stephen Massa, MD, PhD

p75NTR Ligands for Treatment of Traumatic Brain Injury: 4/1/2010 – 3/31/2014

#### Alexander Monto, MD

Viral Associated Liver Disease Phase III  
4/1/2010 – 3/31/2014

#### Mary Nakamura, MD

DAP12 and ITAM Signals in Osteoclastogenesis  
4/1/2010 – 3/31/2014

#### Dennis Oh, MD, PhD

Role of p53 Homologs in DNA Repair in Human Keratinocytes: 4/1/10 – 3/31/14

#### Robert Raffai, PhD

Does Diabetic Hyperglycemia Regulate Atherosclerosis Progression and Regression?  
7/1/10 – 6/30/14

#### Karen Seal, MD, MPH

Neuropsychological Screening of OEF/OIF Veterans in VA Primary Care  
10/1/10 – 9/30/14

#### Rebeka Silva, DMD

Advanced Visuoaptic Surgical Planning for Trauma Surgery: 10/1/10 – 9/30/13

### OTHER GRANTS

#### American Heart Association-Western

#### Ho Seong Seo, PhD

Role of Bacteriophage lysis in Streptococcal Endocarditis: 7/1/2010 – 6/30/2012

#### Yihfen Yen, PhD

Roles of the Asp Proteins in the Export of GspB, a Streptococcal Virulence Factor Associated with Infective Endocarditis  
7/1/2010 – 6/30/2012

#### Purdue University

#### Kenneth Covinsky, MD, MPH

Prognostic Significance of Insufficient ADL Help on Health Outcomes/Utilization  
4/1/2010 – 3/31/2011

#### US Israel Binational Science Foundation

#### Gary Cecchini, PhD

Association of Energy-Metabolism Enzymes with Switch-Motor Complex of Bacterial Flagella  
9/1/2010 – 8/31/2014

#### University of California

#### Daniel Mathalon, MD, PhD

Identifying Intermediate Phenotypes for Compulsive Hoarding  
06/01/2010 – 02/28/2011

#### Vanderbilt Medical Center

#### Gary Cecchini, PhD

Complexities of Complex II: A Vesatile Architecture for Respiration  
3/1/2010 – 2/28/2011

## RESEARCH in review

### A SFVAMC/NCIRE Publication

4150 Clement St., Mail Code 113A, San Francisco, CA 94121

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