Physician-scientists – individuals who devote most of their effort to seeking new knowledge about health and disease through research – play a unique and critical role in translating discoveries into new treatments that benefit patients. Drawing upon his or her mastery of both clinical practice and basic science research in parallel, the physician-scientist is positioned to make advances in the diagnosis, treatment, and prevention of human disease. A generation or two ago, a substantial number of faculty at institutions like UCSF were physician-scientists. Today, physician-scientists are almost an endangered species. Helping the next generation of physician-scientists to be successful will have a major impact on how fully the latest scientific breakthroughs can be applied towards improving human health.

DR. TREVER BIVONA

“As a physician-scientist, everything I do in the laboratory is fueled by the clinical experience,” says Trever Bivona, MD, PhD. Bivona is a medical oncologist who also earned a PhD in cell and molecular biology, and completed postdoctoral training...
Physician-Scientists at UCSF

The UCSF Department of Medicine excels in caring for patients, as well as discovering new treatments for the conditions that afflict them. This issue highlights a few of our outstanding physician-scientists who devote the majority of their effort to finding new knowledge about health and disease. They are intrigued by the underlying causes of diseases that they see in clinic, and passionately pursue these questions over the entire continuum of biomedical investigation – from basic laboratory research to translational and patient oriented research and their application to the health of the population. The explosion of new scientific tools makes this an exciting time to be a physician-scientist, with great potential for unprecedented levels of discovery.

Yet aspiring physician-scientists face many obstacles. Clinical training has become more demanding and logistically complex, and young people must devote a growing number of years to advanced scientific training. They also face a challenging fiscal climate. Budget cuts to the National Institutes of Health and other agencies make grant funding for training and research increasingly tight, while physician-scientists compete head-to-head against investigators whose sole focus is the lab. Today’s physician-scientists are juggling research, patient care and family responsibilities, and some choose to narrow their career focus to clinical care or research alone. For those who truly have the talent and desire to become physician-scientists, this is a great loss.

The UCSF Department of Medicine is developing innovative approaches to supporting promising physician-scientists during training and while they launch successful careers. Philanthropic support plays a key role in these efforts, fueling many endeavors that will ultimately improve treatments, cure illness, and perhaps even prevent some diseases from occurring in the future.

We are deeply grateful for all your support of physician-scientists in the UCSF Department of Medicine. We look forward to their many discoveries, which will help to transform health in the years to come.

Sincerely,

Talmadge E. King, Jr., MD
Chair, Department of Medicine
Julius R. Krevans Distinguished Professorship in Internal Medicine
Epidemic
End the AIDS
Beginning to
Dr. Diane Havlir
faculty profile

Think big, embrace debate, work as a team – these lessons have helped Diane Havlir, MD, become a visionary leader in the HIV/AIDS community.

Havlir (pronounced “HAVE-ler”), chief of the HIV/AIDS Division at San Francisco General Hospital (SFGH) since 2002, arrived at UCSF in 1984 as a resident. “As far as we knew, AIDS was a death sentence,” she says.

“Yet many of us were very inspired by the courage of the patients and the determination of the community. What has really propelled progress against the AIDS epidemic is teamwork – the collective effort of the community, the medical profession and industry.”

Her own research has helped define the most effective treatments for patients with HIV/AIDS in the U.S., and has pioneered novel strategies in Africa for patients with overlapping diagnoses of HIV, malaria and tuberculosis. In addition to overseeing the world-renowned HIV clinic in SFGH’s Ward 86, Havlir also established domestic and international training programs in state-of-the-art HIV medicine.

“Dr. Havlir is leading tremendously important research projects, but as impressive is her mentorship in developing research careers for young faculty members,” says Paul Volberding, MD, director of the AIDS Research Institute at UCSF. “She has played a crucial role in developing the next generation of amazing talent at a challenging time, helping them find a research focus and protecting them from the distractions that are otherwise so hard to resist.”

Pioneering New Approaches

“There is an unprecedented sense of optimism in the HIV/AIDS community,” says Havlir. “A key reason is that using HIV treatments to reduce the amount of HIV in a person’s body also helps limit HIV spread in a community. In 2010, we were the first clinic in the world to offer treatment to persons at all stages of HIV disease to keep them healthy, knowing that it also had the secondary benefit of reducing HIV transmission. Thus far, results are encouraging.”

Havlir and her team are now about to measure the impact that widespread HIV therapy can have to curtail the epidemic in Africa. In 2010, she established the Sustainable East Africa Research in Community Health (SEARCH) collaboration with the World Bank, the National Institutes of Health and the governments of Uganda and Kenya. “We wanted to measure the magnitude of health, economic and education benefits for the individual, community and country if we provided HIV treatment for all those who are infected,” says Havlir. “Our study tests the hypothesis that in a community where HIV treatment is started early, health is preserved, adults stay in the workforce, kids stay in school, and over the long term, health care costs are less.”

The SEARCH study began this spring, and will offer annual HIV testing in 32 communities of 10,000 persons each. Intervention communities offer treatment to all HIV infected persons. Participants also receive bed nets, deworming for children, and screening and treatment for malaria, hypertension and diabetes. “SEARCH takes HIV out of a silo,” says Havlir. “This helps destigmatize HIV disease, and elevates care for other chronic health conditions.

Communities are enthusiastically embracing this approach.”

Turning the Tide Together

Last July, Havlir served as the U.S. co-chair of the 19th International AIDS Conference, held in Washington, D.C. It was the first time the conference was held in the U.S. and followed President Obama’s lifting of the ban barring HIV+ people from entering the country. Nearly 24,000 people attended, and the theme was “Turning the Tide Together” – with an ambitious declaration co-authored by Havlir calling for an end to the AIDS epidemic.

A vital element of the conference was impassioned discussion on ending AIDS. “One of the strengths of the HIV community is that it embraces debate,” says Havlir. “By bringing varying viewpoints together, we have been able to develop consensus on important issues…. In HIV now, it’s all about the ‘how’: what is the best way to begin to end the AIDS epidemic?”

Havlir continues to teach and see patients, and is already beginning to catch glimpses of what a world without AIDS might look like. Recently, a 21-year-old patient called his HIV medicines his “old man pills.”

“I asked him, ‘What do you mean?’” recalls Havlir. “He said, ‘These pills are going to allow me to live to be an old man.’ That was a powerful moment. Our patients both inspire us, and make us think about new questions.”

“In 2010, we were the first clinic in the world to offer treatment to persons at all stages of HIV disease to keep them healthy, knowing that it also had the secondary benefit of reducing HIV transmission. Thus far, results are encouraging.”

— Diane Havlir, MD
Physician-Scientists: Translating Discoveries to Patients

Continued from front page

with UCSF alum Charles Sawyers, MD (see profile on p. 10). He is one of a number of physician-scientists in the Department of Medicine who have chosen this challenging career path. Bivona, who joined the faculty in 2011, spends Friday mornings caring for patients with lung cancer, and the rest of his time developing improved lung cancer treatments in his laboratory.

Lung cancer is the leading cause of cancer mortality worldwide. In the U.S., less than one in six people diagnosed with the disease will still be alive in five years. “Obviously, we have not been doing a very good job of effectively treating patients,” says Bivona. “But over the last 10 years, there has been a sea change in the way we understand the molecular roots of cancers.” Rather than lumping all lung cancers together, scientists are identifying a number of subtypes, each caused by a different combination of genetic mutations.

Instead of treating lung cancers with standard chemotherapy, which is usually ineffective and often produces terrible side effects, Bivona’s lab sequences the lung cancer genome of each clinic patient. His group then identifies mutations that are driving that patient’s cancer, and crafts a treatment plan targeting its genetic vulnerabilities – an example of an emerging field sometimes referred to as “precision medicine.”

Crossing the ‘Valley of Death’

While many patients respond favorably to targeted therapy, almost all of them eventually develop resistance. Bivona is now helping to develop rational combination therapies – the “cocktail therapy” approach used so successfully in treating HIV – which target multiple lung cancer vulnerabilities.

Some drugs may already be available; sometimes the drug doesn’t yet exist. Bivona sees his role as navigating through the “valley of death” – the wide gap between exciting discovery and practical application. For example, his lab has uncovered molecular pathways that drive resistance to Tarceva, a lung cancer drug. He is working with academic and industry partners to develop new drugs that block these resistance pathways.

“Completing the physician-scientist mandate of bringing new therapies to patients requires a collaborative effort,” says Bivona.

Bivona was drawn to UCSF because of its collegial culture. “The amount of scientific exchange and collaboration that happens at UCSF is unlike anything I’ve seen before,” Bivona says. “There is an innovative spirit here that drives science forward into new, unexpected directions.” So far, he has teamed up with Kevan Shokat, PhD, chair of the Department of Cellular and Molecular Pharmacology and an expert in signaling molecules called kinases, and Jonathan Weissman, PhD, a systems biologist; both are also Howard Hughes Medical Institute (HHMI) investigators. “You just mention collaborations to these guys, and we are off and running,” says Bivona.

His work does come with certain costs. “Your personal life definitely takes a backseat,” he says. “It is not a career – it is almost like a vocation.” He receives his greatest inspiration from patients. “We’ve had some of our patients come to the laboratory to meet the team and look at cells under the microscope,” says Bivona. “That is incredibly rewarding – to see a patient who is depending on us, and is the reason why we’re doing what we’re doing. There is nothing more motivating than that.”

He is optimistic about the future. “In 10 to 15 years, I think we, as a community of scientists and oncologists, will be curing most patients with lung cancer,” says Bivona. “There won’t be one therapy that will work for all patients, but I think there will be multiple cures.”

DR. JULIE ZIKHERMAN

“Even as it’s inspiring to see patients and do research, it’s also daunting to spend enough time doing each,” says Julie Zikherman, MD.

Zikherman is a physician-scientist who trained in the laboratory of Arthur Weiss, MD, PhD, the Ephraim P. Engleman Distinguished Professor of Rheumatology and an HHMI investigator. She joined the faculty in 2008, and sees patients one afternoon a week with a wide variety of rheumatic diseases, including rheumatoid arthritis and lupus.

“I see colleagues who are solely focused on clinical work, and they are able to bring a unique amount of expertise to the table,” says Zikherman. “Conversely, sometimes it would be nice to focus completely on research, plan targeting its genetic vulnerabilities – an example of an emerging field sometimes referred to as “precision medicine.”

“To see a patient who is depending on us, and is the reason why we’re doing what we’re doing... there is nothing more motivating than that.”

—Trever Bivona, MD, PhD

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Zikherman considers herself fortunate. She is supported by the Rosalind Russell Medical Research Center for Arthritis which, through its fundraising efforts, provides crucial support to junior faculty such as Zikherman in the Division of Rheumatology.

New faculty members usually receive a startup package to launch their labs, but after that initial funding they are responsible for covering lab expenses and salaries for themselves and their team. However, after an upswing in the 1990s, NIH funding has not kept up with inflation, and more applicants are competing for fewer dollars.

For example, the NIH’s main grant for health-related research is the R01. A decade ago, the NIH’s National Institute of Allergy and Infectious Diseases (NIAID) – one of the main agencies that supports Zikherman’s field of research – had an R01 “payline” of 22 percent, meaning that about 22 percent of proposals submitted were funded.

Feeling the Funding Squeeze
It is increasingly challenging for physician-scientists such as Zikherman to enter the field. It usually takes four to six years for trainees to complete postdoctoral training. Clinical revenue from seeing patients is not enough to cover their salary, and K awards and other transitional grants from the National Institutes of Health (NIH) are highly competitive and relatively small.

because you need long periods of contiguous time to get things done in the laboratory.”

Yet Zikherman loves both parts of her job. “I enjoy asking questions, and designing experiments to try to answer them,” she says. “It’s even more fun if you’re doing something that has clinical implications. There is a lot of freedom and scope for creativity. It’s potentially a very fulfilling career, both from an intellectual and an emotional standpoint, where you have long-term relationships with patients.”

As a physician-scientist, she brings additional depth and focus to both clinic and lab. For example, her scientific training helps her discern what kind of autoimmune disorder might underlie a patient’s disease. “While we see patients who clearly have a disease like rheumatoid arthritis, we also see those who have some sort of autoimmune process that’s hard to pin down,” she says. “Having a basic science focus allows you to step back and think very mechanistically about what’s going on, and how to treat it.”

She is also establishing her own lab, continuing her research into how B cells – a type of white blood cell – develop and respond to foreign antigens and microbes, while maintaining tolerance to the body’s own tissues. “Dysregulation in that process might play a role in some of the autoimmune diseases I see in patients, particularly lupus,” says Zikherman. “Most of the current treatments involve suppressing the immune system pretty broadly, and there is a lot of potential for more specific and targeted therapies.”

“What we can discover in academia and what industry brings to the table are really complementary,” she says. “Biotech companies tend to target final common pathways of disease. In academia, we can focus closely on basic mechanisms of disease pathogenesis. That can lead to new, unexpected therapeutic opportunities that industry might overlook.”

— Julie Zikherman, MD

Zikherman considers herself fortunate. She is supported by the Rosalind Russell Medical Research Center for Arthritis which, through its fundraising efforts, provides crucial support to junior faculty such as Zikherman in the Division of Rheumatology.

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Autoimmunity is complex and not yet fully understood. Mark Anderson, MD, PhD, the Robert B. Friend and Michelle M. Friend Endowed Chair in Diabetes Research, is discovering more about how it develops to create better therapies for patients. Anderson joined the faculty in 2003, and is both an endocrinologist – a specialist in hormone-producing organs – and an immunologist. “Many of the endocrine disorders we see in clinic are autoimmune problems, and I’m trying to unravel the interface of endocrinology with immunology,” he says.

T cells play an important role in curing the body of infections from bacteria, viruses and other living organisms that are “foreign” to the individual. To do this, they have to detect and respond to foreign substances called antigens, but not to self. Each T cell expresses receptors on its surface that identify only one antigen, but there are millions of T cells and together they can detect and respond to almost all foreign antigens.

A central question in immunity is how T cells keep from attacking the body’s own antigens. This does happen sometimes, causing autoimmune diseases such as system lupus erythematosus or type 1 diabetes. In most people, however, T cells ignore host antigens. In part, this occurs during development, when T cells mature in a specialized gland called the thymus. If T cells encounter host antigens during that time, they are eliminated. In essence, the thymus is a “school” where T cells learn to recognize antigens. If a T cell in the thymus recognizes a self antigen, it is expelled from school.

As a postdoctoral researcher, Anderson studied a gene called Aire, which is active in the thymus and helps to expand the group of self antigens that T cells can recognize. Anderson’s lab found that Aire was able to promote the manufacture of small quantities of thousands of such antigens in the thymus – at low levels, but enough to train T cells. If Aire was inactive, T cells were not properly schooled, and they attacked the host.

Building on these discoveries, his lab found other genetic mutations linked with poor “schooling” of T cells and subsequent development of autoimmune disorders. These include type 1 diabetes, in which the body destroys insulin-producing cells in the pancreas, and some forms of interstitial lung disease, a group of conditions involving scarring or inflammation of the lung.

Anderson hopes his discoveries will eventually lead to better treatments. “Having a foot in both the clinical and basic science world, I would very much like to see some evidence of a clinical application of our lab work,” he says.

Training the Next Generation

Anderson wears a third hat, directing the UCSF Medical Scientist Training Program (MSTP). It is one of 43 centers nationally receiving NIH funding to train students earning a combined MD/PhD degree. In its latest grant renewal process, UCSF’s MSTP program was recognized as one of the best in the country. It accepts 12 outstanding trainees annually.

“‘This is what UCSF as an institution is about – translating discoveries to help human health.’
—Mark Anderson, MD, PhD
Connecting the Lab and Clinic: Challenges and Innovations

At the start of my career, it was thought possible to be excellent in clinical care, teaching and research,” says William Seaman, MD, PhD, associate chair for research for the Department of Medicine. “These fields are so challenging now that no one can truly master all. Yet it’s still important to have a group of people who have significant training in clinical care and research.”

Physician-scientists face a double challenge: as clinicians, they need to keep up with the latest treatments of disease, as well as newer fields such as improving the quality, safety and value of care. As researchers they face an unprecedented explosion of scientific knowledge and tools.

“The declining numbers of physician-scientists working at the bench is a national trend – it’s not something specific to UCSF,” says Arthur Weiss, MD, PhD, the Ephraim P. Engleman Distinguished Professor of Rheumatology and an HHMI investigator. “There are huge impediments for young people becoming bench scientists. It’s ironic, because today we have more opportunities than ever before to address human disease-related problems. Technological advances allow us to ask questions that were impossible in the past. But such sophisticated and advanced technologies are not readily accessible to people who have not had scientific training.

“Physician-scientists have experience with disease that you can’t get from experimental models,” says Weiss. For example, lab scientists work with genetically identical mice, a situation that only occurs in humans with identical twins. But real life is much more complicated, as physician-scientists know from seeing many different presentations of disease in clinic. “Patients are very, very heterogeneous,” says Weiss. “Relating animal studies to patients is sometimes very artificial and inappropriate. We need to begin to understand more about how the patient got to the current state of disease.”

For instance, a physician-scientist treating patients with asthma may wonder why some respond well to a certain medication, while others do not. “We now realize that asthma is not one disease,” says Seaman. “It probably comes from many factors that lead to a disease that looks roughly similar between patients – but when you really dig down, you find that the patients differ.” Much of this “digging down” now happens at the molecular level, using relatively new tools to diagnose and treat disease by understanding the way genes, proteins and molecules interact.

Turning Theory into Practice

Physician-scientists are also uniquely positioned to strategize which research avenues are most likely to lead to effective treatments. For example, Joseph (Mike) McCune, MD, PhD, chief of the Division of Experimental Medicine, has cared for patients with HIV/AIDS at San Francisco General Hospital since 1982. He observed that many patients have difficulty adhering to a complicated medication schedule.

“Of all the different hypotheses about how one might make patients who are infected with HIV better, the contact with the patient teaches me that whatever I develop has to be easy to take, affordable and efficacious,” he says. “If that is the goal, one has to move one’s science in that direction.”

While PhD basic scientists have very much expanded their knowledge about disease applications of their research, there are perspectives that you can only understand if you have taken care of patients,” says Seaman. “I don’t think we can succeed by just having basic scientists and clinicians, and then trying to have a bridge between them. It is important to have people who speak both languages.”

Robert Nussbaum, MD, chief of the Division of Genomic Medicine and the Holly Smith Distinguished Professor of Science and Medicine, agrees. “There is a role for physician-scientists in basic research that is distinct from, and
complementary to, that which is done by non-physician-scientists,” he says. “Fundamentally, the difference lies in the utilitarian nature of the questions that physician-scientists are driven to ask, versus the pure curiosity-driven questions that non-physician-scientists usually ask. Both are valuable – I think we need them both.”

Cultivating Future Physician-Scientists

The UCSF Department of Medicine is building on its core strengths – outstanding basic science, excellent clinical care, renowned training programs and a culture of collaboration – to meet the challenges of developing the next generation of physician-scientists.

“In the Department of Medicine, there is a growing recognition that we need to pay more attention to the physician-scientist pipeline, and that a laissez-faire approach just won’t suffice in this day and age,” says Nussbaum. Some of these initiatives include:

- **Molecular Medicine Pathway to Discovery:** UCSF offers trainees the option to pursue a career path combining clinical practice and disease-oriented laboratory research: the Molecular Medicine Pathway to Discovery. This Pathway provides people “…with a strongly mentored, in-depth, full immersion into laboratory-based research,” says Nussbaum, the program’s director.

- **Fast-tracking outstanding new faculty:** One of the most challenging periods for young physician-scientists is the transition from training to junior faculty position. They usually complete one, two or even three postdoctoral fellowships before becoming competitive for such positions. One proposed solution is modeled on the UCSF Fellows Program, which fast-tracks the advancement of recently minted PhDs or MDs with outstanding promise as basic researchers. The program provides lab space and financial support for up to five years, allowing fellows to begin independent research.

- **Fostering community:** The Department of Medicine is spearheading plans for a “College of Physician-Scientists” that would bring together UCSF physician-scientists from many disciplines and levels of career development, from medical students to senior faculty.

Collaborating for Success

In recent decades, basic science has shifted away from single scientists to team-based research. “The techniques that we now can bring to bear on research are so broad that no one can encompass them in their own laboratory,” says Seaman. “Physician-scientists, like basic scientists, are increasingly interactive.”

One particularly vivid example has been the treatment of HIV, which evolved rapidly thanks to close collaborations among scientists, industry and the community. “Patients taught us that the only way you could address this problem was in collaborative teams,” says McCune. “We had to be really attentive of our teammates, in a way that most scientists are not.”

One of UCSF’s stellar strengths is its collegial culture, which makes it especially well positioned to conduct team-based science. “UCSF has traditionally been very collaborative in both the basic and clinical sciences, and it’s a big advantage we have as a research institution,” says Seaman. Some innovative examples include:

- **Organized research units:** UCSF has a number of these disease-focused, interdisciplinary research units, such as the Cardiovascular Research Institute, the Diabetes Center, the Institute for Human Genetics and the Helen Diller Family Comprehensive Cancer Center.

- **UCSF’s Clinical and Translational Science Institute (CTSI):** McCune was also the founding director of CTSI, among the first of 60 such centers launched nationally since 2006 with NIH funding. “CTSI was designed to ask the question, how can we take all this wonderful science and apply it to bring better health to more people more quickly?” says McCune. Now directed by Clay Johnston, MD, PhD, CTSI has established infrastructure, services and training to support clinical and translational research.

- **Patient cohorts:** Over the last several years, the Department of Medicine has provided seed money to develop five patient cohorts – large groups of patients who give permission for scientists to collect and study their anonymized clinical data and blood samples. Cohorts function like a library, making huge amounts of information available to researchers, rather than requiring each investigator to gather data alone.

- **Leadership Initiative:** Started in 2011, this effort enhances the Department’s current leadership capacity by providing professional training, including a 360-degree review and Myers-Briggs Type Indicator test, workshops on leadership skills, and private executive coaching. Says McCune, “I think this initiative is spot on: if people at UCSF want to be leaders, helping trainees and others to succeed in their careers, it’s important that they learn how to be good coaches.”

- **Supporting teamwork:** Collaboration may be the path of the future, but it also raises new challenges. “To be promoted at UCSF, one must show evidence of independent creative scholarship,” says McCune. This is demonstrated by publications not co-authored by a mentor, and serving as principal investigator on an R01 grant. Those rules make it difficult for team-based physician-scientists to succeed, since they may be the 20th author on a 30-author paper, or a collaborator on another investigator’s R01. The Department’s Research Council has proposed changes to Departmental promotion guidelines recognizing such contributions.

Accelerating Discovery

As a premier academic medical center, UCSF plays a special role in bringing forth new treatments to help patients, and physician-scientists are uniquely positioned to accelerate these discoveries. “We have a wealth of diseases to take care of,” says McCune. “I can guarantee you that in the profit-oriented, biotech-pharma environment, interventions that don’t make money will not have a team assigned to fix them. So that’s our province.”

“The opportunities are really there,” says Weiss. “In rheumatology, therapy of arthritis has been revolutionized over the past 10 years. You could say the same thing about HIV and cancer. Physician-scientists play an important role at the interface of disease pathogenesis and developing new therapeutics. There are many examples of successful physician-scientists at UCSF, but for an institution this great, we need more, and we need to invest in the next generation.”
Dr. Charles Sawyers: Targeting Cancer Genes

My role as a physician-scientist is not just to publish another paper and move on to the next project,” says Charles Sawyers, MD, chair of Memorial Sloan-Kettering Cancer Center’s Human Oncology and Pathogenesis Program. “If you really believe your data, you should push it forward into the clinic.”

Sawyers has used this approach to revolutionize the treatment of chronic myeloid leukemia (CML) and prostate cancer, studying the genetic makeup of these diseases to develop new therapeutics.

He began his residency at UCSF in 1985, and vividly remembers caring for leukemia patients during month-long hospitalizations for bone marrow transplants. “You see the same patients every day and form a pretty intense relationship,” says Sawyers. “I took care of young adults – some were cured, and some died, right there in front of you. It was very moving.”

Creating Synergy

He gained his first research experience in the lab of physician-scientist Joel Ernst, MD. Ernst also directed him to Owen Witte, MD, a leading UCLA cancer researcher with whom Sawyers later worked as a postdoctoral fellow.

“In an outstanding group of interns and residents, Charles stood out for his compassion, thoroughness, and dedication to ensuring that all his patients got the best care,” says Ernst, now on the NYU faculty. “In the laboratory, Charles was as exceptional as he was on the wards – he quickly took to the tools and concepts of molecular biology, and it was clear that he would go far. Even with those expectations, Charles’ accomplishments have surpassed anyone’s wildest dreams.”

As a trainee and then a faculty member at UCLA, Sawyers cared for leukemia patients while relentlessly pursuing how a mutated gene called BCR-ABL caused CML. “The questions in the clinic were the same things we were working on in the lab,” says Sawyers. “People tell you that it’s impossible to do both, but there are ways to align them so it’s not only possible, but synergistic.”

He collaborated with Brian Druker, MD, at Oregon Health & Science University, to conduct a clinical trial of Gleevec, a drug that inhibited BCR-ABL in laboratory models. Amazingly, within a week or two, some patients near death walked out of the hospital in complete remission.

“That was an incredibly important experience,” recalls Sawyers, saying it inspired a lifelong focus on translating laboratory discoveries into treatments. “I thought, ‘I’ve got the medical and science training. If I don’t do it, who else will?’ That became the driving motivation of my lab.”

Unfortunately, patients developed resistance to Gleevec and relapsed. Sawyers and his group discovered a large number of mutations that caused resistance. “This resulted in a period of despair,” says Sawyers. “We thought, oh my God, we’ll need 50 drugs to treat this disease!”

Cornering a Shape-Shifter

Then Sawyers began collaborating with John Kuriyan, PhD, at UC Berkeley, an expert in three-dimensional structures of proteins. They found that all the mutations changed the shape of the protein produced by the BCR-ABL gene so that Gleevec could no longer bind to it effectively. But most of these new shapes shared a common feature that might be targeted with another drug.

Sawyers discussed these findings at a scientific meeting, describing what kind of drug might block the protein in this alternate shape. A Bristol-Myers Squibb scientist said one of their drugs, dasatinib, might be a match. Sawyers tested the compound in the lab, then conducted a highly successful clinical trial.

“Gleevec and dasatinib have completely changed the way [CML] is managed, and it was all driven by science,” says Sawyers. “Patients I’d known for years who carried a death sentence had a complete change in their outcome. That has been incredibly satisfying.”

Sawyers also studies prostate cancer that develops resistance to hormone therapy. “This time, no one called me and said, ‘I have the drug,’ so we had to make it,” says Sawyers. He partnered with Michael Jung, PhD, an academic chemist at UCLA, to develop enzalutamide. It won FDA approval in 2012 after a clinical trial showed it significantly increased survival in men with advanced disease.

Sawyers moved to Memorial Sloan-Kettering Cancer Center in New York in 2006, where he continues his research. He was recently appointed by President Obama to the National Cancer Advisory Board, and is president-elect of the American Association for Cancer Research. He is a Howard Hughes Medical Institute investigator, a member of the National Academy of Sciences and the Institute of Medicine, and has received numerous awards, including the Lasker-DeBakey Clinical Medical Research Award.
PAUL VOLBERDING, MD

Paul Volberding, MD was appointed as associate chair for Global Health in the DOM.

In his role, Volberding will take responsibility for the overall planning effort to better identify the needs and opportunities in global health activities and how those efforts might intersect with services being provided or being planned by other groups, including Global Health Sciences and the CTSI.

Volberding is a Professor of Medicine and director of the Center for AIDS Research at the University of California, San Francisco (UCSF) and the Gladstone Institute of Virology and Immunology; and served until 2012 as vice chair of the Department of Medicine. He continues to practice medicine at SF VA Medical Center. He was appointed director of the AIDS Research Institute at UCSF and director of research for Global Health Sciences in 2012. Volberding served as director of the Positive Health Program at San Francisco General Hospital (SFGH) for 20 years. He received his undergraduate and medical degrees at the University of Chicago and the University of Minnesota, respectively, and finished training at the University of Utah and at UCSF, where he studied for two years as a research fellow in the virology laboratory of Dr. Jay Levy, later a co-discoverser of HIV.

beth harleman, md

Beth Harleman, MD, was appointed as associate chair for strategic planning and implementation for the Department of Medicine (DOM).

In her new role, Harleman will take responsibility for the continued success of the DOM’s overall strategic plan. The DOM developed its first formal strategic plan – Planning Together for Excellence – three years ago. So far, implementation of the strategic plan has involved developing new structures to enhance communication and collaboration across the DOM, specific initiatives in each strategic priority area, implementation of the Leadership Initiative, and planning for a new program aimed at reducing medical costs, “Choosing Wisely.”

Harleman earned her medical degree from the UCSF School of Medicine (SOM), was a resident at UCSF and a chief resident at San Francisco General Hospital (SFGH). She currently practices both inpatient and outpatient medicine at SFGH and serves as the associate program director for curriculum and program evaluation for the DOM Residency Program. A member of the Academy of Medical Educators, she has worked extensively in education for the past ten years, creating a highly regarded course in the UCSF SOM, mentoring hundreds of medical students and residents and spearheading programmatic innovations. Beth also served as co-champion of the education pillar of the strategic plan from 2010-12.

Stephen J. McPhee, MD Endowed Chair Created

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“Steve [McPhee] has an almost encyclopedic knowledge of medicine, and was very accessible,” says Ross Jaffe, MD, who trained under McPhee as a UCSF resident in the mid-1980s. “If you had a challenging case, to sit down and talk with Steve for 10 minutes about it was a wonderful educational experience. He has been a great role model and mentor to generations of internal medicine residents at UCSF.”

Jaffe is a co-founder and a managing director of Versant Ventures, a health care-focused venture capital firm. He and his wife, Eve Epstein Jaffe, LCSW, a former UCSF clinical social worker, made a significant early gift to the endowed chair fund. “When Steve Schroeder approached me, the answer immediately was, ‘Yes – how can I help?’ By donating to this chair in Steve McPhee’s honor, we hope to support other faculty members who will make similar valuable contributions to clinical care, education and research at UCSF.”

McPhee’s accomplishments at UCSF were manifold. Beloved by his patients, he was a consummate general internist, and received recognition as a Department of Medicine Master Clinician. In 1999, he co-founded the UCSF Palliative Care Service, including the Comfort Care Suites. From 2000-2008, McPhee co-edited “Perspectives on Care at the Close of Life,” a landmark series in the Journal of the American Medical Association, later published as a textbook, Care at the Close of Life.

He has been an outstanding teacher and mentor to hundreds of UCSF residents and junior faculty. He served as one of the first directors of the primary care general internal medicine residency program, and received the first UCSF Lifetime Achievement in Mentoring Award. He is a leading editor of core clinical textbooks, including Current Medical Diagnosis & Treatment, a bestselling general medical text for practicing physicians published annually in 11 languages, and The Pocket Guide to Diagnostic Tests and Pathophysiology of Disease: An Introduction to Clinical Medicine for medical students, among others.

He has been the principal investigator on nearly 70 grants and contracts, with a primary focus on disease prevention and palliative care. In 1986, he co-founded the UCSF Vietnamese Community Health Promotion Project, a research program for which he received the Chancellor’s Award for Public Service in 2003.

“This endowment is not just a personal honor, but also a gift back to the Division of General Internal Medicine,” says McPhee. “We need more such chairs, because without primary care, you don’t really have good clinical care for patients…. The Affordable Care Act relies on having a supply of primary care physicians, and in order to do that, we need to train them. That is something we have done very well at UCSF for more than 30 years.”

To contribute to the Stephen J. McPhee, MD Endowed Chair, please contact Senior Director of Development Olivia Herbert at (415) 476-9878, or oherbert@support.ucsf.edu.
Improving Health Care Delivery

While many faculty are translating laboratory findings into patient treatments, other physician-scientists are studying health care systems themselves – often using UCSF as their “laboratory” to pioneer ways to improve health care delivery.

“UCSF has a number of faculty who are involved in what we call health services research,” says Niraj Sehgal, MD, MPH, associate chair for quality improvement and patient safety. “They are well equipped to answer questions that are becoming increasingly important with health care reform, such as how do we provide the highest quality and safest care to patients with a limited set of resources?”

R. Adams Dudley, MD, MBA
R. Adams Dudley, MD, MBA, a pulmonologist and the associate director for research at the UCSF Philip R. Lee Institute for Health Policy Studies, has developed measures of quality of care and worked on initiatives to make quality matter in the market. One of the best-known is CalHospitalCompare.org, which includes ratings for clinical care, patient safety and patient experience for more than 232 California hospitals. “Health care has not been an industry to track its own performance,” says Dudley. “Comparative information is very important. If you just tell a doctor or hospital, ‘The death rate in your ICU is 13 percent,’ they don’t know what to do with that. Helping them to understand where they fit in the spectrum of performance, with data they believe is accurate, enables them to get better.”

Working in partnership with hospital executives, insurance companies, consumers and many other stakeholders, CalHospitalCompare developed a way of measuring and risk-adjusting mortality for ICU patients, then shared the data in a series of quality improvement collaboratives. “Improvements happened at a really rapid rate, and we lowered the statewide ICU death rate by about 2 percent over three years,” says Dudley. Many other improvements were spurred by making accurate comparative information easily available. “It’s all about multiplication,” he says. “Getting information all the way to key policymakers really extends your impact.”

Ralph Gonzales, MD, MSPH
Ralph Gonzales, MD, MSPH, associate chair for ambulatory care and clinical innovation, is an expert in implementation science – the science of translating evidence into practice. “With the goal of designing a much better ‘1.0’ version of a health care intervention, implementation science provides a framework for understanding the patient, provider and systemic factors related to what we are trying to improve,” says Gonzales. “Also, because no two places are alike, we tailor and adapt previous evidence to the local environment and circumstances.”

Gonzales has developed strategies for reducing overprescribing of antibiotics. “Many years ago when I moonlighted at Kaiser urgent care, I found how hard it was to resist pressure from patients to give them antibiotics I didn’t feel were appropriate,” says Gonzales. He and colleagues developed educational pieces for physicians and patients, including exam room posters emblazoned with the Centers for Disease Control and Prevention (CDC) logo explaining that antibiotics aren’t effective for bronchitis, and increase antibiotic resistance in the individual and the community. “Doctors told us that these interventions made it easier for them to do the right thing – it was no longer the doctor saying ‘no’, it was the CDC and poster saying ‘no’,” says Gonzales. These education programs have been scaled up, the CDC now offers this content on their website, and total antibiotic prescribing for respiratory conditions has dropped by about 20 to 25 percent nationally over the last 15 years.

Urmimala Sarkar, MD, MPH
Urmimala Sarkar, MD, MPH, an internist at San Francisco General Hospital, is working to help people living at home with chronic conditions manage their health more safely. Patient safety has been a focal point in the hospital setting, but Sarkar is one of a handful of researchers studying patient safety in the outpatient setting – such as outpatient medication complications. “With patients who take 20 medications a day, there is the potential for confusion and drug interactions,” says Sarkar. “For someone who is low-income, doesn’t speak English and can’t afford glasses, the likelihood that they’re going to experience medication problems is much higher.”

She analyzes large data sets and interviews patients who recently visited the emergency room to determine the scope and underlying causes of the problem. “I envision there will be a multilayered solution, involving a combination of technology, care teams to support patients in their medication self-management, and workflow changes to allow providers to think about patients who are not right in front of them,” says Sarkar. “This work requires a very supportive and forward-thinking enterprise, and I can’t imagine doing this kind of research anywhere else.”
Stephen J. McPhee, MD, a founding member of the Division of General Internal Medicine (DGIM), has been a beloved and highly respected clinician, educator and researcher during his 31-year career at UCSF. As tribute to his exceptional legacy, more than 250 colleagues, friends, family and trainees contributed funds to create the Stephen J. McPhee, MD Endowed Chair, which will be awarded to a faculty member in the DGIM who shares McPhee’s dedication to patient care, education, and research.

“Dr. McPhee has been an inspirational teacher and doctor, and has really been part of the fabric of the division,” says Steven Schroeder, MD, the founding chief of the DGIM who hired McPhee in 1980. Schroeder is currently the Distinguished Professor of Health and Health Care and directs the Smoking Cessation Leadership Center. “When he had to step down, I thought it would be nice to create a lasting memory in his honor. That led quite logically to the thought of establishing a chair, and it has been wonderful to see the resultant outpouring of support.”