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DETAILS

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NEWS

A

AWARDS

VOLUME XV Summer 2022

FOCUS on Research

Endocrine Research Gets Down to the Bone

When breakthrough research is announced or published, it is usually the laboratory experiments, innovative technology or novel treatments that are highlighted.

Rarely mentioned are the figurative bridges that connect information and stir ideas among the scientists with varied expertise. They assure the collaborations that are necessary to accelerate research from the laboratory to the clinic.

For NCIRE-supported scientists at the San Francisco Veterans Affairs Healthcare System's (SFVAHCS) Endocrine Research Unit, those invisible bridges are as much a part of the laboratory design as are the spaces for bench work, imaging equipment, and specimen storage.

In the Endocrine Research Unit at SFVAHCS's Mission Bay location, the scientists—many of whom have their own research niches and projects—share space and equipment and sometimes funding as Co-Principal Investigators. They hold weekly conferences to discuss their current studies of endocrine (hormone) systems, share data, and shape future research. "We've learned over the years that we work best when we work together," said Daniel Bikle, MD, PhD, a renowned scientist, and member of the SFVAHCS Endocrine Research Unit. "It's a non-insular environment that has strengthened both the basic science and clinical research efforts of the unit."

Keeping order in the body

Hormones are the chemical messengers that manage and affect many of our bodily processes, including metabolism, growth, and development. The endocrine system is tightly regulated to keep hormones and their effects at the right levels. When the system goes even slightly awry—disrupting



Members of the SFVAHCS Endocrine Research Unit, (L-R) Chialing Tu, PhD, Wenhan Chang, PhD, Dolores Shoback, MD, Tsui-Hua Chen, and Zhiqiang Cheng, MD, PhD.

the delicate balance of hormones in the body—the result can be an endocrine disorder or disease. And while University of California, San Francisco (UCSF) and SFVAHCS scientists study a wide range of conditions and diseases linked to hormones, the SFVAHCS Endocrine Research Unit is particularly prominent for exploring the hormonal regulation of calcium metabolism, bone development, and fracture repair.

Swift healing of fractures is important to Veterans, who are at risk of many illnesses affecting bone health, including diabetes, vascular diseases, and osteoporosis. The Endocrine Research Unit Laboratory Scientists have studied key mechanisms underlying the regulation of bone fracture repair in mice, and they collaborate with their clinical research colleagues to translate their discoveries into therapies for Veterans.

Key researchers in the unit include:

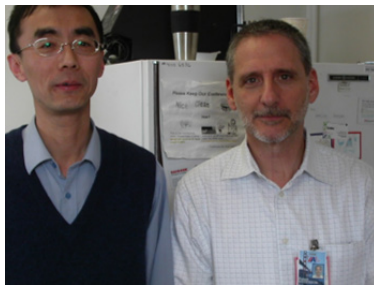
Daniel Bikle, MD, PhD, UCSF Professor of Medicine and Dermatology and SFVAHCS Staff Endocrinologist, who in five decades has published hundreds of research articles and received numerous honors for his bone and calcium



*Daniel Bikle, MD, PhD
Professor of Medicine
and Dermatology, UCSF
Staff Endocrinologist, SFVAHCS*

metabolism research. His laboratory has made landmark discoveries of the mechanisms by which parathyroid hormone (PTH) and insulin growth factor (IGF-1) regulate bone formation, the response of bone to mechanical loading and unloading, and the ability of an analog of PTH to heal fractures.

and Physiology and a Research Chemist at the SFVAHCS, studies “cell signaling”, the process of cellular communication driven by cells releasing and receiving hormones. He and colleagues are identifying new pathways to activate osteoblasts—the cells that make new bone—to more effectively treat osteoporosis and accelerate fracture repair. They have found that activation of one of these pathways will result in a massive increase in bone formation and in the size of bones.



Robert Nissenson, PhD (right), pictured here with Zhiqiang Cheng, MD, PhD, a member of the SFVAHCS Endocrine Research Unit.

Dolores Shoback, MD, UCSF Professor of Medicine and SFVAHCS Staff Physician, has uncovered secrets of the parathyroid glands, which produce PTH—a key player in the regulation of calcium levels in the blood. Naturally, calcium plays a critical role in bone formation and growth.

As a laboratory scientist, she has also made key discoveries

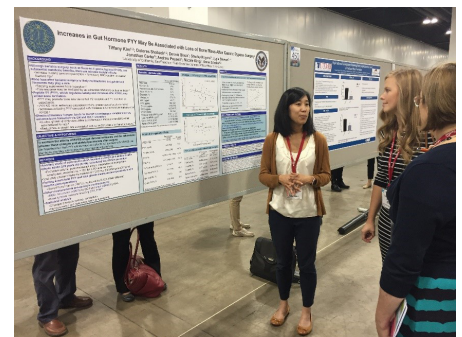


*Dolores Shoback, MD
Professor of Medicine, UCSF
Staff Physician, SFVAHCS*

about calcium-sensing receptors (CaSRs), molecules on the membranes of cells that painstakingly monitor the level of calcium in the blood and in bone microenvironment and communicate this information to the inside of cells. That information is critical as the body tries to control and balance the levels of calcium in the bloodstream. Too little calcium or too much PTH can deplete the bones of minerals and lead to osteoporosis. Too much calcium can be toxic to the functioning of countless body tissues. As a clinical researcher, she leads clinical trials of novel treatments developed from her laboratory work and that of her colleagues in the Endocrine Research Unit.

Wenhan Chang, PhD, UCSF Professor of Medicine and Director of the SFVAHCS Bone Imaging Core facility, also explores the role and impact of CaSRs on skeletal development and the capacity of bone cells to repair cartilage and bone after traumatic injuries. In the 1990s, he was a post-doctoral fellow mentored by Dolores Shoback, and later, he developed unique laboratory cultures to study parathyroid glands and cells. He also developed mice models to study parathyroid-related diseases. Chang now employs all these strategies to advance his independent research program, which is supported by a VA Biomedical Laboratory R&D Research Career Scientist Award.

Tiffany Kim, MD, UCSF Assistant Professor of Medicine and a SFVAHCS Staff Physician, focuses on osteoporosis and bone metabolism. She currently investigates the effects of improved glycemic control on bone marrow fat and skeletal health in people with Type 2 diabetes. With growing evidence that bone disease is a complication of Type 2 diabetes, the research has implications and potential benefits for Veterans.



Tiffany Kim, MD, presents a study co-published by the SFVAHCS Endocrine Research Unit at the annual meeting of the American Society for Bone and Mineral Research.

According to the Veterans Health Administration, nearly one in four Veterans (1.6 million individuals in the U.S.) receiving care at its health facilities has diabetes. For a study funded by a VA Career Development Award, Kim is enrolling and following some 75 Veterans with Type 2 diabetes to gain insight into the mechanisms of diabetic bone disease and potential preventive and therapeutic treatments.

Anne Schafer, MD, UCSF Associate Professor of Medicine and of Epidemiology and Biostatistics and Chief of Endocrinology

and Metabolism, at the SFVAHCS, is an endocrinologist focusing on bone metabolism and skeletal health. Schafer explores the relationship between bone, fat, and glucose metabolism, including the effects of obesity and diabetes on bone.



Anne Schafer, MD
Associate Professor of
Medicine and of Epidemiology and
Biostatistics, UCSF
Chief of Endocrinology and
Metabolism, SFVAHCS

Within this domain, she studies the effects of bariatric surgery for weight loss on calcium metabolism and bone health. While the surgery produces long-term weight loss, improves obesity-related comorbidities, and even improves survival, the operation has negative effects

on bones because it dramatically reduces the intestine's ability to absorb calcium. She has completed a clinical trial of a prebiotic intervention to improve calcium absorption after surgery. And she is currently conducting two studies: one to define the effects of sleeve gastrectomy—typically a laparoscopic procedure to remove a large part of the stomach—on intestinal calcium absorption, bone mineral density and bone structure; and the other is to test the effects of an osteoporosis drug on premenopausal women and older men undergoing bariatric surgery. While Type 1 diabetes is associated with lower bone mass and heightened fracture risk, the underlying reasons are not known, and that hampers prevention efforts. Schafer is also currently the Principal Investigator of a study to understand this skeletal fragility and identify strategies to mitigate fracture risk in adults with Type 1 diabetes and diabetic kidney disease.

Moving research from bench to bedside

Anne Schafer acknowledges that discoveries by her basic research colleagues of the inner workings of the parathyroid gland and its associated hormones and receptors have informed her clinical studies and those of her clinical researcher colleagues. A classic example of the successful bench to bedside research translation is a current clinical trial led by Dolores Shoback, to test a novel combination drug therapy for osteoporosis in men.

While osteoporosis primarily affects women, some two million men in the U.S. have osteoporosis, and 600,000 men suffer fractures annually due to their low bone mass. Osteoporosis is common and problematic for male Veterans. In addition to osteoporosis risk, Veterans also have other injuries, such as having a greater risk for vascular insufficiency, diabetes, gastrointestinal disorders, smoking and alcohol-related diseases—all of which can cause vitamin D and calcium deficiencies, which increase bone fracture

risks. Men are more at risk for the disease later in life than women; yet because of the misconception that osteoporosis is a “women’s disease”, “men are rarely tested for osteoporosis before fractures occur,” said Shoback. “The consequences of osteoporotic fractures are more severe in men than women. And hip fractures in men are particularly devastating. Mortality for a man with a hip fracture is nearly 38 percent in the first year after that fracture.”

Although there are several drugs to treat osteoporosis in women, few therapies have been studied in men. Shoback is testing a new combination drug regimen that has the potential to improve bone mass and structure in men. The regimen combines two drugs: an active fragment of parathyroid hormone and a drug that activates CaSRs in bone cells. These clinical trials draw on discovery by Shoback’s lab and her colleagues that found CaSRs and other cells play an important role in controlling bone formation and mineralization. And it was in the mouse models, developed in collaboration with Wenhan Chang, that the Endocrine Research Unit scientists figured out what calcium is doing to bone cells by removing CaSRs selectively from different types of bone cells.

Beyond bone

Bone development and fracture repair certainly are not the only targets of the Endocrine Research Unit’s basic and clinical research. Daniel Bikle’s lab examines the mechanisms by which calcium and vitamin D promote skin wound healing. Studies in mice are also applied to skin cancer development.

Dolores Shoback’s team is conducting a Phase 3 multicenter clinical trial of a new formulation of PTH for adults with hypoparathyroidism, a rare disease that causes deficiencies of calcium and phosphorus in the blood. Disease symptoms include muscular spasms and cramps, fatigue, and weakness. The majority of cases are due to neck surgery when parathyroid glands are injured or destroyed. Autoimmune diseases are the second most common cause.

Wenhan Chang’s lab uses his mice models to assess the role of CaSRs and other signaling molecules in the development of neuronal injury. The hope is to eventually develop new therapies for ischemia and traumatic brain injury.

With the collaborations built by the team at the SFVAHCS Endocrine Research Unit, researchers are working together in a synergistic way to bridge discoveries to clinical therapies that help our Veterans and ultimately the greater good of all.

Q and A: An Interview with Dr. Natalie Purcell



Natalie Purcell, PhD, MPA
Assistant Professor,
Social Behavioral Sciences, UCSF
Integrative Health Program Director, SFVAHCS

Q: How does one with a background in sociology and humanities wind up at the San Francisco Veterans Affairs Healthcare System (SFVAHCS), where most of your colleagues are research scientists and clinicians?

A: The San Francisco VA is the perfect place for a sociologist to be! I may be the only sociologist here right now, but every SFVAHCS research and clinical team I've had the opportunity to work with is interdisciplinary in the truest sense of the word. Here, the physicians, psychologists, nurses, health coaches, and many other professionals are accustomed to collaborating closely with team members who have very different training from their own and bring unique perspectives from their areas of expertise.

We're always learning from one another. It facilitates creativity and innovation, and it forces us to figure out how to communicate in ways that translate across disciplines. It

also keeps us humble because we're surrounded by experts in areas that we know very little about.

As for how I got here, I came to San Francisco VA right out of graduate school as a Presidential Management Fellow. My graduate work focused on the social psychology of violence and its relationship to trauma. I was really interested in joining the VA, in part because of the VA's Veterans Justice Outreach (VJO) program, in which VA clinicians work closely with courts, jails, and prisons to support Veterans involved in the criminal justice system and disrupt cycles of recidivism.

Working with this program turned out to be an amazing real-world application of my graduate training; and I was fortunate to have the opportunity to work with our local VJO program during my fellowship before eventually moving into my current role as a program director in integrative health.

Q: A large part of your research is focused on moral injury, particularly its effect on war Veterans who are impacted by violence and combat trauma. How did you become interested in this fascinating topic?

A: As a result of my work with Veterans in the VJO program, and my work in patient advocacy, I became very interested in the spiritual impact of war and

the possibility for integrative, community-based healing.

When we think primarily in terms of physical or mental illness, we can miss some important dimensions of trauma. An "illness" model locates the problems that Veterans experience after combat trauma primarily in their own bodies and minds. Yet a more expansive and integrative model invites us to also consider trauma as a social and spiritual affair, and to think of healing as a collective project that involves mind, body, soul, and community.

To me, the concept of "moral injury" opens these possibilities in ways that more established, medicalized concepts of illness don't always do. It focuses on spiritual trauma and goes to the very heart of what makes us interconnected human beings—our moral values and ethical obligations to one another.

Moral injury shows us how deeply we can suffer when we, or those we place our trust in, act in ways that violate our sense of what is good and just. Coming back from that requires a real reckoning with who we are and how we can reintegrate into a community that shares our values.

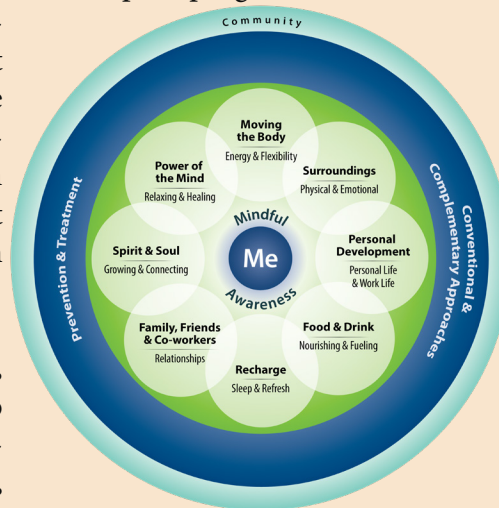
Q: But you don't just study the problem, you seek and test solutions. What are some promising approaches for those who have suffering or have been impacted by that kind of trauma?

A: I am especially excited about VA's "Whole Health" model of care, which is holistic and dedicated to bio-psycho-social-spiritual care in service of each Veteran's goals for their own health and well-being. A Whole Health approach is innately team-based and adds integrative options to conventional medical and mental health care. Often, these options involve mind-body approaches to healing that help Veterans learn and practice different techniques for self-healing—often in groups with other Veterans, or with the support of Veteran peers and Whole Health coaches.

In the Whole Health model, we recognize that there is no single solution or one-size-fits-all approach for any problem, including moral injury; so we offer a variety of different options—along with strong peer and community support—for building resilience and grappling with the impacts of trauma in our lives.

Some of those options include mindfulness-based stress reduction, yoga and other movement-based modalities, arts and humanities programs, and a wide variety of skill-building and support groups. These are not substitutes for conventional medical and mental health care, but are powerful when integrated with them.

I am proud to have been involved in San Francisco VA's Whole Health program, and to have played a part in founding and leading our local Integrative Health service line, alongside our Chief, Karen Seal, MD. Seal is also a researcher, so we work closely together to study the Whole Health and integrative health programs we've launched and to evaluate the impact they are having on Veterans' lives. This field is still young, but we are encouraged by what we are seeing in terms of improved wellness and reduced stress among participants in our pilot programs.



VA "Whole Health" model provided by the Veterans Health Administration Office of Patient Centered Care & Cultural Transformation.

Q: You have also developed a research interest in the well-being of health care employees and caregivers. How did that evolve?

A: These days, I think it's hard to work in a medical center without thinking about the well-being of health care workers. I've seen the incredible demands on our clinicians and other frontline workers over the course of the pandemic. The psychological

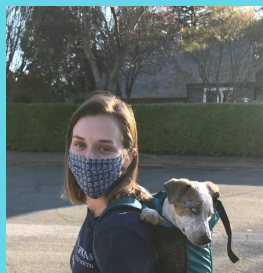
toll on them is increasingly well-documented; and it is not an understatement to say that many frontline workers have experienced real trauma.

Thankfully, I think the VA recognizes this and is stepping up in important ways to support workers. This is integral to the Whole Health model—the recognition that you cannot provide optimal care to Veterans if you are not also cared for. One of my current research studies, funded by the National Institutes for Occupational Safety and Health, examines moral injury and post-traumatic stress among frontline healthcare workers at VA medical centers across the country. We plan to use our findings to develop a blueprint for moral injury awareness, prevention, and mitigation, which we will share with VA healthcare leaders and administrators.

Q: What would most people be surprised to know about you?

A: Growing up, I became a big fan of metal music and even turned an undergraduate research project into a book on the topic. Music has been an important part of my life and I think that's part of what brought me to the world of integrative health. It showed me that music and the arts can have incredible healing power, especially when embedded in an engaged community. And metal fans are definitely a community!

In the Helix



Laura Muratore
NCIRE Staff Research Associate III

Q: What's the best piece of advice you've ever been given?

A: The best advice I've been given is "Follow what brings you joy!"

Q: What qualities do you value in the people with whom you spend time?

A: I value authenticity in others. It makes me happy to be around people who are living their authentic, true selves.

Q: If you could eat only one meal for the rest of your life, what would it be?

A: Cookies. I would truly just eat cookies for the rest of my life (barring any health repercussions).



Johanna (Jo) Madjus
NCIRE Office Manager/Executive Assistant to
Diana Truran-Sacrey

Q: What's the best piece of advice you've ever been given?

A: The best piece of advice I've ever been given is "Always do your absolute best at everything you do."

Q: What qualities do you value in the people with whom you spend time?

A: The qualities that I value the most in people are kindness, a sense of humor, and a sense of adventure!

Q: If you could eat only one meal for the rest of your life, what would it be?

A: If I had to eat only one meal for the rest of my life, it would definitely be Detroit style pizza, Caesar salad, and water.

Department Updates

IRS increases mileage rate for remainder of 2022

The Internal Revenue Service (IRS) has announced an increase in the optional standard mileage rate for the final 6 months of 2022. Taxpayers may use the optional standard mileage rates to calculate the deductible costs of operating an automobile for business and certain other purposes. For the final 6 months of 2022, the standard mileage rate for business travel will be 62.5 cents per mile, up 4 cents from the rate effective at the start of the year. The new rate for deductible medical or moving expenses (available for active-duty members of the military) will be 22 cents for the remainder of 2022, up 4 cents from the rate effective at the start of 2022. These new rates become effective July 1, 2022. The IRS provided legal guidance on the new rates in Announcement 2022-13, issued on June 9, 2022. In recognition of recent gasoline price increases, the IRS made this special adjustment for the final months of 2022. The IRS normally updates the mileage rates once a year in the fall for the next calendar year. For travel from Jan. 1 through June 30, 2022, taxpayers should use the rates set forth in Notice 2022-03. Midyear increases in the optional mileage rates are rare, the last time the IRS made such an increase was in 2011. For more information visit the IRS.gov Newsroom Page: <https://www.irs.gov/newsroom/irs-increases-mileage-rate-for-remainder-of-2022>

Purpose	Rates Jan 1, 2022 - June 30, 2022	Rates July 1, 2022 - Dec 31, 2022
Business	58.5	62.5
Medical/Moving	18	22
Charitable	14	14

Finance Department Updates

NCIRE Promotions

- As of July 1, 2022, Controller **Joanna Zhao, MBA** has been promoted to Chief Financial Officer. Joanna has been with NCIRE since 1998. Joanna also serves as the Secretary and Treasurer to the NCIRE Board of Directors.
- Linda Huang** also received a promotion on July 1st from Accounts Payable Specialist to Accountant.
- As of March 28th, **Julia Yu**, who has been with NCIRE for eight years, was promoted from Accounts Payable Specialist to Sr. Accounts Payable Specialist.

Congratulations on your recent achievements!

New Personnel Funding Change Form

- The NCIRE Finance Department has updated its Personnel Funding Change form.
- The form is available on the NCIRE Intranet SharePoint, in Accounting under the Payroll section or [here](#).

2022 NCIRE Employee Survey Results

**YOUR
VOICE
MATTERS**

NCIRE staff members shared their voices in our annual survey, conducted from April 15 – May 27, 2022. This survey continued efforts started in 2021 to gather feedback in a consistent and confidential way to identify what we are doing well, and where we can invest in the future of our staff.

Please visit [Employee Engagement Survey Results](#) for a full summary.

**Thank you to all staff for participating in our annual survey.
Your voice matters in achieving our goal to be
an amazing and diverse place to work!**

Year to Year Comparison

Question	2021	2022
Do you feel that NCIRE cares about your health and safety?	53%	56%
My experiences at NCIRE have led me to become more understanding of differences among my coworkers.	44%	54%
I understand how my work impacts the organization's business goals.	49%	51%
My Principal Investigator or manager gives me opportunities to develop and grow.	44%	48%
Management shows that diversity is important through his actions.	36%	48%
Benefits are an important reason why I remain here.	36%	44%
I am satisfied with the culture of my workplace.	38%	41%

Ranking of Benefits

Ranking	Benefit	Percentage
1	Paid Holiday	88%
2	Vacation Pay	88%
3	Sick Pay	85%
4	Paid Personal Days	83%
5	Health Insurance	82%
6	Flexible Work Schedule	80%
7	Dental Insurance	79%
8	Telework/Work From Home	78%
9	403b Retirement Savings Plan	74%
10	Vision Insurance	73%

Highlights from Comments section:

"I really enjoy working for NCIRE, I feel valued and appreciated and I enjoy doing my job."

"I really appreciated NCIRE's decision to grant employees a floating holiday. I think that went a long way to acknowledge the various holidays celebrated by other cultures."

"More teambuilding and encouraging employees to bring their whole selves to work."

Survey Participation

47% RESPONSE RATE

Out of 230 employees surveyed 108 responded.

Compared to 38% in 2021

Message from the Chief Executive Officer

Sunshine and summer days are upon us. I hope you enjoy the Summer 2022 edition of the NCIRE Newsletter. Thank you to all the contributors: Drs. Anne Schafer, Daniel Bikle, and Dolores Shobak of the SFVAHCS Endocrine Research Unit, and Dr. Natalie Purcell. Their willingness to share their research and provide their time is much appreciated.

June is usually the month in which there are the most grant submissions each year. I am pleased to share that in June 2022, there were 16 grant application submissions. For reference, the same number of applications were submitted in June 2021.

In April, the NCIRE Board of Directors supported the relocation of the NCIRE Core Office staff to Buildings 210 and 3. This move ensures NCIRE will remain on campus to support the research community. Starting June 15th, NCIRE will begin relocating from Building 14 and will continue the staggered move over the summer.

In May, NCIRE published its second annual PI Survey. The survey closed on May 31, 2022; the response rate was 28%. For comparison, the 2021 survey had 43% response rate.

The goal of the survey was to engage the Principal Investigator Community at SFVAHCS to garner feedback and comments on NCIRE's role in supporting and facilitating research.

NCIRE is efficient at expediting my requests.

- 47% of respondents strongly agreed
- 39% of respondents agreed

NCIRE provides appropriate staff support.

- 39% of respondents strongly agreed
- 42% of respondents agreed

Overall, I am satisfied with NCIRE as my grant administrator.

- 45% of respondents strongly agreed
- 45% of respondents agreed
- 8% of respondents disagree

Over the next year we will work to continue to provide consistent grant and administrative staff support and to provide financial projections for all research projects. A goal for next year will be to increase survey participation to at least 50%.



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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Please send comments to dna@ncire.org