



UCSF Department of Medicine ZUCKERBERG SAN FRANCISCO GENERAL

EXCELLENCE IN COLLABORATION: COMBINING EXPERTISE TO ADVANCE HEALTH

Collaboration is essential to tackling the most challenging health problems in San Francisco and afar. This issue features two exemplary centers – led by ZSFG Department of Medicine faculty – which bring together teams of experts to tackle important health problems and address health disparities, both locally and globally.

EPPIcenter: Accelerating Understanding of the Dynamics of Infectious Disease Transmission

Infectious diseases such as malaria, Zika and COVID are incredibly complex, involving large populations, evolving pathogens, and the need to collect and analyze huge amounts of data. To accelerate discovery in the field, two faculty in the ZSFG Division of HIV, Infectious Diseases and Global Medicine established the Experimental and Population-based Pathogen Investigation Center (EPPIcenter) in 2019.



Isabel Rodriguez-Barraquer, MD, PhD

“Too often, infectious disease research is focused around individual labs, with silos of microbiologists, immunologists, mathematic modelers, and people in the field working independently,” said Isabel Rodriguez-Barraquer, MD, PhD, Assistant Professor and EPPIcenter co-founder and co-director. “A lot is lost, because each group is working with a narrow view of the process. It makes much more sense to work together with people with different areas of



Interactive activity illustrating bioinformatics concepts to research and public health personnel in a regional East Africa training session on malaria genomics in Uganda orchestrated by the EPPIcenter.

expertise who are trying to answer similar questions, but from different perspectives. We hope this center helps everyone move faster and more cohesively in the same direction.”

Bryan Greenhouse, MD, MA, Professor and EPPIcenter co-founder and co-director, agrees. “During my early career, I was interested in combining sophisticated data analysis with laboratory work, but had a hard time finding ways to get that training,” he said. “Everyone I met who did that kind of work got a PhD in one field, then got trained in another field as well. When I joined UCSF, I was fortunate enough to find two mentors – Phil Rosenthal, who does fieldwork and has a strong lab background, and Grant Dorsey, a really good epidemiologist. Even so, I still needed more train-

ing, so I went to UC Berkeley and got a master’s in biostatistics. Eventually, through lots of effort and different mentors, I was able to have a career that straddles and synthesizes both epidemiology and lab science.”

Dr. Greenhouse and Dr. Rodríguez-Barraquer are longtime collaborators with complementary areas of expertise. “We wanted to create something that was a combination of both our strengths, as well as to create a broader environment for trainees,” said Dr. Greenhouse. With support and encouragement from Diane Havlir, Chief of the ZSFG Division of HIV, Infectious Diseases and Global Medicine, and the ZSFG Department of Medicine, they launched the EPPIcenter in 2019.



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UCSF Department of Medicine



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Hospital and Trauma Center

EPPICenter

The center now has about 15 faculty, staff and trainees who bring together expertise in field epidemiology, data science, computational analysis, lab science and other related fields; they also have many partners both at UCSF and globally. “Our goal is have a place where we can work together across disciplines,” said Dr. Greenhouse. “We also want to create an immersive environment for trainees so they have mentorship from peers and senior researchers from a wide range of fields who can help them think creatively about problems.... It’s as if we were trying to compose a piece of music. Ideally, you’d bring the lyricist and composer together from the very beginning. It allows you to bounce ideas off each other in an environment that’s fun. That keeps motivation high and stimulates creativity.”

Developing Innovative Tools and Approaches

Because of its broad range of expertise, the EPPICenter can leverage emerging technologies



Bryan Greenhouse, MD

to develop new approaches for epidemiological research. For example, team members are developing novel assays to measure antibodies in blood samples. “Right now, with molecular technologies,

it’s possible to measure not just one antibody at a time, but multiple antibodies,” said Dr. Rodríguez-Barraquer. “But for these assays to be useful, we need to collect the right samples, test the assays to understand how they work, and use computational tools to make sense out of the big data.

We all have a common goal, but we’re working on different fronts to move this technology forward so we can better understand disease transmission and where to target interventions.”

The EPPICenter is also working on developing ways to glean new information from existing resources. For example, early in the COVID pandemic, they wanted to develop better ways to estimate the prevalence of exposure to SARS-CoV-2 in the general population. They were able to obtain blood samples left over from routine blood draws at UCSF Health and ZSFG, and tested them for COVID. “People always say, “This is a biased sample, and not truly representative of the population,” said Dr. Rodríguez-Barraquer.

To help mitigate that bias, the EPPICenter team used demographic data in the electronic medical record to select samples that more closely reflected the population of San Francisco. “Because residual samples are collected all the time, the volumes are much greater compared with going out [in the community] to collect a tiny number of samples,” said Dr. Rodríguez-Barraquer, noting that this approach could provide another tool for routine disease surveillance. The EPPICenter is now a coinvestigator with Kaiser Permanente Southern California on a recent multicenter grant funded by the Centers for Disease Control and Prevention. They are testing this approach for outbreak analytics and disease modeling, using residual sera from the very large Kaiser network.

Reducing Malaria Transmission, Improving Overall Health

A particular strength of the EPPICenter is malaria epidemiology. Another EPPICenter faculty member, Jessica Briggs, MD, MA, Assistant Professor in the ZSFG Division of HIV, Infectious Diseases

and Global Medicine, is leading research to better understand how malaria is transmitted from person to person, incorporating human antibody responses, malaria genetics and other elements to develop a statistical model of transmission. This could someday help to evaluate whether specific interventions are effective in reducing the transmission rate.

Both Dr. Rodríguez-Barraquer and Dr. Greenhouse are affiliated with the Chan Zuckerberg Biohub, giving them access to advanced technologies and expertise in genomics. For example, they are trying to understand how children develop immunity to malaria, which often occurs only after dozens of infections. In partnership with other groups, the EPPICenter is able to collect serial blood samples from the same children over many years, and to genetically sequence every malaria parasite in those blood samples, as well as how they relate to that child’s immune response and antibodies.

They are also using a systems immunology approach, employing a metagenomic approach to sequence all the pathogens in a blood smear or nasal swab. This includes not just malaria, but other diseases such as SARS-CoV-2, influenza, RSV and other infections. “Since we’re following these same kids over years, we can look at immune responses to these other infections to better understand how they might interact with one another or with malaria, and how the immune response changes in the same kid who has now had malaria, influenza, and other diseases,” said Dr. Greenhouse. “We’re very fortunate to have access to these great resources where we can follow these kids in detail over time, collect different types of samples, and work with brilliant people who can analyze the data and put it all together.”



Andres Aranda-Diaz from EPPICenter training some scientists in Uganda on sequencing.

“In settings such as sub-Saharan Africa, the burden of malaria, HIV and TB are so high that unfortunately, every other disease gets neglected,” said Dr. Rodríguez-Barraquer. “This type of study is nice, because it provides information on what else might be there that may have been ignored until now.” The goal is ultimately not just to reduce the burden of malaria, but to increase population health overall. “Eventually it would be ideal if we could come up with strategies to tackle more than one disease at a time,” she said. “We’re not there yet, but we’re trying to think more integrally”

Building Skills at Home and Abroad

In addition to conducting cutting-edge research at the intersection of multiple disciplines, the EPPICenter is committed to growing the next generation of infectious disease researchers. “Training is at the core of our mission,” said Dr. Rodríguez-Barraquer. “We have training opportunities at all stages, including post-baccalaureates, PhD students, postdoctoral scholars, and clinical fellows. We’re always looking for people who want to join us.”

For example, one center alum had expertise in mathematical modeling and data analysis, but was

excited to learn about laboratory science. “She didn’t do the lab work herself, but was sitting next to and embedded with people who were, so she understood it more fully and helped design studies,” said Dr. Greenhouse. “She helped us write a few grants, and we started doing a number of additional types of research that wouldn’t have been possible if we hadn’t all been nestled together, sharing ideas. She’s now a very successful faculty member at Johns Hopkins, and we still collaborate closely.”

Another lab alum was a microbiologist who learned about data science, genomics and bioinformatics through the EPPICenter. “He synthesized all these skills, and now in his work as a full-time professional researcher, he is both developing tools and making them accessible to people in low- and middle-income countries,” said Dr. Greenhouse. “He is running workshops in multiple countries in Africa, and expanding access to these techniques beyond the EPPICenter, which is one of our main goals.”

This focus on training and capacity-building aims to make the latest tools available to colleagues worldwide. The EPPICenter posts free software tools and extensive documentation on how to use them on its website, and works with partners globally to teach them how to incorporate these technologies into their work.

They have also built training courses on malaria genomics, presenting them both in person and virtually. With funding from the Bill and Melinda Gates Foundation, they are now developing a free online training course on this topic. “The best part is that it’s not just a series of lectures, but incorporates interactive activities,” said Dr. Greenhouse. “By mid-2024, we hope to go live with eight modules covering everything from the basics of epidemiology to data analysis, bioinformatics and sequencing techniques. It will be recorded in four languages, and include many of our colleagues so

it won’t just be voices from the Global North. It’s been fun to see how we can translate this material to the broader community – not just researchers, but public health professionals.”

The EPPICenter also hosts a monthly seminar series, which features researchers who are leading novel investigations in infectious disease and provides a forum for networking and discussing topics of mutual interest.

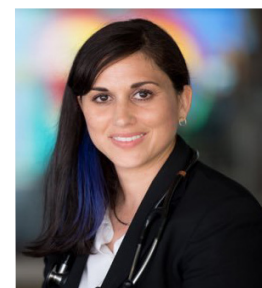
“We’re trying to tackle questions relevant to infectious disease from an interdisciplinary perspective, so we can come up with solutions faster and in a more creative manner,” said Dr. Rodríguez-Barraquer. “We really want to generate a space for trainees so they can get a more holistic training with exposure to different pieces of the puzzle. We’re very excited to be part of the General, and growing.”

“UCSF is a place where collaborations are encouraged,” said Dr. Greenhouse. “Creating an interdisciplinary center fit in with the ethos here. In the next five years, I look forward to being even more creative, answering scientific questions and producing resources of value for our colleagues.”

PRISE Center: Bringing Benefits of Medical Science to our Patients and Community

Too often, proven approaches that can improve health – such as COVID vaccines and cancer screenings – fail to reach the people who most need them. To help bring more scientific discoveries all the way to our patients and community, UCSF established the Partnerships for Research in Implementation Science for Health Equity (PRISE) Center in fall 2020.

“When bringing evidence-based interventions to safety net health care settings like the General, it is often difficult to implement them because of financial and resource constraints, as



Neeta Thakur, MD, MPH

well as the complex social aspects that many of our patients face, such as lack of housing or access to good nutrition,” said Neeta Thakur, MD, MPH, Associate Professor in the ZSFG Division of Pulmonary and Critical Care Medicine and co-director of the PRISE Center.

“We are focused on how to use methods to keep people from falling through the cracks, whether that’s in the health care setting or elsewhere,” said Margaret Handley, PhD, MPH, Professor in the Department of Epidemiology and Biostatistics and the ZSFG Division of General Internal Medicine and co-founder and co-director of the PRISE Center. “The emphasis is on adapting interventions to make them fit better for a particular community. We do that by listening, being attentive to barriers, and applying skills and approaches to translate evidence from one setting to another, in a way that improves health and quality of life.”

This field of study is known as implementation science, and the PRISE Center serves as a hub for



Margaret Handley, PhD, MPH

promoting these tools to improve health equity both locally and globally, whether it’s improving health of essential workers in San Francisco or reducing the burning of plastic in Guatemalan households. “We’re trying

to bring together a community of researchers and community members who are interested in doing this work together,” said Dr. Thakur. “People don’t need to be experts in implementation science – it’s just a tool which can support our effort to address health disparities and promote equity.”

The center does this by offering education and training, forging partnerships with community members and other stakeholders, and conducting



novel research in implementation science.

Practical Tools for Tailoring Interventions

Dr. Thakur and Dr. Handley hope to make the tools of implementation science more accessible to clinical teams so that evidence-based interventions can be more successfully adapted to specific patient populations. “Implementation science doesn’t have to involve a large, time-consuming research project,” said Dr. Handley. “It can be a phase, with an emphasis on digging deeper into components that involve humans, such as qualitative interviews to better understand why people might be hesitant to implement an intervention.”

For example, Dr. Handley and Lucía Abascal, MD, PhD, MS, now a postdoctoral fellow at UCSF, volunteered as contact tracers with the San Francisco Department of Public Health during the pandemic. Using tools of implementation science, they spoke with many monolingual Spanish-speaking essential workers, asking what might help or hinder them from sheltering in place, getting tested for COVID, isolating when sick, and eventually, getting vaccinated. “We were sampling a very vulnerable population which had some of the highest burden [of risk], but were also in positions to spread COVID while working,” said Dr. Handley.

Because of their implementation science expe-

rience, Spanish language skills and position as contact tracers affiliated with the San Francisco Department of Public Health (SFDPH), they were able to earn people’s trust and gently ask follow-up questions to get a deeper understanding of their situation. “When I asked how many people were in their household, they might say, ‘Four,’ but when I asked them how many rooms were in their house and then asked how many people lived in each room, eventually that number would go from four to 10,” said Dr. Handley. “I looked at the data, and knew many people lived in high-density households.

People would eventually tell me, ‘Yes, there are a lot of people living here, and it’s hard to isolate.’ We were able to feed all that information back to the Health Department.”

Knowing how to ask the right questions to identify barriers and enablers of implementing interventions can shape strategies to tailor an intervention for a certain population. “This was a nice way to add more contextual evaluation, and ended up getting modeled for contact tracing not just across the state but across the country,” said Dr. Thakur.

Another example was conducting focus groups in adult English as a Second Language classrooms about the best ways to encourage Spanish-speaking women who developed gestational diabetes to get screened for diabetes after giving birth. “A public health person might say, ‘You’re recommended to get screened,’ but after discussing these issues in the focus group, women wrote scripts that we used to make videos,” said Dr. Handley. “The scripts had one woman telling her friend, ‘I’m good, my baby’s good,’ and her friend telling her, ‘You know, it’s good to get screened for diabetes after you have your baby.’ It was a different conversation, because it came out of how people were living their lives and how they use language. We call it ‘re-storying’ – reframing in a way that reflects stakeholder perspectives.”



True Partnerships

This participatory approach is very different from traditional models, where experts develop an intervention in one study population, then expect other communities to enthusiastically adopt a one-size-fits-all model. Dr. Handley noted that in implementation science, people’s lived experience shapes the public health response. “This helps promote equity, because there is buy-in, truth, and more justice in developing programs and interventions,” she said.

“At its core, implementation science is about how an intervention works in a certain context,” said Dr. Thakur. “By default, you have to bring in community members and other stakeholders as co-designers, to identify levers for promoting successful implementation. That’s huge. There aren’t many scientific fields that value community perceptions as highly as implementation science does.” In addition to community members, stakeholders may include health system leaders, nursing administrators, patients and others. “Understanding the entirety of the context through careful listening and documenting inputs and outputs is essential,” she said.

“We do a lot of work on adapting interventions,” said Dr. Handley. That could range from a very light adaptation, such as providing health counseling by a peer instead of a clinic nurse. Other times it could involve more substantial changes. She helped adapt the Diabetes Prevention Program, a well-established, intensive intervention that requires many meetings and homework. “Vulnerable populations may not have that kind of time, so we and others have been making lighter versions, such as offering the program at a community site like the YMCA rather than a research study site, doing health coaching over the phone, and tailored callbacks and narrative recorded messages with recipes and social support,” she said.

Elevating People and Programs

UCSF has a deep bench of experts in implementation science, and the UCSF Department of Epidemiology and Biostatistics already offers robust training in this area co-designed by faculty in the ZSFG Department of Medicine, including

a two-day short course, certificate program, and degree programs.

The PRISE Center has developed additional opportunities to incorporate implementation science techniques into existing work. For example, they offer workshops on topics like how to successfully develop community-academic partnerships, a forum to get peer feedback on implementation science grant proposals, and networking “speed dating” events. The center also has a T32 training grant for postdoctoral scholars, pairing each one with a mentor who provides expertise on technical aspects of implementation science. Dr. Handley is a lead faculty member on the Research in Implementation Science for Equity (RISE) training program, funded by an NIH R25 grant and directed by Alicia Fernandez, MD, Professor in the ZSFG Division of General Internal Medicine. It helps underrepresented junior faculty across the country obtain K and R grants by cultivating implementation science research skills during summer institutes hosted by ZSFG’s Center for Vulnerable Populations.

The center is also building many partnerships, meeting with health systems leaders at ZSFG and the San Francisco Health Network to understand priority areas for incorporating implementation science approaches. They provided support to Delphine Tuot, MD, MAS, Associate Chief Medical Officer, Specialty Care and Diagnostics, to obtain grant funding from the Patient-Centered Outcomes Research Institute (PCORI) to support evaluation of implementation science projects. “Delphine led the effort, but we helped bolster the application process,” said Dr. Thakur. “It’s a great example of partnership-building.”

The PRISE Center also works closely with SDFPH. For example, they identified barriers and enablers to receiving COVID vaccines among high-risk San Franciscans, particularly Spanish-speakers, and uncovered ways to increase their capability, opportunity and motivation to get vaccinated. Dr. Thakur has received a PCORI grant to support her work with the San Francisco Department of the Environment and community groups serving neighborhoods disproportionately affected by climate change. Together they are identifying community members’ priorities for the best ways

to mitigate the effects of extreme heat and wildfire smoke.

The center is also collaborating with the California Department of Public Health on trainings. “Qualitative data can be really useful for contextualizing a situation or why an approach might not be working, but it takes time to use a theory-informed approach to analyze that data,” said Dr. Thakur. “We’re planning a workshop on a method called rapid ethnographic assessment, which helps quickly translate qualitative work into intervention design or implementation strategies.”

The center seeks to connect people across its affiliated networks with complementary areas of expertise. “There is so much innovative programming going on at the General, and we hope to partner leaders in the clinical space – who have contextual and content expertise – with experts in implementation science,” said Dr. Thakur. “One of our long-term goals is to help elevate these amazing projects, provide an evaluation framework, and talk about how these types of programs could be replicated in other settings.”

“Implementation science tools are user-friendly, and we want to support people applying them in a way that works for them,” said Dr. Handley.

Elizabeth Chur

Editors: Neil Powe, Laurae Pearson, Kevin Weil

SPOTLIGHT

Binh An Phan, MD, Division of Cardiology was awarded the Henry J. Kaiser Awards for Excellence in Teaching.

Congratulations to Neil Powe, MD, for receiving the AAMC’s Herbert W. Nicksen Award. This award is given to an individual who has made outstanding contributions to promoting justice in medical education and health care equity in the United States.

UCSF at ZSFG Faculty & Staff Appreciation Event will be held on November 29th, 11:30 am – 1:00 pm in UCSF Pride Hall – 1st Floor conference rooms 1930,1940,1950

Join the Fall 2023 StoryCore event on November 15th at 12:30 pm to learn about Keeping in Real – Real Staff, Real Journey’s, Real Stories. Register at https://ucsf.zoom.us/webinar/register/WN_mFZh-4ceZSEKsc72TKzr-kQ#registration

