

CTSC@connections

Building research teams of the future to improve human health • 2017 • Volume 7, Issue 1

PROGRAM PROFILE

CTSC KL2 Program – A path to independence

THE CTSC KL2 PROGRAM offers a research training experience to help junior faculty members become independent investigators. Funded by the National Institutes of Health (NIH) with support from the UC Davis School of Medicine Dean’s Office, the program offers up to three years of mentorship and protected time to conduct multidisciplinary, patient-oriented clinical research.

The KL2 program encourages applicable coursework, offers access to workshops, and provides a variety of resources to help scholars learn the complexities of conducting research and obtaining future grants. Beyond the training they receive as researchers, the program aims to help participants

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CTSC KL2 SCHOLARS

24 alumni
+6 current
30 scholars

JANUARY, 2017

Grant Productivity

20 NIH grants have been earned by 14 scholars:

» **3 RO1s** » **2 R21s** » **9 K awards**
» **6 other NIH research awards**

PATENTS

3

Publication Productivity

CTSC KL2 Scholars
30

Total Scopus
1,325

Total Citations
25,771

Average H-Index
14

Total Scopus: Number of publications indexed in Scopus. **Total Citations:** Number of times the publications of the scholars have been cited. **H-Index:** Maximum number of papers (N) that have at least (N) citations. For example, a scholar with an H-index of 14 has published 14 papers, each of which has been cited in other papers at least 14 times.

DIRECTOR’S MESSAGE

Lars Berglund, M.D., Ph.D.

IN LATE 2006, UC DAVIS was honored to be among the first 12 institutions to receive a coveted NIH Clinical and



Lars Berglund, M.D., Ph.D.

Translational Science Award (CTSA), marking an important recognition of the rich, collaborative culture at UC Davis. During

the years that followed, the consortium of CTSA academic research institutions has expanded to 62, located in 30 states and the District of Columbia. The grant, renewed in 2011 and 2016, is now one year into its 3rd 5-year funding period.

Initially the CTSC served as an incubator of ideas and a catalyst for partnerships at UC Davis and beyond. Today, the UC Davis CTSC offers a robust toolbox of resources that faculty, trainees and staff across the scientific

and medical spectrum can use to enhance research and improve health and health-care delivery. Our mission is “building research teams of the future to improve human health.”

The CTSC generates and supports strong scientific projects,



Ted Wun, M.D.

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develop the skills to become leaders in the next generation of clinical and translational investigators and future mentors themselves.

A trail of success

Over the last 10 years, the KL2 program has trained 24 scholars in addition to the six who are currently enrolled. The program is successful, as evidenced by notable metrics. Former scholars continue to be actively engaged in clinical and translational research, and have been awarded 20 NIH grants (including

The KL2 program encourages applicable coursework, offers access to workshops, and provides a variety of resources to help scholars learn the complexities of conducting research and obtaining future grants.

three R01 awards, two R21 awards, and nine K awards), as well as prestigious foundation grants. Program scholars produced more than 1,300 Scopus-indexed publications with nearly 26,000 citations, and three patents. Past scholars have assumed various leadership roles, including NIH program officer, associate dean, and positions with professional societies, scientific advisory boards and state agencies.

“The KL2 program’s impressive record reflects the excellence of our scholars, as well as that of the mentors and the entire CTSC staff,” said James Holmes, co-director of the CTSC KL2 program and professor in the Department of Emergency Medicine. “I wish that this program had been available when I was a junior faculty member embarking on a career combining clinical medicine and research.”

Holmes added that the KL2 program and other research development awards are important for attracting high-quality junior faculty to UC Davis. The program has garnered a reputation

for nurturing new investigators and successfully leading them down the road to independence. The program is competitive, currently accepting only 2 new scholars annually – approximately 20-25% of those who apply. Holmes hopes that the program will be able to accommodate more scholars in the future.

Balancing life

The KL2 program protects 75 percent of scholars’ time for research activity. Even with dedicated research time, the pull of clinical work and research can be strong for scholars committed to caring for patients as well as investigating new ideas. There is, however, a tradeoff. Most participants must devote long hours, and this can conflict with family time and a social life. And the struggle for work-life balance is a continuing issue when scholars receive independent research funding. Thus, perfecting time management skills and prioritization become keys to success for scholars seeking a career in research.

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DIRECTOR’S MESSAGE *continued from page 1*

a well-developed cadre of translational trainees, and community partnerships serving a broad range of investigators and research projects. Firmly embedded in the institutional framework, the CTSC serves as an honest and resourceful broker and efficient catalyst, collaborating with schools and colleges engaged in life science and translational research. During our decade-long existence, we have become an agent of change focusing on translational research and bringing value through a robust workforce development program, process facilitation and streamlining, and key shared functions such as informatics,

biostatistics, and regulatory assistance.

I am extremely proud of the CTSC and believe strongly in its value, mission, and capability. I also recognize the contributions of staff and faculty leaders to the program. These efforts underscore one of my proudest achievements – a superb team that will ensure continued success of the CTSC. This support becomes even more important, since with increased responsibility as interim dean for the School of Medicine, I now find it necessary to relinquish my role as PI. My colleague, Ted Wun, M.D., has agreed to accept the role and continue the legacy.

Dr. Wun is a professor of medicine, division chief, and the associate dean of research at the UC Davis School of Medicine. I have had the extreme pleasure of working with Dr. Wun since the 1st CTSA grant and consider him to be a most suitable candidate to assume the role of PI for the CTSC. Dr. Wun has been a strong partner in research and excellent co-collaborator over the last 11 years, assuming various roles as best fit the need throughout our history. I believe he will drive the CTSC toward continued success with the mission of building research teams of the future to improve human health. §

CTSC KL2 Program Principal Investigator

AFTER SERVING SEVERAL YEARS in a program leadership role, Jim Holmes, M.D., M.P.H., became the principal investigator on the most recent CTSC KL2 grant awarded in July 2016. The KL2 is an NIH-



supported training program for junior faculty who wish to incorporate research into their medical career. As a researcher himself, Holmes reminds his mentees that although research is not easy, it is rewarding. He believes the biggest keys to success are 1) finding a good mentor, 2) making time to get appropriate training,

and 3) conducting the preliminary studies. Holmes emphasizes not only the importance of mentoring, but also finding a mentor who has performed research and is willing to focus on success of the mentee. He believes he benefited from great mentorship and reminds his mentees that research is a long-term commitment requiring dedication – not something “done on the side.”

As a physician with an emphasis on pediatric trauma, Holmes focuses his research on appropriate resource utilization, particularly identifying criteria that indicate the need for a specific diagnostic test or admission to the hospital. His interest in research began with a longstanding sense of curiosity and the desire to find answers. Combining this inquisitiveness with his role as a physician in the emergency department keeps him engaged in delivering the best care possible to his patients.

After leading several large observational studies, getting his first federal grant was a major source of pride. He still enjoys the data analysis through which he can see how all the hard work leads to study results that have an impact on health care.

On a personal level, Jim has a long history as a triathlete. Although raising a family cuts into this endeavor, someday he hopes to return to the physical challenges offered by training and competition. Also an avid birder, he is a world traveler who enjoys watching and recording avian species in their natural environments. He has further combined these interests with medicine and served as ship's doctor on multiple expedition trips, travelling not only across both the Pacific and Atlantic Oceans, but also to Antarctica. Notably, he has visited all seven continents. §

CTSC KL2 Program *Continued from page 2*

“Successfully obtaining awards that lead to a large volume of work and commitments is a good problem to have,” laughed Holmes. “But seriously, balancing an abundance of riches takes effort, and CTSC staff members are available to help in whatever way they can.”

An ongoing challenge

Fred Meyers, UC Davis associate dean for precision medicine, serves with Holmes as co-director of the CTSC KL2 program and is a national thought leader in fostering the future scientific workforce. Instrumental in guiding a

national emphasis on support for junior investigators, Meyers noted that current funding for training is more robust than for independent research. With that in mind, he encourages junior faculty to take advantage of the opportunities available for training, and at the same time, urges more senior researchers to step up to provide the mentorship that is essential to a successful program.

Transitioning to the next step – to obtain independent funding – is always a challenge and a goal that KL2 scholars and their mentors must keep in mind. Stephen Henry, Jared Jagdeo, Oanh Meyer and Michael Schivo (all featured

in this issue) are just a few examples of former KL2 scholars who successfully procured NIH grants to pursue their own research.

“The researchers highlighted in this issue are a highly accomplished group, diverse in disciplinary excellence,” added Meyers, who is also a UC Davis professor of internal medicine/hematology-oncology. “The UC Davis KL2 program is clearly successful in developing the next generation of accomplished scientists who will make a big difference in clinical medicine.” §

Seeking solutions for chronic pain management

THE FIRST PATIENT that Stephen Henry saw when he started delivering clinical care 10 years ago was a man with a history of drug abuse seeking long-term opioid treatment for chronic chest pain.

“It was a difficult interaction,” recalled Henry, now assistant professor in the Division of General Medicine, Geriatrics and Bioethics. “I immediately had internal conflicts and doubts not generally felt with the average patient, including ‘Is he being honest?’”



Stephen Henry, M.D., M.Sc.

But over the next three years of caring for this individual, he now remembers the experience as one of his most rewarding in medicine. With careful and compassionate communication, Henry helped his patient quit smoking and put his life back together. “Without taking the time to look past the issues to the human being, the outcomes would not have been so favorable,” he added.

This experience sparked Henry’s research focus on patient-clinician communication about chronic pain management in the primary care setting. According to Henry, discussions between physicians and patients about chronic pain management are often contentious and unproductive. In preliminary research, he found that 41 percent of visits dealing with opioid management of chronic pain are rated as “difficult” by physicians, more than double the rate of other patient visits.

Mismatched goals

Henry received a UC Davis Clinical and Translational Science Center (CTSC) KL2 scholar award with the ultimate goal of identifying communication best-practices and then developing training for physicians dealing with chronic pain management. He started by video-recording clinic visits between primary care residents and patients taking opioids for chronic pain.

When analyzing the encounters, he realized that doctors and patients differed in their underlying goals. As a primary goal, patients typically want their pain alleviated, while doctors placed greater emphasis on improving function and reducing medication side effects.

Henry noted that the mismatch between physician and patient goals is intensified by recent state and federal guidelines published in response to the epidemic of opioid abuse and overdose to discourage focusing primarily on reducing pain intensity. California’s prescription drug monitoring program, known as CURES (Controlled Substance Utilization Review and Evaluation System) requires reporting of all controlled prescriptions. New state laws will soon mandate

that California physicians check a prescription database for controlled medications to ensure that individual patients are not “shopping around” for extra drugs.

The conflicts between patient, physician and government priorities create enormous challenges for physicians – who typically receive little training in establishing clear, shared treatment goals – when discussing pain treatment with patients, according to Henry.

Designing interventions

Henry’s KL2 research led to a 2-year (\$470,000) R21 grant awarded in 2016 and a 3-year (\$590,000) K23 award funded by the National Institute on Drug Abuse in 2017.

With the R21 grant, Henry is video-recording patients with chronic pain who successfully discontinued opioids or tapered down to a low dosage. The videos will form the basis for an innovative, story-based intervention targeted to primary-care patients to facilitate opioid tapering and discontinuance.

The aim of the K23 award is to design a clinician training intervention that will improve pain-related communication, pain management and opioid prescribing in primary care. Using trained actors to serve as standardized patients, the intervention will provide immediate feedback to doctors to enhance their skills and gain comfort in difficult situations. This approach was pioneered by Henry’s primary research mentor, Richard Kravitz, co-vice chair of research for the UC Davis Department of Internal

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Putting the red light on skin scarring

FLIPPING THROUGH A SKYMALL catalog on a long flight several years ago, Jared Jagdeo came across devices harnessing red light-emitting diodes (LEDs) to purportedly miraculous effect, from regrowing hair to making wrinkles disappear.

“Could any of this be true?” he wondered. This thought was quickly followed by another, “Could we use this in medicine?”

His ponderings provided him a focus for research, which last year led to a 4-year (\$775,000) K23 award from the National Institutes of Health (NIH) to study the effects of red LEDs on skin fibrosis.

Scars are not just cosmetic

Jagdeo, associate professor of dermatology at UC Davis, sees many patients with functional skin scars – fibrosis that thickens and constricts skin, causing disfigurement and hampering movement. In the autoimmune disease scleroderma, for example, patients develop such tight skin that their facial features change and they may be unable to open their mouth normally.

“Fibrosis – or skin scarring – is not merely a cosmetic issue,” Jagdeo

emphasized. “It can significantly impact quality of life.” He added that skin fibrosis is an important component in more than 75 conditions, including injury, burns and graft-versus-host disease.



Jared Jagdeo, M.D., M.S.

Current treatments for fibrotic scarring – including topical and injected corticosteroids, cryotherapy with liquid nitrogen, and radiation – tend to be expensive and involve undesirable side effects.

LEDs – common but unusual

LEDs are nearly ubiquitous in modern life – in our living room lamps, in our car headlights – replacing incandescent lights about as fast as ... well, the speed of light. Being cost-effective,

long-lasting and energy-efficient gives them an advantage over conventional lighting.

Their monochromatic quality – delivery of a narrow band of wavelength – provides the potential for therapeutic use. Incandescent lights emit a wide range of wavelengths and colors that cancel out to a colorless light, while LEDs can be manufactured to a nearly single wavelength that emits a very pure color. Each color LED may elicit a different effect on plant and animal tissues; certain wavelengths of light can cause mushrooms to manufacture vitamin D, for example, while others can help normalize a person's circadian rhythm.

In pursuit of answers

During laboratory research performed in collaboration with the UC Davis Clinical and Translational Science Center (CTSC) KL2 program, Jagdeo showed that red LEDs reduced two critical aspects of skin scarring: collagen production and skin cell proliferation. These processes, which cause accumulation of proteins under the skin, produce the thickness and rigidity of fibrotic scarring.

(Continued on page 8)

Chronic pain *from page 4*

Medicine. Henry credits Kravitz's support and mentorship as a key component of his early successes at UC Davis. “I cannot overstate how helpful it has been to work with a nationally-renowned mentor who shares my research interests and is also committed to my career success,” noted Henry.

Key to success: strategic thinking

With more than two dozen published papers and two current NIH grants, Henry attributes his success to remaining vigilant on his research career goals.

“Being given the option to participate in the CTSC KL2 program was an important factor for accepting a faculty position at UC Davis,” he said. Knowing he would have the opportunity to develop into an independent investigator gave him confidence. Henry also noted the importance of protected time to focus on his research.

He also credits James Holmes, director of the program, for providing the advice to consider the next steps when pursuing research grants. He added, “Jim taught me that in addition to doing day-to-day research, you must always think strategically about the future.” §

Reducing caregiver stress to enhance well-being

GROWING UP IN A LARGELY

monolingual Vietnamese-American community, Oanh Meyer saw firsthand the difficulties her community faced, particularly surrounding mental health issues. The fourth most numerous among Asian minorities in the U.S. (following Chinese, Asian Indian and Filipino), Vietnamese Americans tend to have low socioeconomic status and poor English proficiency – both risk factors for depression and other psychological illnesses. The older generation suffered severe trauma in the past, and many are unaware of mental health services available to them.

“I’ve been interested in mental health issues for a long time,” said Meyer, now assistant professor of neurology at UC Davis, “particularly in underserved populations that are usually the least able to access quality care.”

Helping caregivers give care

Meyer spent several years focusing her efforts on a subgroup of a minority population, one that received little attention from traditional sources – caregivers for elderly Vietnamese with Alzheimer’s disease. Meyer noted that they, along with other ethnic minorities, are more likely to turn to family members to assume the burden of caregiving. However, reliance on family members leads to caregivers who are less likely to be aware of available resources or access respite care.

“Alzheimer’s disease is a public health issue that affects everyone, but certain groups are more vulnerable to the stress that comes with it,” Meyer said. “Very little intervention work has focused on addressing caregiver needs in these populations.”



Oanh Meyer, Ph.D., M.A.S.

With an eye to conduct research addressing these needs, Meyer entered the UC Davis Mentored Clinical Research Training Program (MCRTTP), which then led to a CTSC KL2 scholar award. Meyer conducted multiple interviews with caregivers, gathering details about the challenges they faced, some of which are unique to the Vietnamese culture. “These programs allowed me to complete the formative work needed to obtain independent funding to initiate translational research,” said Meyer.

A focus on intervention

Meyer is now finishing her first year of a 4-year (\$515,460) K01 grant from the National Institute on Aging. She also obtained a 3-year (\$150,000) award from the Alzheimer’s Association. These funds will enable her to design and pilot test a community-based intervention targeting Vietnamese caregivers based on her earlier studies. While evidence-based dementia caregiving interventions already exist, cultural validity for the Vietnamese community has not been assessed.

Her 6-week intervention program is designed to reduce distress and enhance well-being in Vietnamese dementia caregivers and their care recipients. The premise is that a caregiver who is less stressed and can maintain his/her own well-being will be of greater benefit to patients. The program provides support, education and information on accessing resources. General stress management techniques are taught, such as breathing exercises, as well as culturally specific ones, such as Tai Chi. The intervention will be detailed in a manual for use by others and may be applicable to other Asian minorities, according to Meyer.

The program is a work in progress, and Meyer’s grants provide her the time to fine-tune her approach in order to maximize its utility. “We will be examining the feasibility, acceptability and effectiveness of the pilot intervention,” she stressed.

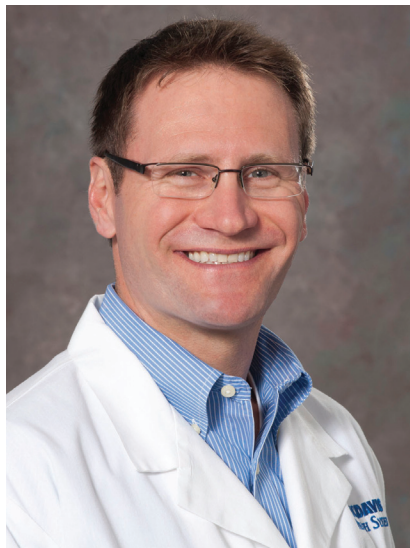
Mentor and peer support

Meyer is especially grateful for the structured mentoring she accessed in her training programs. “Being able to talk with mentors and CTSC leadership about my work and to seek advice was invaluable,” she said. “Because I was in these programs, I felt freer to ask for the help I needed.”

She also expressed appreciation for the opportunity for camaraderie with other junior researchers who were facing similar challenges. “Research can be isolating,” she emphasized. “To have peer support as we were developing into independent investigators was good for me, both personally and professionally.” §

Developing breath analysis for diagnostics

PATIENTS WITH CHRONIC OBSTRUCTIVE pulmonary disease (COPD) or asthma are evaluated frequently for exacerbation of symptoms. Do they have a mild cold virus or something more serious, such as influenza or a bacterial infection?



Michael Schivo, M.D., M.A.S.

Determining the cause of breathing issues is important for prescribing appropriate therapy promptly and avoiding the unnecessary use of antibiotics. To help with diagnosis, a variety of methods can provide clues. However, X-rays, blood tests and sputum sample analysis all involve a trip to the doctor and entail some risk or involve a time lag to learn results.

When UC Davis pulmonary medicine specialist and assistant professor of medicine Michael Schivo learned of an opportunity to develop a potentially new diagnostic paradigm using analysis of volatile organic compounds (VOCs) emitted in the breath, he jumped at it.

Schivo joined the UC Davis Mentored Clinical Research Training

Program (MCRTP) with Nicholas Kenyon, professor and division chief of pulmonary, critical care and sleep medicine, and Cristina Davis, professor of mechanical and aerospace engineering, as his research mentors. He later became a T32 Research Fellow in the pulmonary division, and went on to obtain KL2 funding from the CTSC to continue this line of research.

Unlocking the breath's secrets

Most people think of VOCs as fumes emanating from agricultural pesticides or smoke from automobile exhaust. But Schivo explained that VOCs – a generic term for carbon-containing compounds in vapors – are also released from the airway with every breath. Analysis of airway epithelial cells can detect specific interactions with viruses and bacteria, or the presence of cancer cells. Although Schivo is not researching cancer diagnostics, he noted that breath VOC analysis could also be developed for this purpose.

“We don’t know exactly what’s in the breath,” said Schivo. “It may offer a whole new way to understand biology and help us to better diagnose and even treat pulmonary diseases.”

Grant project launched

Last year, Schivo was awarded a 3-year (\$525,000) K23 grant from the National Heart, Lung and Blood Institute. With this funding, he will be able to further advance his investigations using airway epithelial cells obtained from bronchoscopies of patients with asthma, which are then grown in tissue culture and infected with influenza A and human rhinoviruses.

“We intend to develop the complexity of this unique model so that it closely mirrors how cells function in the body,” said Schivo. “This will open up this new field of research to others for a variety of applications.”

Schivo will also obtain breath samples from patients and test his diagnostic models against polymerase chain reaction (PCR)-based tests, currently regarded as the gold standard for diagnosis – but are too costly and slow for routine clinical use. Another exciting feature of this developing technology is the likelihood of portability for home use. Schivo anticipates the capability to link a phone adaptor so that data collected from the breath analysis can be sent to the doctor’s office for further assessment. “A breath VOC analysis device will be an invaluable tool for patients with chronic lung disease so that they can avoid a trip to the doctor’s office every time their symptoms worsen,” said Schivo. “It may also greatly speed up the time for patients to start the therapy they need.”

Collaboration is key

Schivo emphasized that his project relies on many extraordinarily talented people, including engineers, chemometricians, airway biologists, and clinicians. He also credited Jeffrey Elias, Director of the School of Medicine Grants Research Facilitation Unit and Betty Guo, Grants Coordination Officer, for very practical assistance in developing his grant applications. “They must have read my grant application 40 times,” Schivo recalled with a chuckle. “They were really invaluable in helping me translate the science into a readable and compelling story.” §

Skin scarring *continued from page 5*

This research led to several published papers and an NIH K23 award to bring his promising findings to Phase I and II clinical trials with a focus on reducing skin scarring following surgery. Red LED phototherapy is expected to offer similar advantages as conventional treatments, but without the risk of burning, harmful radiation or systemic side effects.

Assuming that the trials show the expected benefits, Jagdeo anticipates that applications of red LED therapy will be expanded to inhibit and treat scarring in patients with burns, other traumatic injuries and immune-mediated diseases. It may one day offer a portable, safe and inexpensive option to treating skin scars that may even be amenable to home application.

“Harnessing red-light LED offers a potentially paradigm-changing therapy

for skin scars caused by a huge variety of conditions,” said Jagdeo. “It may be a new frontier in dermatology treatment.”

An environment of support

Jagdeo credits the CTSC with his success by providing an environment to turn his curiosity during airplane travel into fruitful research. While funding was critical, he emphasized it was the support beyond that which made the biggest difference.

“UC Davis provides an amazing environment that focuses on incubating and nurturing young talent,” he added. “There is an incredible culture of support, from the cadre of caring leadership to the dedicated and committed people who run the CTSC. We look forward to translating research discoveries made as part of the CTSC KL2 program to benefiting the lives of patients with scars.” §



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