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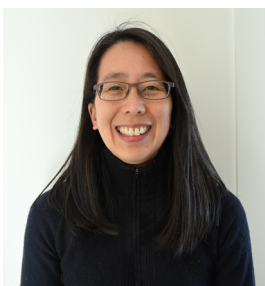
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AWARDS

VOLUME XVIII Spring 2023

Focus on Research

Team Aims to Correct Health Disparities by Including More Veterans in New Cancer Trials



Sunny Wang, MD
*Professor of Clinical Medicine in the
Division of Hematology and Oncology,
UCSF/SFVAHCS*
*Chief, Division of Hematology and
Oncology, SFVAHCS*

The battle against cancer has been long and sometimes arduous, but basic and clinical research over the years have spurred innovative therapies.

However, for some vulnerable populations, including Veterans, the disease and access to new treatments are complicated. Cancer is more prevalent among Veterans than in the general population (11.4 percent to 10 percent diagnoses, respectively, according to the Department of Veterans Affairs); and their cancers are often associated with radiation and chemical exposures during their years in service.

Many Veterans face barriers to receiving guideline-based cancer care due to complex comorbidities, including economic and social challenges. As a result they are underrepresented in clinical trials which further hampers the delivery of the newest and most effective life-improving therapies to Veterans.

NCIRE-supported researchers in the SFVAHCS Division of Hematology and Oncology aim to correct these inequities by increasing the number of clinical

trials for Veterans. “By including Veterans and a more diverse group of patients in the latest clinical trials, we will make discoveries that will directly benefit their health in the long-term,” said SFVAHCS Hematology and Oncology Service Chief Sunny Wang, MD, who is also a UCSF Professor of Clinical Medicine.

“Research and evidence-base medicine are integral to achieving the highest standards of care,” said Wang whose own research focuses on barriers to lung cancer screening, diagnosis and treatment, particularly for older patients. “We will assess novel treatments, so we can push to the forefront more effective and less toxic treatments for our Veterans, and patients in general.”

But the Division’s research is much more than evaluating new drugs or the latest diagnosis technology. From genomics to outcomes analysis, the research team applies a wide range of expertise to focus in on the best treatments for their cancer patients.

Precision oncology

Veterans suffer a higher rate of lung cancer and lower rate of survival than the general population.

Precision oncology, which uses patients’ unique genetic profiles from their tumors to tailor individualized treatments, may be a key to thwarting difficult cancers. Wang is Project Director of the SFVAHCS hub site for the National VA Lung Precision Oncology Program (LPOP). The San Francisco hub coordinates with the

Fresno, Sacramento, and Reno VAs, offering lung cancer screening for high-risk Veterans and genetic testing for those with advanced lung cancer. But a key objective is connecting Veterans in these regions to clinical trials and innovative treatment options.

Franklin Huang, MD, PhD

Associate Professor, Department of Medicine, Department of Urology, Helen Diller Family Comprehensive Cancer Center, UCSF

Principal Investigator, SFVAHCS/ UCSF Precision Oncology Center of Excellence

Investigator, Chan Zuckerberg Biohub, UCSF



Staff Physician, SFVAHCS

Similarly, for prostate cancer—the most diagnosed cancer among Veterans—Franklin Huang, MD, PhD, is the Principal Investigator of the Prostate Cancer Foundation (PCF) Precision Oncology Center of Excellence at the SFVAHCS and UCSF. The public-private collaboration also aims to deliver the best precision oncology treatments to Veterans.

A Clinician-Scientist, Huang is also studying why African American men have the highest risk of prostate cancer in the U.S. and are twice as likely to die of the disease than white men. In laboratory studies, Huang has found that some gene mutations may cause a tumor to grow more aggressively, metastasize, or respond to different treatments. He has also observed that prostate cancer cells in African American men may acquire a different spectrum of mutations than similar cells in white American men. “These genetic differences may help explain why the disease affects the two populations differently,” Huang says.

He hopes his lab studies will inform clinicians how to better match patients with the most effective treatments.

Listening to our elders

Biology is just one piece of the cancer puzzle, and hematology and oncology researchers encourage a whole health approach that supports patients’ well-being and is aligned with their goals.

“A cancer diagnosis, and often the ensuing cancer treatment, affects every part of a patient including the physical, social, emotional, and spiritual aspects,” said Carling Ursem, MD, a Principal Investigator with the SFVAHCS Hematology and Oncology research team. “A cancer diagnosis and treatment are often

layered on top of many other medical comorbidities and treatments. For our cancer care to be effective, we need to also be equipped to address all of these aspects through our multidisciplinary team.”

“An important study that we currently have open is ‘Lung Cancer in Older Adults: Treatment Toxicity Through the Patient’s Lens’ (conducted with UCSF collaborator Melisa Wong, MD),” said Ursem. “This study uses patient questionnaires and geriatric assessments to try to understand the experience of patients age 65+ receiving lung cancer treatment and specifically the impact of treatment on their functional status.”

Li-Wen Huang, MD, Principal Investigator with the Hematology and Oncology research team, is also passionate about improving care for older patients with cancer. Her research focuses on understanding the interactions between cancer, cancer therapy, and geriatric syndromes such as cognitive impairment. Her ultimate goal is to improve the care of older adults with cancer and cognitive impairment.



Li-Wen Huang, MD

Assistant Clinical Professor, Hematology and Oncology, UCSF/SFVAHCS

Staff Physician, SFVAHCS

Rooting for the underdog

A deep-rooted passion for their VA patients—and a penchant for fighting for vulnerable populations—drives this research and care team.

Sunny Wang, who has spent the large part of her career at the SFVAHCS, has developed an affinity for Veterans and is motivated “to give back to those who served our country so bravely.”

Besides his research and clinical titles, Franklin Huang is co-founder of Global Oncology, a non-profit working to improve cancer care for underserved patients around the world.

Carling Ursem noted that her grandfather is a Veteran who received excellent care at the Cincinnati VA. “His experience motivated me to pursue a career at the VA; therefore, starting my time here already with an appreciation of our nation’s Veterans and a strong desire to provide them with the highest quality cancer care.”



Carling Ursem, MD
*Assistant Professor,
 School of Medicine, UCSF/SFVAHCS
 Staff Physician, SFVAHCS*

Ursem also recalls her time during medical school when she rotated at an Indian Health Services site. “It was in a very rural location and the majority of the patients we served had very limited resources,” she said. “At a time when I was learning about all of the

advances in medicine it was quickly clear that these advances were of little value if they didn’t get to the patients who needed them most.”

“We have worked on building a strong community with our patients in our clinics, building relationships based on trust and empathy,” said Wang. “By listening to our patients, we have also tried to develop research projects that focus on our patients’ specific needs and addressing gaps in care,” she said. “I think we have been able to achieve significant diversity in our trials enrollment at our center which I hope will be highly impactful to improving health care for all our patients.”

NCIRE Award Spotlight

In this new section we celebrate the award-winning achievements of our supported Researchers

Kristine Yaffe, MD winner of the 2022 John B. Barnwell Award

Leadership and commitment to Alzheimer’s and dementia care and research

Over the course of her more than two-decade research and clinical career, Kristine Yaffe, MD, has become an internationally recognized and highly influential expert in the epidemiology of dementia and cognitive aging.

Among her prestigious honors in recent years: election to the National Academy of Medicine, the American Academy of Neurology’s Potamkin Prize for Alzheimer’s Research (often called the “Nobel Prize of Alzheimer’s research”), the National Institutes of Health’s Robert S. Gordon, Jr. Lectureship Award, and the National Institute on Aging’s Leadership Award for Alzheimer’s Disease and Related Dementias Research (ADRD).



Kristine Yaffe, MD

*Scola Endowed Chair and Vice Chair, Department of Psychiatry, UCSF
 Professor of Psychiatry, Neurology, and Epidemiology, UCSF
 Director of the Center for Population Brain Health, UCSF
 Director of NeuroPsychiatry, SFVAHCS
 Director of the Memory Evaluation Clinic, SFVAHCS
 NCIRE Board Director*

And Yaffe’s most recent honor—the 2022 John B. Barnwell Award

from the VA’s Clinical Science Research and Development service, in recognition of her significant leadership in the field of Alzheimer’s disease and related dementias—is especially dear to her.

“As a clinician who has cared for Veterans for over 25 years, this is an immense honor,” said Yaffe, an NCIRE-supported scientist, and Board Director. “My clinical and scientific work with the VA has been very rewarding; so I’m thrilled to receive this honor, especially as the first female recipient of the Barnwell Award.”

National model, service and mentorship

“I started at the VA as a trainee and established the Memory Evaluation Clinic,” said Yaffe. “At the time, Veterans with cognitive problems may have been seen by different services and their

care was very fragmented. We really wanted to improve clinical services for these Veterans; and as a result, we formed a multidisciplinary team of neurologists, psychiatrists, geriatricians, neuropsychologists, nurses, and social workers to really provide more comprehensive care and address Veterans' multifaceted needs."

"Now, the Memory Evaluation Clinic serves as a model across the country," she said. "In caring for our patients early on in my training, there was also very little that we could tell them in terms of prevention. So, this has been the primary focus and driver of my research program."

"Her service and mentorship activities are also exceptional," said VA Chief Research and Development Officer Rachel B. Ramoni, DMD, ScD. "Her mentees have, in turn, become leaders in dementia research. She plays critical leadership and advisory roles at SFVAHCS. She is a major asset for the VA and the Veterans we serve."

Yaffe is the Principal Investigator on multiple grants from NIH, the U.S. Department of Defense, and several foundations, and delivered testimony as a subject expert to the U.S. Senate Special Committee on Aging. She served as co-chair of the National Academy of Medicine's Committee on Cognitive Aging, which assessed the public health dimensions of cognitive aging and released a report, "Cognitive Aging: Progress in Understanding and Opportunities for Action," in 2015, and was appointed to

the Governor's Task Force on Alzheimer's Prevention and Preparedness by Gavin Newsom in 2019.

Her work focuses on the identification of modifiable risk factors—including cardiovascular and metabolic risk factors, sleep disturbances, and traumatic brain injury—and the critical role they play not just in late life, but across the entire lifespan. Her research has also provided important insight into the pathways that increase dementia risk.

Yaffe is also the Principal Investigator for the UCSF Population-Based Research for Alzheimer's Innovation (Pop-BRAIN) Program, a multidisciplinary program that highlights new strategies for prevention, underscores the underpinnings for health disparities in risk of AD/DRD, and offers new insights to the life course etiology of AD/DRD. The program also fosters the careers of junior investigators from a variety of disciplines focused on population health for AD/DRD by providing mentoring, didactics, research design and biostatistics guidance, pilot funding, and career development activities across several departments at UCSF in a unified hub dedicated to population health.

Challenges ahead

Yaffe is not one to rest on her laurels; and she continues to take on new research or clinical challenges as they emerge. "Despite tremendous advances in brain science over the past two decades, there is still so much to learn," she said.

What are some of the current research challenges? "Drug development, definitely," said Yaffe. "Investigators are starting to make significant headway, but it's been decades of work."

"We also need more research with diverse and underrepresented communities," she said. "This is both a challenge and a major priority. So far much of the data from the field is based on fairly homogeneous populations, but we know that the burden of dementia is greater for certain racial/ethnic communities and for adults with lower socioeconomic status.

"Understanding the role of multimorbidities, especially among Veterans, has also been a challenge. Often relatively healthy participants are enrolled in research studies which, similarly, does not reflect the population at greatest risk," she said.

"We really need to increase our efforts in these areas if we want to have a significant impact on dementia prevention and care."

Yaffe is currently the Roy and Marie Scola Endowed Chair and a Professor of Psychiatry, Neurology, and Epidemiology at UCSF, as well the Department of Psychiatry and Behavioral Sciences' vice chair for the Weill Institute for Neurosciences. She is also the Director of Neuropsychiatry and Director of the Memory Evaluation Clinic at the San Francisco VA Health Care System and Director of the UCSF Center for Population Brain Health.

Judith Ford, PhD winner of the 2022 William S. Middleton Award

An inside look at schizophrenia

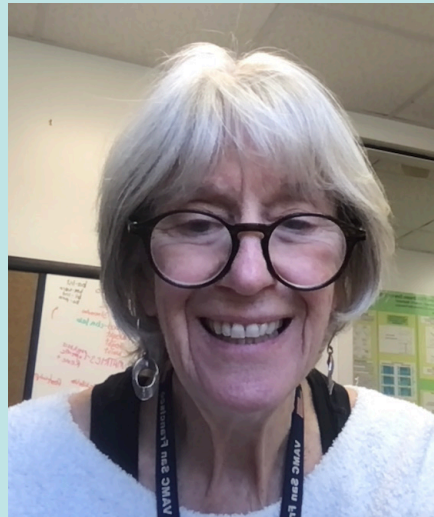
In the early 1970s, at the beginning of her illustrious psychiatry and neurosciences research career, Judith Ford, PhD, believed that schizophrenia was a “choice” and not a brain disease. She thought “studying the neurobiology of schizophrenia would be a fruitless effort.”

Ford was skeptical when her Stanford University Department of Psychiatry Laboratory Director at the time, Dr. Bert Kopell, claimed that their methods for studying patients were at the “interface of psychology and physiology” and a “window into the brain.”

But her mind changed. During her work in the mid-80s at the Palo Alto Veterans Affairs Hospital with Dr. Adolf Pfefferbaum, she found herself at the forefront of neuroimaging and electrophysiological research for neuropsychiatric disorders.

“Through exposure to Veteran patients themselves and to the biological data we were analyzing, I began to realize that people with schizophrenia have a serious brain disorder, reflected in neural signals missing or misfiring.”

Ford would go on to carve her own research niche, using electroencephalogram (EEG) and magnetic resonance imaging (MRI) to uncover underpinnings of key symptoms of a variety of psychiatric conditions, including schizophrenia. She has spent her entire 50-year research career



Judith Ford, PhD

Professor, Department of Psychiatry and Behavioral Sciences, UCSF
Senior Research Career Scientist, SFVAHCS

within the VA System—at the Palo Alto VA, the VA Connecticut Healthcare System as Director of the Schizophrenia Biological Research Center, and now as a Senior Research Career Scientist for the Mental Health Service at the San Francisco VA Health Care System (SFVAHCS).

Ford served as a faculty member at Stanford and Yale before she came to UCSF in 2007, where she is now a Professor in the Department of Psychiatry and Behavioral Sciences. Ford also co-directs the UCSF Brain Imaging and Electroencephalography Laboratory (based at the SFVAHCS) with her husband Daniel Mathalon, PhD, MD.

Honored for research by VA

Last fall, Ford was named a winner of the 2022 William S. Middleton Award by the U.S. Department of

Veterans Affairs. It’s the highest honor awarded annually by VA’s Biomedical Laboratory Research and Development Service to recognize outstanding scientific contributions and achievements in the areas of biomedical and behavioral research relevant to the health care of Veterans.

Ford was feted for her translational research in psychiatry, which has transformed the understanding of psychotic illnesses in Veterans. She is credited with explaining the basic neural mechanism that enables animals to distinguish between “self-generated” and “other-generated” sensations.

This finding facilitated groundbreaking research that found people with schizophrenia demonstrate altered responses to self-generated sensations like sound and speech, due to an inability to predict these sensations. Sensations that are not predicted may be attributed to external sources. In this way, thoughts may become audible. Her work has reassured patients and their families that their symptoms have a neurobiological basis.

“Dr. Ford’s research has provided fundamental insights into the pathophysiology of schizophrenia-spectrum disorders,” said VA Chief Research and Development Officer Rachel Ramoni, DMD, ScD. “She is a visionary scientist whose discoveries have assisted Veterans and others diagnosed with mental health disorders.”

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A complex brain disorder

Schizophrenia is a mysterious and serious disorder that is notoriously difficult to diagnose and treat because it manifests so differently in people. It's a chronic condition that affects how a person thinks, feels and behaves. People with schizophrenia often seem like they have lost touch with reality.

In the U.S., approximately 3.5 million, or 1.2 percent of the adult population is diagnosed with schizophrenia. Among Veterans, rates are much higher. In VA Medical Centers nationwide, up to 4 percent of Veterans have a diagnosis of schizophrenia, according to some U.S. estimates. With EEG and fMRI data from psychiatric patients, Ford has

used brain signals to understand how people hear voices when no one is talking, or auditory verbal hallucinations, cardinal symptoms of schizophrenia. "These signals are an 'early warning system' or a 'cc to self' that tell a person that the resulting sensations or thoughts are self-generated," said Ford. "This signal is reduced in patients with schizophrenia, suggesting that they may have abnormal sensory responses to the results of their own actions."

Among the goals of Ford and co-researchers at the Brain Imaging and Electroencephalography Laboratory (BIEGEL) are to identify biomarkers to predict who may be at risk for schizophrenia and to develop novel treatment

targets for early intervention.

Even with decades of successful research under her belt, Ford looks to expand studies. "(At BIEGEL), I continue to use brain imaging tools to ask questions about Long-COVID, the effects of a ketogenic diet on neural stability in people with psychosis, and the effects of mindfulness on responses to emotional stimuli in people with schizophrenia and depression," she said.

Ford flashed back to 1970. "When Bert Kopell told me that EEG methods were a window onto the brain, I laughed quietly to myself," she said. "Now I realize how prophetic and true that comment was."

In the Helix



Chantal Kloth
NCIRE Research Assistant II

Q: What brought you to NCIRE?

A: I was graduating from the University of Minnesota and was planning on spending 5 months in 2020 backpacking through Latin and South America, but unfortunately COVID had other plans for me. So I applied for jobs and accepted an offer in San Francisco. Now, 3 years later, with almost 1 year of working here in the lab, I'm very grateful to be here!



Spero Nicholas
NCIRE Programmer/Analyst

Q: What would your superpower be and why?

A: I can't decide if this means which of my abilities is most super, like maybe my unfortunate bottomless appetite for pizza, or what my fantasy superpower would be, which is being able to talk to animals. My family's two cats barely understand me at all.



Natalie Viola
NCIRE Administrative Analyst I

Q: If you could instantly become an expert in something, what would it be?

A: If I could instantly become an expert in something it would be cooking. My meals would be delicious every time. I'm not a bad cook! My skills are just "limited" and I'd want to expand them.

If you or someone you know is an NCIRE employee and would like to be featured in *In the Helix*, contact us at dna@ncire.org.

NCIRE Office of Sponsored Research Update

New Team Member – Adan Pinedo

We're excited to share with you, the newest member of NCIRE Office of Sponsored Research (OSR). Please help give a warm welcome to Adan Pinedo! In December 2022, Adan joined OSR as a Contracts & Grants Specialist III. He brings with him 15+ years of experience in contracts and research grants management. A few notable organizations he's been with are Fred Hutchinson Cancer Research Center, Seattle Children's Hospital, and most recently, Seattle Children's Research Institute.

New Federal Funding Awards

Congratulations to the following Principal Investigators for your recently funded awards!

Anne Richards, MD, MPH

Project Title: Using High-Density EEG to Identify Sleep-Dependent Cortical Replay of Laboratory Analog Trauma and Effects on Distressing Dreams and Intrusive Memories

Sponsor: Department of Defense (USAMRAA)

Activation Date: 3/1/2023

Michael Weiner, MD

Biomarker Evaluation in Young Onset Dementia from Diverse Communities (BEYONDD)

Sponsor: NIA via Subaward from UCSF

Activation Date: 3/20/2023

Robert Raffai, PhD

Project Title: Characterization of Beta-Cell-Specific Extracellular Vesicle Cargo as Functional Biomarkers for Type I DM Disease

Sponsor: NIDDK via Subaward from Massachusetts General Hospital Corporation

Activation Date: 5/4/2023

Funding Opportunities

Industry Opportunities

Please contact Newton Ong, newton.ong@ncire.org or at x23892, for further information on the following Industry Opportunities.

AN2 Therapeutics, Inc

A Phase 2/3, Randomized, Double-blind, Placebo-controlled, Multicenter, Prospective Study to Assess the Efficacy, Safety, and Pharmacokinetics of Orally Administered Epetaborole in Patients With Treatment-refractory Mycobacterium Avium Complex Lung Disease

Please visit this link for the full list of Industry Opportunities: <https://ncire.sharepoint.com/sites/crc/Industry%20Opportunities/CRC%20Opportunities.pdf>

Federal Funding Opportunities

Please contact Jessica Schmidt, jessica.schmidt@ncire.org or at x24514, for further information on the following Federal Funding Opportunities.

NIH: Research Supplements to Promote Diversity in Health-Related Research (Admin Supp - Clinical Trial Not Allowed)

<https://grants.nih.gov/grants/guide/pa-files/PA-18-586.html>

Please visit this link for the full list of Federal Funding Opportunities: <https://ncire.sharepoint.com/sites/grants/Shared%20Documents/Open%20Federal%20Funding%20Opportunities.pdf>

Message from the Chief Executive Officer

So far 2023 has brought a fair amount of heavy rain, flooding, and winds here in the Bay Area. With the inclement weather, we also had many rainbows. The balance of these two events is always a wonder to behold.

Thank you for the contributions to the Spring Newsletter from Sunny Wang, MD, Carling Ursem, MD, Kristine Yaffe, MD, and Judith Ford, PhD. It is serendipitous this edition features the research and accomplishments of this group, given March is a Celebration of Women.

In December 2022, Dr. Theodora Mauro concluded her term as Board Chair. We thank her for her leadership over the past few years. She will retain her role as a director on the Board. In January 2023, Dr. Michael Shlipak, Associate Chief of Medicine for Research Development at SFVAHCS, and Scientific Director, Kidney Health Research Collaborative and Professor of Medicine, Epidemiology & Biostatistics at UCSF, has assumed the role of NCIRE Board Chair.

The annual financial audit, which includes Federal Awards, was recently completed for the fiscal year 2022 (10/1/21-9/30/22). The audit report was issued with an unqualified opinion indicating a clean report. NCIRE demonstrated compliance with Uniform Guidance (2 C.F.R. Part 200): 2 C.F.R Part 200 establishes uniform administrative requirements, cost principles, and audit requirements for Federal awards to non-Federal entities.

The Nonprofit Program Office, which provides oversight and guidance for the VA-affiliated Nonprofit Research and Education Corporations, visited NCIRE for a triennial review 2/28/23-3/2/23. Their review provided positive feedback on our policies and processes and financial growth. In their review they also identified an issue with IPAs indicating that these agreements must be fully executed by all parties prior to the start of the agreement. We will be working collaboratively to improve the timeline.

Thank you for taking time to read our Spring 2023 Newsletter. Please let me know if you have any questions or comments.



Rebecca Rosales, MBA, CRA
Chief Executive Officer

About NCIRE

NCIRE - The Northern California Institute for Research and Education has one mission and one goal: Advancing Veterans Health. We sustain a scientific community of clinicians and researchers and support over 200 researchers who have joint faculty appointments at the University of California, San Francisco (UCSF) and the San Francisco VA Health Care System (SFVAHCS) and are working to foster innovation through leadership in the field of Veterans health research. Our broad portfolio of projects receives generous support from the National Institutes of Health, the Department of Defense, and individual donors, making us the largest nonprofit research institute devoted to Veterans health in the US.

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