Envisioning the Future

2016 Report to Our Community

Stanford MEDICINE | Department of Medicine

Department of Medicine in Numbers

14 Divisions

414 Faculty
(103 University Tenured and Nontenured Line, 101 Medical Center Line, 172 Clinical Educators, 38 Instructors)

29 Endowed Professors

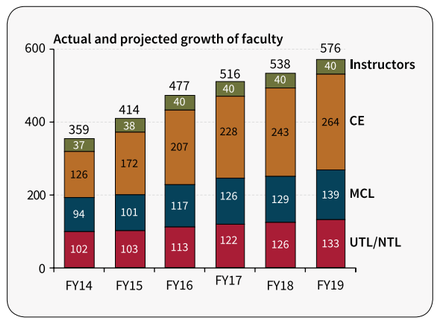
572 Staff & Research Associates
(492 Staff, 80 Research Associates)

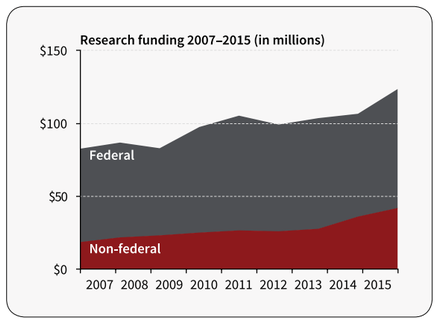
396 Trainees
(121 Residents, 131 MD Fellows, 144 Post-docs)

418 Non-academic Staff
(256 Research, 162 Administrative)

$123.8M Sponsored Research
($81.8 million in federal grants, $42 million in non-federal grants and clinical grants)

366 Grants
(3 Program Projects, 56 R-01s, 31 Ks, 15 Us, 11 Training, 150 Non-Fed, & 100 Clinical Trials)





On the cover: *Ami Bhatt, MD, PhD in her lab; Stephanie Harman, MD, and Karl Lorenz, MD, MSHS on Stanford's Discovery Walk.*


Robert Harrington, MD

What you're holding is neither a yearbook of our recent accomplishments nor an annual report replete with facts and figures. It's most like an anthology, giving readers glimpses of some recent progress we've made as we addressed Stanford Medicine's tripartite mission: to teach our students and trainees, to do research, and to care for our patients.

As we move toward the future, it's important to reflect on the past, which created the culture of the Stanford Department of Medicine. Thus we start this compendium with Stan Schrier, who was here before some current faculty members were even born. Even today Stan consults in the clinic, mentors residents, and interviews housestaff candidates.

We organized this report to follow the department's four strategic priorities:

1) invest in science & research;
2) elevate the culture of clinical care;
3) connect science to the clinical;
4) educate & train the next generation.

Within these domains you'll meet some of the people and read about some of their activities.

Read about Ron Levy's work to combine immune therapies and targeted therapies to defeat certain cancers and Marcella Alsan's fascinating theory about the role of the tsetse fly in altering the economies of Africa.

We include articles about important clinical advances that may change the future for patients with familial hypercholesterolemia or metabolic bone disease. The creation of Stanford Health Care-ValleyCare in Pleasanton gave us an opportunity to introduce an academic hospitalist program and integrate our faculty into the community.

Work that connects science to the clinic includes the new Center for Population Health Sciences, promising to blend campus-wide efforts to address significant health issues and create a learning health care system. Shai Friedland's pioneering work with Korean colleagues on gastric cancers may reduce the need for surgery in certain patients.

Nothing that we do at the bench or in the clinic will matter if we don't bring along a new generation of scientists to take up where we leave off. Read about global health opportunities for our residents and the creation of new pathways that match residents' clinical, research, or education interests.

I'm pleased to share this brief look at a few of our recent projects with you. Whether you're new to learning about our Department of Medicine or you've been on campus for decades, I hope that you sense the excitement in the department—and mostly in the people—who will drive the missions forward.

Let me know if you have questions or suggestions for future editions.

Sincerely,
Robert Harrington, MD
Chair, Department of Medicine


Ray Lyman Wilbur, MD

"Envisioning the future, building on our past" is the theme of this report. The recent achievements of the Department of Medicine would not be possible without the work of many past leaders, starting with Ray Lyman Wilbur, MD, the first dean of the Stanford University School of Medicine. As you read about those who are advancing our field today and into the future, we acknowledge the great progress made here in the not so distant past. So, with a nod to those who built this department, we've inserted historic photos in selected locations within this report, including the section headers on pages 4, 12, 20, and 26.

Remembrance of Things Past

Stan Schrier wasn't around a century ago when Marcel Proust was writing, but to listen to Schrier's recollections, it's as if the octogenarian might have been.

"I got to Stanford on July 9, 1959, and I went to my first Department of Medicine meeting, where I think there were about 12 other people. It was pretty clear that we had a very small department and the place was going to build," recalls the emeritus professor of medicine.

The medical school had just relocated to Stanford's main campus in Palo Alto from the tattered Cooper Medical College and Lane Hospital buildings in San Francisco.

"I actually never worked a day in my life at the Cooper Lane Hospital in San Francisco. I went up there to steal the equipment as the place was falling down," Schrier confesses.

"There was some laboratory data lying around as well as large numbers of mice that had escaped from the experimental laboratories. So I went up there with my car, and I brought back equipment to help furnish my new laboratory.

"My impressions of what went on at Stanford in the city was that it was a very small service at the Cooper Lane with another Stanford service at the San Francisco General and a smaller service at the VA at Fort Miley. It was really quite small, and the one thing that I learned talking to the people who lived and worked there was they had extraordinarily good feelings about each other."

Schrier had been recruited to Stanford from the University of Chicago where there was a very substantial Department of Medicine.

"I'd been at Hopkins, the University of Michigan, and the University of Chicago. These were well-established departments of medicine with fellowship programs, house staff training programs, and grand rounds. They had research conferences. And we got down to Stanford and we had none of that. And so we looked around and said, 'My goodness gracious, we're going to have to put all these things in place. We have to have a house staff program in medicine. We have to have rounds. We have to have a fellowship program. We have to have research conferences,'" Schrier remembers.

Saul Rosenberg, MD, Maureen Lyles D'Ambrogio professor of medicine (Oncology), emeritus, also came to Stanford at that time.

"I was one of the new assistant professors as was Stan, and that was a remarkable group of young faculty, mostly recruited by Hal Holman during the 60s. We had an assistant professor club, and there were 10 or 12 of us, and they were the seeds of a tremendous growth of this Department of Medicine and Stanford Medical School," Rosenberg said in "The Mozart of Hematology," a 2010 film by Jason Gotlib, MD (associate professor, Hematology), about the fascinating life and work of Schrier.

"It was terribly exciting because as young assistant professors with not many of the older faculty around we had enormous leverage. We proposed programs that, in fact, took place, and that have led to what we see now—an enormously powerful department with strengths in basic science and translational medicine," Schrier says.

With the move from San Francisco came a complete revamp of the medical school curriculum that was prompted by Stanford president Wally Sterling and other university leaders including provost Fred Terman, radiation therapy pioneer Henry Kaplan, MD, and pharmacology department chair Avram Goldstein, MD.

"The curriculum that we built was heavily based on the idea that there was very strong basic science. We were now on the main campus and could interact with the basic scientists," says the 86 year old.

During his 56 years at Stanford, Schrier has witnessed phenomenal change.

"We're an extraordinarily different place today. Instead of 12 or 15, there are 400 in the Department of Medicine. We have people at ValleyCare Medical Center, and we have people at the Palo Alto VA, to say nothing of the enormous expansion of Stanford Hospital. The department now is in the top category of med schools in the country because it's managed to combine very good science with translational medicine and the clinical trial program, which had been a little bit sluggish in getting started, but is now going very well," he observes.

Comparing the clinical programs of today with those of the early 1960s is "as though we were dealing with two separate realities," notes the former Chief of the Division of Hematology as he refers to the advances that took place under his leadership.

Among those he credits are immunologist Rose Payne, PhD, who helped develop the HLA system that allowed for transplantation to take place. He also talks fondly of Judith Pool, PhD, who discovered the cryoprecipitate that for many years was the standard treatment method for hemophilia.

With an emergent hematology division within a growing department of medicine, Schrier was able to work with Ron Levy, MD, Robert K. and Helen K. Summy professor of medicine (Oncology), to recruit people like Karl Blume, MD, who established what Schrier proclaims as "probably the best bone marrow transplant unit in the country."

Blume hired one of Schrier's fellows, Rob Negrin, MD, professor of medicine, who is now chief of the division of blood and marrow transplantation. Other notable Schrier recruits were Peter Greenberg, MD, (professor, Hematology), emeritus, who became an expert in myelodysplastic syndrome; Larry Leung, MD, current Maureen Lyles D'Ambrogio professor of medicine, who followed Schrier as hematology division chief and set up strong programs now with the VA; and Linda Boxer, MD (professor, Medicine), who performed research in the molecular abnormalities underlying lymphomas and rose to hematology division chief and now vice dean.

But if what's past is prologue, then Schrier's recollections foretell even better days to come for the Department of Medicine. In his own case "the best time of my life is now, and though I'm supposed to be retired, I'm actually an 'active emeritus.'"


Stan Schrier, MD

During his 56 years at Stanford, Schrier has witnessed phenomenal change.

Bob Harrington, MD (professor and chair, Medicine), met recently with Schrier to discuss an upcoming search for a new chief of hematology.

"As Stan sat across the table from me, his eyes lit up and he said 'oh, my goodness, what a great time to be at Stanford! We're moving to the South Bay, we're moving to the East Bay, campus is growing. What a great time to think about building hematology here at Stanford,'" Harrington relates. "For somebody who came here more than 50 years ago and who helped build this place, he is the past. But he's the future, too, and his enthusiasm for the future says a lot about who we are at Stanford and who we want to be."

While Schrier no longer sees patients on the inpatient service, he still sees patients in consultation in the hematology clinic.

Furthermore, he still has plenty of teaching opportunities. As one of the department of medicine's core reviewers, he reviews house staff candidates and is one of 18 in the residency program's faculty mentorship program. He spends two sessions a week with the house staff on the hematology med 8 service (which he started almost 25 years ago), where he answers their many questions, and he also meets them at the microscope, where he shows them how morphology can aid in diagnosis and management.

"Stan sets the expectation about what it is to be an academic hematologist and a life-long learner, and I have tremendous respect for that," says Gotlib, who views Schrier as a mentor in his role as the hematology fellowship program director. "His example is what I try to model. Showing up at conferences to teach is how you make sure that a program has the respect of its fellows and faculty."

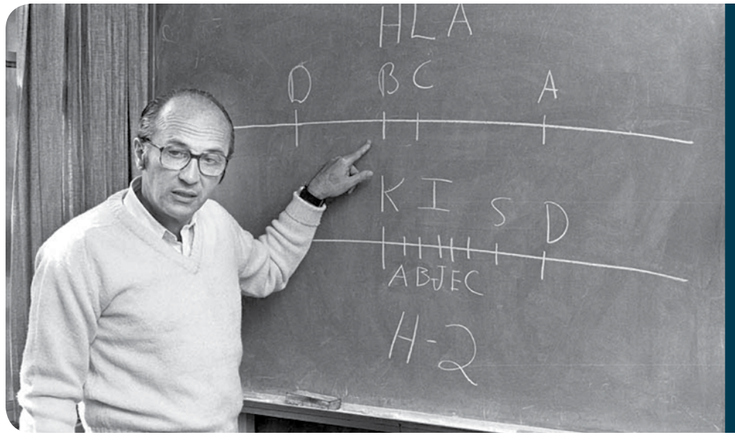
Schrier notes that he also has "an interesting job in the Stanford Cancer Institute," where he serves as vice chair of the Scientific Review Committee.

As if that's not enough for a man in his ninth decade, he proudly boasts: "I'm funded by the NIH, would you believe?"

The Program for Anemia, Clinical and Translational Trials in the Elderly (PACTTE) is funded by the National Institute on Aging. Schrier chairs a PACTTE consortium of institutions that are dealing with anemia of the elderly. The consortium is studying the impact of anemia on about 20,000 elderly patients who have congestive heart failure.

"We think we're going to be able to make some interesting observations that will allow us to improve the care of elderly patients with heart failure," he says.

Looking to help the elderly is a noble activity for a youngster like Stan Schrier. ■



Invest in Science & Research

Hugh McDevitt
Stanford Professor of
Microbiology and Immunology

Responsible for the discovery of immune response genes and the first definitive physical map of the Major Histocompatibility Complex (MHC).

Making Bone Marrow Transplantation Safe

Bone marrow transplantation is so dangerous and so toxic that it is reserved for people with life-threatening diseases. Despite the dangers of a transplant, including rejection of the new, disease-free cells in the transplanted tissue, more than 50,000 patients get bone marrow transplants each year because it is the only curative treatment possible for patients with inherited disorders of blood formation; for immunodeficiencies such as severe combined immunodeficiency disease (SCID); and for many types of cancer.

The need to deliver DNA-damaging treatments, and the possibility of graft-vs-host disease remain the biggest hurdles in bone marrow transplants, as an average of 10 to 20 percent of bone marrow transplant patients die from complications. Prior to the transplant, patients will receive chemotherapy or radiation to make space in the bone marrow for the healthy donor cells. Patients also receive medications to suppress donor lymphocytes from attacking the transplant recipient's body, which can cause life-threatening graft-vs-host disease.

At Stanford, researchers are developing a safer bone marrow transplantation approach, which will begin clinical trials next spring. Instead of chemotherapy and radiation, the trial will use the first biologic agent to eradicate the disease-producing stem cells to treat children with SCID; patients will then receive grafts of pure blood-forming stem cells from a donor. The mixed cell grafts will be processed so that only pure stem cells will be infused, devoid of contaminating donor lymphocytes that cause graft-vs-host disease.

> "This is the most exciting thing I have done in my life"

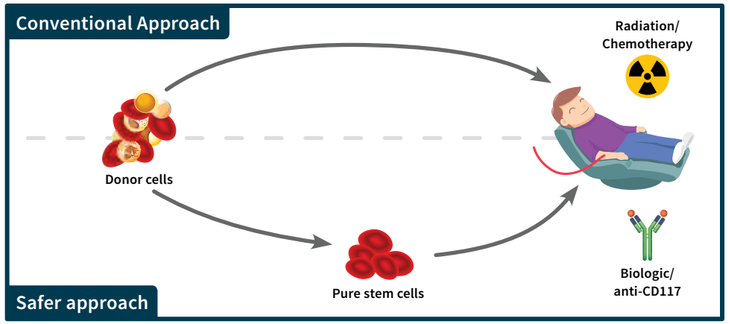
"This combined approach could be the 'holy grail' of transplantation," says investigator Judith Shizuru, MD, PhD (associate professor, Blood and Marrow Transplantation), who was awarded a $20 million grant from the California Institute for Regenerative Medicine (CIRM) to develop this antibody-based therapy. The discovery could lead to safe, long-term treatment for a multitude of inherited blood disorders and cancers, and expand treatment options for autoimmune diseases like multiple sclerosis, lupus, and childhood diabetes.

Making bone marrow transplantation safer so that patients benefit from the procedure without toxicity, and expanding the procedure to treat a range of autoimmune diseases have been the goals of Shizuru's research for more than a decade.

This is an exemplary story of the promise of translational medicine, starting with studies of the basic biology of blood-forming cells at Stanford; then the laboratory discovery of the antibodies to target stem cells; and then adapting the development of those antibodies by off-campus biotech companies, with the empowering support from CIRM that allows Shizuru's team to deliver these new treatment options to patients.

This research builds on groundbreaking discoveries in mice by Irving Weissman, MD, director of Stanford's Institute for Stem Cell Biology and Regenerative Medicine and a consultant to the Shizuru team. In the late 1980s his laboratory developed methods to isolate mouse stem cells by sorting them, using the fluorescence-activated cell sorter technology developed at Stanford. His team subsequently founded a company that applied these methods to isolate human stem cells.

Next, a Stanford medical student working in the Weissman lab, Agnieszka Czechowicz, identified the target antibody that the researchers will soon test in a clinical trial. Czechowicz's project was to test different antibodies to see if any of them could remove the blood-forming stem cells as well as or better than chemotherapy would do in humans (or radiation would do in mice). She discovered that an antibody that recognizes the CD117 molecule, which is present on blood-forming stem and progenitor cells, could accomplish this goal. "We have always envisioned that antibodies could replace toxic treatments, and targeting CD117 seemed ideal," Shizuru explains, "and we began to investigate if a similar antibody that targets human stem cells could be tested in a clinical trial."

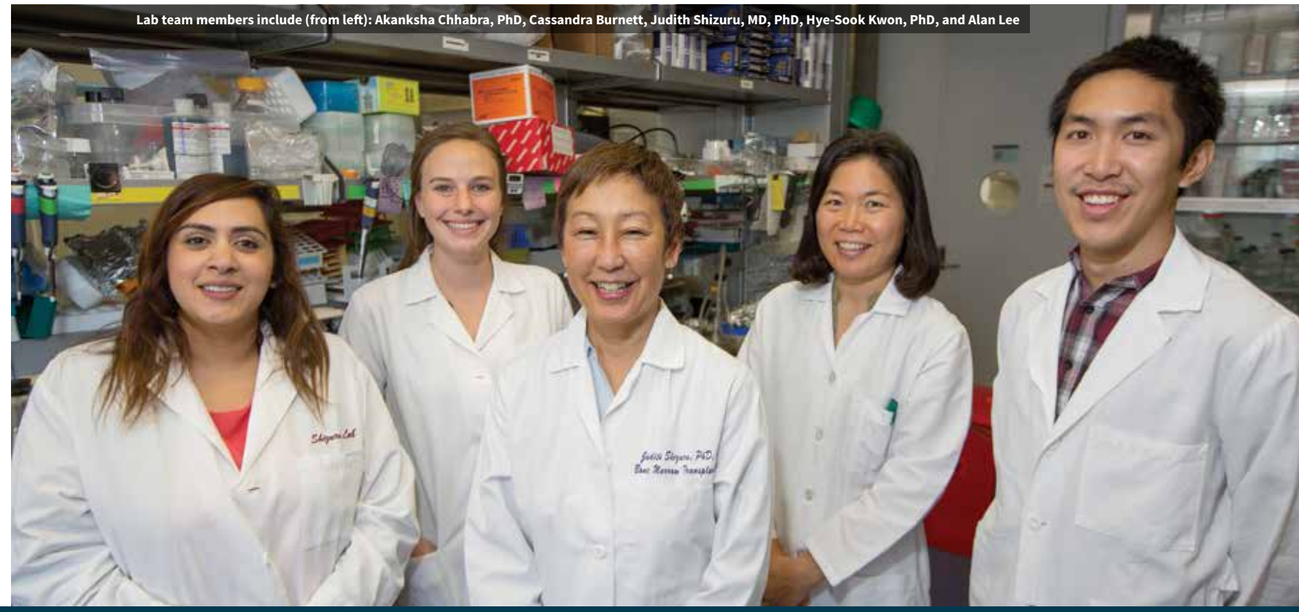


The next lucky discovery was that a local biotech company had already developed and safety-tested a human antibody to target human CD117, but for treatment of inflammatory disease and not for bone marrow transplantation. Scientists at the company agreed to collaborate in Shizuru's investigations, and openly shared their biologic and safety tests with the antibody. This vital assistance from the company has accelerated the ability of the Stanford team to move to clinical trials, and CIRM funding has supported the many steps needed to obtain FDA approval for the study, including testing to validate use of the human anti-CD117 antibody in patients.

"This is the most exciting thing I have done in my life," Shizuru says. "One important reason why I became a bone marrow transplanter was so I could help to cure autoimmune disease, and diabetes was my PhD topic."

Shizuru began her career as a technician in a Stanford lab, where her mentors encouraged her to pursue a PhD. She then completed her studies to become an MD at Stanford and became a physician-scientist after receiving advice and support from the founding members of the Juvenile Diabetes Foundation. "If we can make bone marrow transplants safer, that offers a potential way to cure autoimmune disease, including diabetes," says Shizuru.

Shizuru has set out to change the field of bone marrow transplantation, and she is confident this work will create the pathway. "I want to make the transplantation procedure an order of magnitude safer, and to achieve this end-goal we have to evolve from the current toxic, DNA-damaging approach and infusion of undefined cell populations to a more targeted and nuanced one." ■


Lab team members include (from left): Akanksha Chhabra, PhD, Cassandra Burnett, Judith Shizuru, MD, PhD, Hye-Sook Kwon, PhD, and Alan Lee

The World Within Us

How the Microbiome Influences Human Disease and Patient Outcomes

As a child, Ami Bhatt, MD, PhD (assistant professor, Hematology, and assistant professor, Genetics), found herself drawn to science. "I was always curious, and I wanted to apply my curiosity in a way that could help people," she recalls. These dual instincts led her to medicine, where she found her calling as a physician-scientist. Today Bhatt runs her own laboratory at Stanford, where she studies how shifts in the microbiome—the vast community of bacteria and other microscopic life that live on the body—affect human disease and patient outcomes.

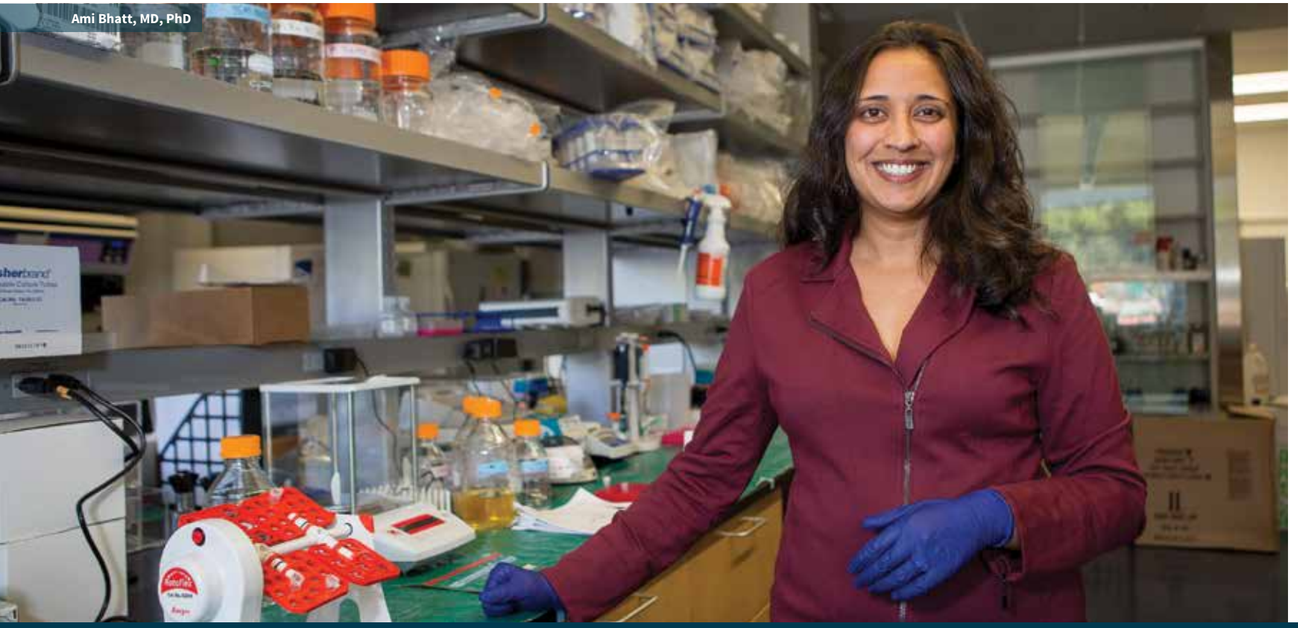
Bhatt first became interested in the intersection of infection and malignancy as a medical student at UCSF. "At UCSF I saw a lot of patients with HIV who died of opportunistic infections," she explains. Several years later she encountered a similar trend while on rotation for Brigham and Women's Hospital's bone marrow transplantation service. "A lot of the bone marrow transplant patients were getting sick with syndromes that seemed like infections, but we weren't able to identify the infectious triggers because we didn't know what we were looking for."

Bhatt's search for answers led her to the laboratory, where she used genomics to understand the diseases that had presented in those bone marrow transplantation patients. Her investigation led to an important discovery—the genome of a new bacterium—and set the stage for her current research. "That's the moment when my eyes started to open. I realized that there are many more types of bacteria and viruses and fungi that live within us, in our microbiome, than we know about."

Bhatt and her colleagues use cutting-edge genetic sequencing technologies and a sophisticated understanding of diseases to try to "solve mysteries that occur in immunocompromised patients. The fundamental thesis that drives our research," she explains, "is that patient outcomes are manipulated or modified by the alterations in their microbiota, and that we can discover these microbes using sequence-based technologies." Once the microbes are identified, Bhatt's team works to clarify the mechanistic underpinnings of the microbiota-disease relationship. This information is then used to alter the microbiota through targeted drugs or treatments.

Another of Bhatt's initiatives aims to unravel a particularly interesting question: What molecular changes occur during a fecal microbiota transfer? To answer this, Bhatt and her colleagues have developed a computational pipeline that will provide a time-based characterization of what actually happens during a transfer.

While her research goals are ambitious and varied, the source of Bhatt's passion remains the same. "I'm still committed to the idea of being able to help people using science," she says. "It's been exciting to see our lab grow from just me in an empty room to a vibrant, interactive environment. We currently have eight talented staff members from all over the world. It's a fun and bustling place. I feel like I am one of those lucky few who get to do exactly what they want to do." ■



Ami Bhatt, MD, PhD

Ronald Levy, MD, today (top) and in 1981 (below)

Drug Synergy May Upend Cancer Treatment

For decades, scientists have diligently been working toward new treatments for cancers by pursuing two lines of research: harnessing the power of the immune system to seek out and destroy tumors, or suffocating the tumors by blocking molecular pathways vital to the cancers' survival. The best way to cure a cancer, though, may involve combining these two lines of attack, according to new research led by Stanford oncologist Ronald Levy, MD (professor, Oncology).

"Individually, these two kinds of therapies are already changing our cancer therapy paradigm," says Levy. "But when combined, I think they're really going to change things."

The idea behind so-called cancer immunotherapies is that the human body already has built-in defenses that can abolish foreign entities; just as the immune system can fight off a cold virus, many researchers theorize that it can be coaxed to fight off a cancer. In the past few years, drugs based on this idea—which boost the activity of the immune system or trick it into attacking cancer cells—have begun to hit the market.

At the same time, targeted therapeutics are emerging that take advantage of the growing knowledge that scientists have gained about the genetics of cancers. When studies discover a particular mutation in a cancer cell's DNA that allows it to thrive, researchers can develop drugs that reverse the effects of the mutation, stopping a cancer's growth in its tracks.

> "the immune system is ready to attack cancers if we give it a nudge"

Levy and his colleagues wondered what would happen when they combined drugs based on these two approaches. While immune therapies are only effective in some patients, they can lead to long-term remissions. Targeted therapies, on the other hand, usually cause short-term improvements, but work in more patients.

"We thought that putting the two together had the potential to get the best of both worlds," says Levy.

So the team launched a preclinical study using anti-PD-L1 antibodies, an immunotherapy, together with the targeted drug ibrutinib.

Both of these drugs have been approved by the FDA and are actively being used in the clinic now. Together, the drugs were even more effective.

In mice with lymphomas, breast cancers, and colon cancers, the combination of anti-PD-L1 and ibrutinib shrank tumors and cured the animals. The therapies were revving up the immune system's T cells to successfully destroy existing cancer cells. Even in cancers that didn't respond to either drug alone, the combination yielded positive results. Moreover, the drug combination successfully taught the animals' immune systems how to fight off the cancers in the future: when new cancer cells were injected into the mice after their original tumor had disappeared, they successfully destroyed the cells before they formed a new tumor.

"It seems that what some people have been hypothesizing all these years—that the immune system is ready to attack cancers if we give it a nudge—is completely true," Levy says.

Now, the Stanford team is collaborating with the companies that produce anti-PD-L1 antibodies and ibrutinib to launch clinical trials of the drug combination in humans; seven trials are already in progress, including two that will be based at Stanford.

"I think this is the future of cancer therapy," says Levy. "I hope this will allow us to replace chemotherapy and all those bad side effects that they cause." ■

Applying the Science of Health and Wellbeing


John Ioannidis, MD, DSc

To date, wellness has been difficult to define scientifically because it encompasses all the delicate and exciting experiences that make life worth living. Physical vitality, mental alacrity, social satisfaction, a sense of accomplishment and personal fulfillment all contribute to wellness.

"Health seems like a no-brainer, but it is more than the absence of disease," says John Ioannidis, MD, DSc, director of the Stanford Prevention Research Center (SPRC). The Wellness Living Laboratory (WELL) is the flagship effort of SPRC, and it aims to draw on the strengths and insights of world-renowned researchers at Stanford, using the best that rigorous science has to offer in approaching this important concept. "There's clearly a lot of enthusiasm for obtaining actionable information about healthy living," says Ioannidis.

The SPRC is particularly interested in diminishing health inequalities and serving disadvantaged populations, thereby contributing to Stanford University's service to society. SPRC is a unique gem within the vibrant Stanford community. For nearly half a century, SPRC has been making leading contributions to the field of disease prevention.

WELL aims to be the definitive platform to investigate, promote, and extend wellness for people across the socioeconomic spectrum. Studies in genetic science suggest that less than a quarter of health is dictated by immutable genetics, leaving over seventy-five percent influenced by other elements, such as lifestyle choices. Great scientific strides have been made in managing disease; yet, the real question is how do we prevent illness in the initial state.

WELL will engage tens of thousands of volunteers—called "citizen scientists"—in two initial locations: Santa Clara County, California, and Hangzhou, China, with plans to expand to other sites as additional funding is secured. The citizen scientists participating in this effort will contribute information to improve our understanding of what makes lives healthier.

> "Health... is more than the absence of disease"

Santa Clara County was selected because it is one of the most diverse counties in the United States and is home to people of many cultures and income levels. This diversity provides unique opportunities for investigators to increase current understanding of the complex range of factors that affect the health and wellness of individuals and communities.

Although the benefits of economic development have created substantial gains in living standards, health outcomes, and health care systems, it has also created new health problems that cannot be solved through disease-focused investment, but only through emphasizing prevention and wellness at the population level. This dynamic is nowhere more evident than in China, where the rapid rise of obesity, diabetes, and other non-communicable diseases threatens hard-won gains in both health outcomes and social equity. "Researchers selected China because of its large population, rapidly expanding economy, and its concomitant growth of chronic disease," says Ioannidis.

The next generation cohorts of WELL that are being built in multiple countries will help dissect what affects wellness both for individuals and for large populations. Participants will be encouraged to engage in studies that will assess in a rigorous way diverse interventions that may be influential in shaping wellness. WELL's initial funding is through a gift from the Nutrilite Health Institute Fund provided by Amway.

WELL seeks to scientifically determine the interaction of relevant evidence-based wellness domains to establish best wellness practices to improve health and quality of life among all segments of populations, positively impacting individuals, communities, and policies by using the three-pronged approach of observation, intervention, and biology.

WELL's aim is to apply the science of health and wellbeing into concrete, scientific evidence that can improve the quality of our lives. WELL is a cutting-edge effort to define, redefine, expand, and materialize wellness. ■

New Plays to Tackle Inflammation and Infection

It's a natural—and usually beneficial—response of the human body to react to a wound or pathogens with angry, red swelling. A sore knee or stomach, while an annoyance for anyone, is a sign that the immune system is sending all its molecular soldiers to defend and repair an injury. But, around the world, there are times the immune system falters, letting infectious diseases take their toll on populations. Likewise, there are times the immune system becomes a belligerent, over-responsive army—lashing out at the body it's meant to defend when there's nothing to attack. In both cases, clinicians have struggled to develop ways to treat these conditions; the immune system is complex and has many unknowns.

Now, a new generation of researchers, including fresh faces in Stanford's Division of Infectious Diseases, are coming at the immune system, as well as invading pathogens, with new energy and new approaches. Their research has implications for conditions as common as diabetes and as globally far-reaching as tuberculosis.

In 2013, Paul Bollyky, MD (assistant professor, Infectious Diseases), launched his lab at Stanford to understand how the body responds to wounds and infections. He homed in on a molecule called hyaluronan, found in the nooks and crannies between cells, as being vital to mediating immune responses.

"You make hyaluronan in abundant quantities at the sites of injuries," Bollyky explains. "If you've ever twisted your ankle or gotten a bad burn, all that swelling and edema is basically caused by hyaluronan." The molecule, he's found, recruits both water and immune molecules to injuries. And blocking hyaluronan, his research team recently reported in the *Journal of Clinical Investigation*, can control chronic inflammation—the kind that's not benefitting the body at all.

Bollyky's basic findings have the potential to treat autoimmune diseases like multiple sclerosis, characterized by inflammation of the nervous system. And they also may revolutionize the prevention of something far more common: type 1 diabetes. In patients with this autoimmune disease, inflammation of the pancreas is an early precursor to more severe symptoms. Blocking the hyaluronan, and therefore the inflammation, Bollyky thinks, could slow the progression of the disease.

But while treating inflammation is one lofty goal, diagnosing infectious diseases can be just as tricky. Jason Andrews, MD (assistant professor, Infectious Diseases), is tackling this challenge. He's developing and evaluating low-cost diagnostic tools that can be used in settings like rural Nepal where electricity, water, and high-tech laboratories are hard to come by. These include an electricity-free, culture-based incubation and identification system for typhoid and an easy-to-use molecular diagnostic tool that does not require electricity. With his technology in development, Andrews is continuing epidemiologic research on diseases like tuberculosis to get a better handle on how they spread and what weak spots in their transmission cycles might lend themselves to intervention. ■


Paul Bollyky, MD

How a Pesky Parasite Impacts Africa

Stanford Assistant Professor of Medicine Marcella Alsan had always wondered why the mineral-rich African continent—with so many natural resources, diverse climates, and arable land—remains so poor.

She launched into extensive research while working on her PhD in economics and has now come up with an intriguing theory: A pesky parasite prevented many precolonial Africans from adopting progressive agricultural methods, a phenomenon that still impacts parts of the continent today.

The tsetse fly has plagued Africa for centuries—having sent millions of people into the confusing stupor of sleeping sickness, while killing the cows and other livestock needed to plow their fields and feed their families.

Alsan writes in a paper published in *The American Economic Review* that the tsetse fly, which today is found only in Africa, drove precolonial Africans to use slaves instead of domesticated animals for agriculture. This limited their crop yields and the ability to transport goods.

"Communicable disease has often been explored as a cause of Africa's underdevelopment," writes Alsan, who is the only infectious-disease trained economist in the United States and a core faculty member of the Center for Health Policy/Center for Primary Care and Outcomes Research.

"Although the literature has investigated the role of human pathogens on economic performance, it is largely silent on the impact of veterinary disease," she notes. "This is peculiar, given the role that livestock played in agriculture and as a form of transport throughout history."

The economic impact caused by the parasite of the trypanosome vector is estimated to be as much as $4 billion a year. The Food and Agricultural Organization estimates 37 African countries are affected by the tsetse fly and that its trypanosomosis kills around 3 million livestock per year.

The World Health Organization reports that the sleeping sickness delivered by the tsetse bite in humans is hard to diagnose and treat. Some 60 million people were once at risk with an estimated 300,000 new cases each year.

Sleeping sickness causes headaches, fatigue and weight loss; confusion and personality disorders occur as the illness progresses. If left untreated, people typically die after several years of infection.

Fortunately, sustained control efforts have reduced the number of new cases, dropping below 10,000 annual cases for the first time in 50 years in 2009. This is in part due to an eradication effort using radiation sterilization techniques adopted by the International Atomic Energy Agency.

But the lingering economic impact from the tsetse has been monumental.

For her research, Alsan used geospatial-mapping software to mine data gathered by missionaries and anthropologists in the 1800s. She found that farming methods used in other developing regions of the world—such as the agricultural revolution in England—were not widely adopted in Africa.

"They pulled plows and carried carts. Their manure was used for fertilizer," Alsan said. "They helped transport people and goods across land."

She found that ethnic groups inhabiting tsetse-prone African regions were less likely to use domesticated animals to plow their fields, turning instead to the slash-and-burn technique still used in many parts of the continent today.

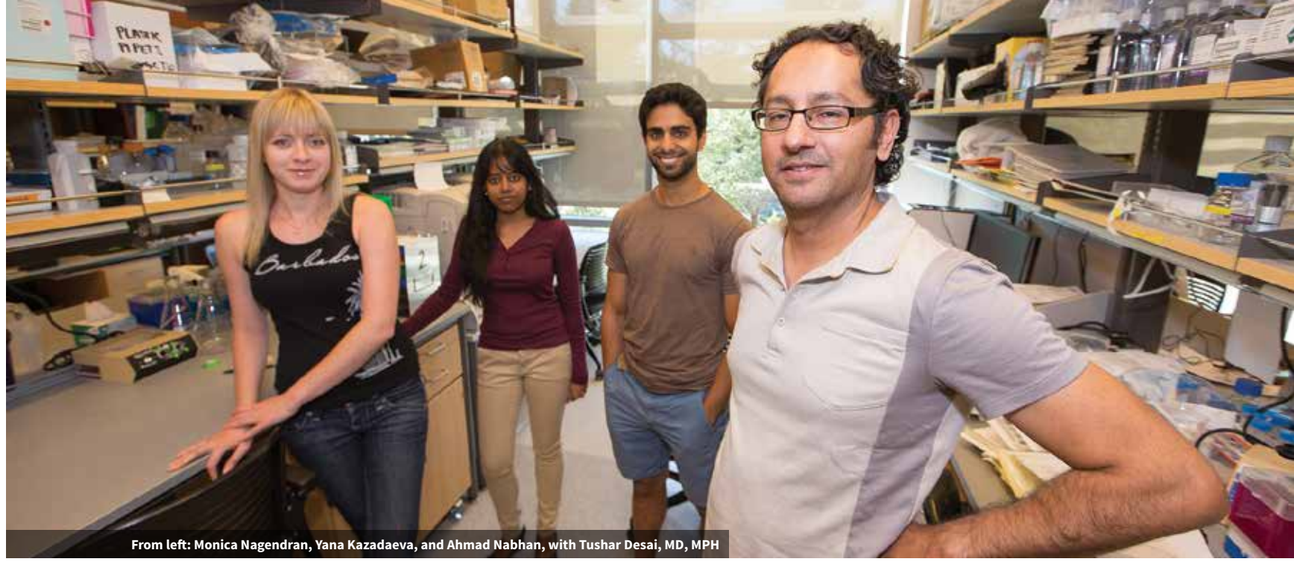
"These correlations are not found in the tropics outside of Africa, where the fly does not exist," she writes. "The evidence suggests current economic performance is affected by the tsetse through the channel of precolonial political centralization."

The FAO estimates that the tsetse fly infects nearly 10 million square kilometers in sub-Saharan Africa. Much of this large area is fertile but left uncultivated, a so-called green desert not used by humans and cattle. Most of the tsetse-infected countries are poor, debt-ridden, and underdeveloped.

And this is what triggered Alsan's interest in the tsetse fly: How its deadly bite has altered the socioeconomic impact of a continent.

"It's incredibly important to shine light on issues that are Africa-specific and therefore may not garner as much attention as those economic and medical issues that affect wealthier regions of the world," she said. ■

Lee Sanders, MD, and Marcella Alsan, MD, PhD, MPH



From left: Monica Nagendran, Yana Kazadaeva, and Ahmad Nabhan, with Tushar Desai, MD, MPH

Painting a New Picture of Lung Development

From the outside, the lungs develop like the roots of a plant; branching airways expand and grow increasingly more intricate, until they've filled every space they can with ever smaller passageways to capture oxygen from a breath of air. But inside the cells that make up these airways, an even more amazing molecular dance is taking place, one that creates new lung cells—as an embryo develops and, later, in adult lungs. It's only in the past few years that researchers have begun to understand the details of this story, thanks to an interdisciplinary team at Stanford. And what they're finding may allow clinicians to learn how to repair lungs in patients with conditions like emphysema and pulmonary fibrosis, or even treat lung cancer.

"You can take intermittent snapshots of what a tissue looks like as it develops, but to really understand it, you want to know what's happening at a molecular scale between those snapshots," says Stanford pulmonologist Tushar Desai, MD, MPH (assistant professor, Pulmonary and Critical Care). "To reveal that molecular level of development, though, is very painstaking, time consuming, and hard to get people excited about."

Most researchers, he said, have skipped from the visual snapshots of lung development to genetic experiments. By engineering mice to lack certain genes, and then studying the effect on the lungs, they can elucidate what genes and molecules are key to the process. But that's not the same thing, Desai argues, as understanding each sequential event in lung formation. So, after a medical fellowship in pulmonology and then a post-doctoral research fellowship in the lab of Stanford biochemist Mark Krasnow, MD, PhD (professor, Biochemistry), Desai made it his goal to paint a new, more detailed, picture of how lungs develop.

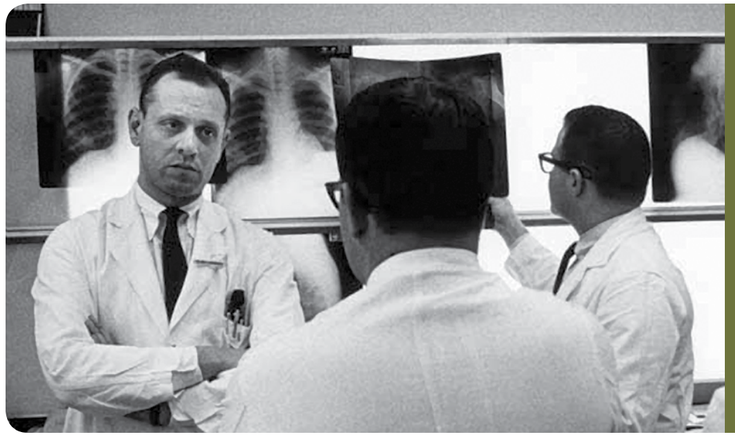
Inside each tiny airsac of the lung, two types of cells help the body breathe air. Alveolar type 1 (AT1) cells lie flat on the surface of each airsac, enabling the exchange of carbon dioxide and oxygen. Chunkier alveolar type 2 (AT2) cells studding the walls and ceilings produce surfactant, a fluid that coats the airsacs and keeps them from collapsing.

Scientists had previously hypothesized that progenitor cells in the developing lungs acted as the precursors for AT2 cells, and that some AT2 cells could then form from AT1 cells. But when Desai, in collaboration with Krasnow, traced the origin of lung cells, he discovered that a single alveolar progenitor cell directly formed both cell types. In the lungs of adults, however, these precursor cells were nowhere to be found. Instead, some AT2 cells acted as stem cells—able to form both new AT2 and AT1 cells. The results were published last year in the journal Nature.

"One of the most surprising things was that rare AT2 cells seem to be bifunctional," says Desai. "Not only are they acting as stem cells, but they're also apparently still secreting surfactant and keeping the lung functional that way."

Desai went on to capture the transcriptome—levels of genes being used by a cell—in precursor and newly forming AT1 and AT2 cells. By determining what genes are turned on and off during this dynamic process, he thinks he may be able to find the molecular switch that's flipped to generate new AT1 and AT2 cells.

Answering that question, Desai says, will not only satisfy his quest for understanding lung development, but could lead to new therapeutics for lung diseases. ■



Elevate the Culture of Clinical Care

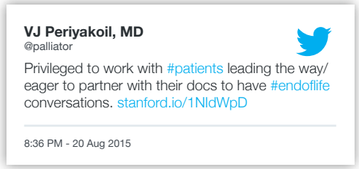
Saul Rosenberg
Stanford Professor and clinician

Started clinical trials for Hodgkin's disease 53 years ago that would lead to significant improvements in survival.

A Unified Vision for Palliative Care

Just as Stephanie Harman, MD (clinical associate professor, General Medical Disciplines), began medical school, her father-in-law was diagnosed with metastatic lung cancer, unexpectedly sparking her interest in palliative care. As his illness progressed, she accompanied him to his appointments; reviewing his treatment options, discussing how he wanted to spend his remaining time, and eventually witnessing his transition to hospice care. "I had this internal realization that this process was so important," she recalls. This realization stuck with Harman as she progressed through medical school and residency, where she continued to seek out hospice and palliative care training.

In 2007, Harman and a handful of multidisciplinary experts established Stanford Health Care's first-ever inpatient consultative palliative care service. As palliative care gained momentum and recognition in hospitals and health care system nationwide, the program experienced tremendous growth. "We've grown from three team members to over 25," Harman says, "and the number of patients we're seeing has more than quadrupled."



Today, Harman and her colleagues are working to scale up Stanford's infrastructure to address this growing demand. "We're in the process of building and designing a new inpatient hospice unit," she explains, "and we're partnering with a community hospice agency, Pathways, to create a program to help patients transition from the hospital to hospice." She continues: "We now have outpatient teams in three different sites, including clinics in our two Cancer Centers, led by Kavitha Ramchandran, MD (clinical assistant professor, Oncology), and our newest clinic at Hoover Pavilion led by Joshua Fronk, MD (clinical instructor, General Medical Disciplines). All of our teams reflect a multidisciplinary model to address the complex needs of patients and families, including physicians, nurses, social workers, and chaplains."

Across town, Karl Lorenz, MD, MSHS (professor, General Medical Disciplines), who is based at the Veterans Affairs Palo Alto Health Care System (VA), is waging his own campaign to change the culture of palliative care.

Lorenz's passion for these issues began in 1998, when he heard his mentor Joanne Lynd speak at UCLA about the failure of the SUPPORT study – an ambitious, $29 million effort sponsored by the Robert Wood Johnson Foundation to improve end-of-life care. Like Harman, he had a significant realization: "I realized for the first time that I was a bad provider of end-of-life care. But part of the reason was that I'd never received any training, and that I had never thought about it as an aspect of practice that I should be good at. I suddenly realized that I was going to have one crack at making a difference, and I wanted to be doing something that no one else was paying attention to, because I realized what a cost it had been in the past for my patients and me. And I didn't think that was right."

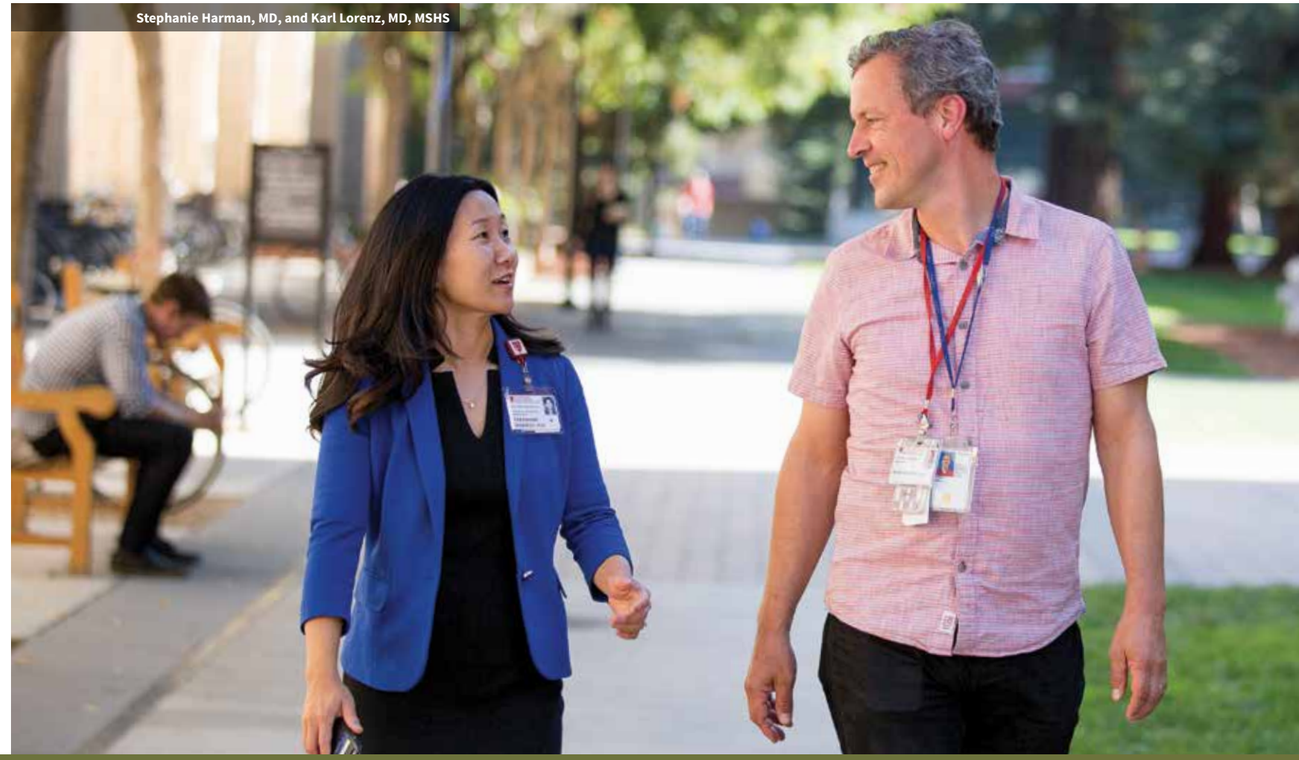
Lorenz committed himself to the field of palliative care, and began to work closely with leadership from the VA. "One of my earliest experiences was meeting James Hallenbeck, the associate chief of staff for Palo Alto VA, and sharing in some of the early meetings that established palliative care training programs through the VA's Office of Academic Affiliations," he recalls. Along with Randall Gale, PhD, an investigator at the Palo Alto VA, Lorenz now directs a national resource center that develops provider-facing informatics tools for the electronic health record to improve palliative care.

The VA and Stanford Health Care palliative care programs each bring great strengths to the table. "Traditionally the two programs have operated fairly independently," says Harman. "Collaboration will be a great opportunity to share best practices and resources, to learn from each other, and also to build up a much more robust academic section with research, education, and clinical programs." The teams are evaluating the current palliative care landscape to develop a core set of program priorities and goals. As Lorenz explains, "We're currently in the middle of an assessment process. One of our goals is to think through the advantages of our existing programs and resources and identify where the gaps are to prioritize some direction for us as a group."

They also have plans to expand education and training efforts and leverage new technologies to support palliative care. "This is a great opportunity to innovate and to think more broadly about using technology in palliative care training, education, and delivery," says Harman. Lorenz agrees, adding: "We'll get to test and identify the technologies and models of care that will best serve the needs of patients and their families."

Research is another key component of the combined VA-Stanford palliative care program. Several projects are already in the pipeline, including an examination of ways to spread palliative care within cancer practice by Manali Patel, MD (instructor, Oncology) and Risha Gidwani, DrPH (consulting assistant professor, General Medical Disciplines); and innovative research on end-of-life communication modes by VJ Periyakoil, MD (clinical associate professor, General Medical Disciplines). "We want to be doing cutting-edge research that is not only cited elsewhere but is adopted," notes Lorenz.

A robust and effective academic partnership will be a reflection of Stanford's commitment to palliative care, says Lorenz. "This will be an opportunity to think about what palliative care can really mean within the Stanford Health Care system. Veterans, patients, and their families all have much to gain from a growing program aspiring to excellence in palliative and end-of-life care." ■


Stephanie Harman, MD, and Karl Lorenz, MD, MSHS

The Future of Primary Care


Lauren Cheung, MD, MBA

If recent news headlines are any indication, primary care is at a crossroads. A combination of rising health care costs, antiquated care models, increased patient demand, and an anticipated shortage of physicians has stressed existing systems, creating what many refer to as a "primary care crisis."

In the face of this grim picture, health care providers are rethinking the primary care paradigm, coming up with new, innovative ways to deliver care and improve patient experiences. Stanford has been at the forefront of this movement, working to transform and revitalize the field.

Primary Care 2.0

Imagine a place where your health care is tailored to your lifestyle. Your minor medical issues can be handled remotely, your physician works with a multi-disciplinary team, and your care is continuous, affordable, and preventive. That's the idea behind "Primary Care 2.0," a new Stanford initiative dedicated to providing high-value patient care.

"Primary Care 2.0 aims to rethink and transform the way we practice," says Megan Mahoney, MD (clinical associate professor, General Medical Disciplines)."Today's primary care field is somewhat broken; patients feel that they don't get to spend enough time with their provider and that physicians are less focused on wellness and prevention."

The current system also puts a strain on providers. As Mahoney explains, "Providers feel very burnt out. Primary Care 2.0 has given us the chance to ask: How do we increase the value of what we're doing?"

Primary Care 2.0 is a blueprint for the future. It builds on Stanford's commitment to excellence in patient care while improving coordination of care, access to services, and patient experience. "It's more than a system, it's a new way of operating," says Mahoney. "It's flexible, so patients will be able to access us how they choose; it's proactive, so we'll be reaching out to patients between visits; and it's designed to ensure continuity."

Today, a team of physicians, designers, pharmacists, and others are working to bring this blueprint to life. The team is planning a clinic demonstration site that will be intuitively designed to incorporate the principles of the Primary Care 2.0 model. "For example, if a patient came in for a visit and they wanted to sign up for MyHealth—Stanford's web-based health management platform—we would have a tablet in reception for them to sign up, as well as a video that would walk them through the process. As soon as they registered, their information would be sent to their care team." Once the demonstration site opens, the Primary Care 2.0 team will continue to iterate their new model. "We'll be learning from our clinic," says Mahoney, "and we'll be able to improve and perfect what we're doing."

ClickWell Care

ClickWell Care, a new virtual online clinic staffed by Stanford physicians, is another innovation designed to upend the traditional primary care model. Armed with a laptop or a cell phone, patients who are enrolled in the ClickWell program can choose to meet with their doctors virtually, without having to take time out of their day to travel to a clinic. Or they can opt to meet their clinician in person. "ClickWell leverages technology to make care more accessible and convenient," explains Sumbul Desai, MD (clinical assistant professor, General Medical Disciplines). "We empower patients to connect with us in the way they see fit."

So far, the program seems to be working. "We've had really good traction, and a lot of return business. About 90–95% of patients who start with ClickWell stay with ClickWell." Providers have also expressed enthusiasm. "The mix of in-person, phone, and video seems to create less burnout for physicians. They find that it's a nice way to interact with their patients," says Desai.

Another aspect of ClickWell that has been well received is the virtual wellness coaching. Wellness coaches—usually fitness trainers and nutritionists—can work with patients to help them meet specific health goals, like losing weight or training for a marathon. They're also an integrated part of the patient's care team, and they work closely with the primary physician. "Patients can see a wellness coach as frequently as they want," says Desai, "and they're really able to see the coach as a partner in their overall health."

Inspired by their recent success, the Click Well team is now working to expand their program. "Going forward, we'll continue to test and tweak the model with larger patient populations." ■

A Good News Story*

It's not often that a story contains both good news and an asterisk. This article, about patients with life-threatening familial hypercholesterolemia (FH), is one such story.

> **Robert Harrington**
> @HeartBobH
> "@StanfordMed: Cardiologist Joshua Knowles discusses the potential of using #genetics to improve cardiac health: stan.md/1ERksGg"
>
> 5:24 AM - 26 Feb 2015

The sad truth is that over 90% of the estimated 1.3 million patients in the US with the genetic disease do not know they have it. Often the first sign is a fatal heart attack; sometimes it is quadruple bypass surgery in a person in only the fourth decade of life. The FH Foundation, a patient-led charity, was founded to address these critical problems. Joshua Knowles, MD, PhD (assistant professor, Cardiovascular Medicine), serves as the Chief Medical Advisor for the FH Foundation, which is a major driving force behind a project funded by the American Heart Association, the Stanford Data Science Initiative, and Amgen that aims to identify patients with FH. The project is being led at Stanford by Knowles and Nigam Shah, MBBS, PhD (assistant professor, Biomedical Informatics).

This project combined the skills of Knowles and Shah to create an algorithm capable of scanning electronic medical records (EMRs) and picking out FH patients. The computer "learns" what an FH patient looks like by being shown examples of true positive patients. Then it picks out other patients with similar "patterns" in the EMR. Knowles explains: "We can scan all types of data in the EMR (lab results, clinic notes, text, etc.), which is in itself exciting. Because we don't know the features of FH that it will identify as important, we also get insights into the disease process. Some will make a lot of sense (like LDL levels) while others will be head scratchers."

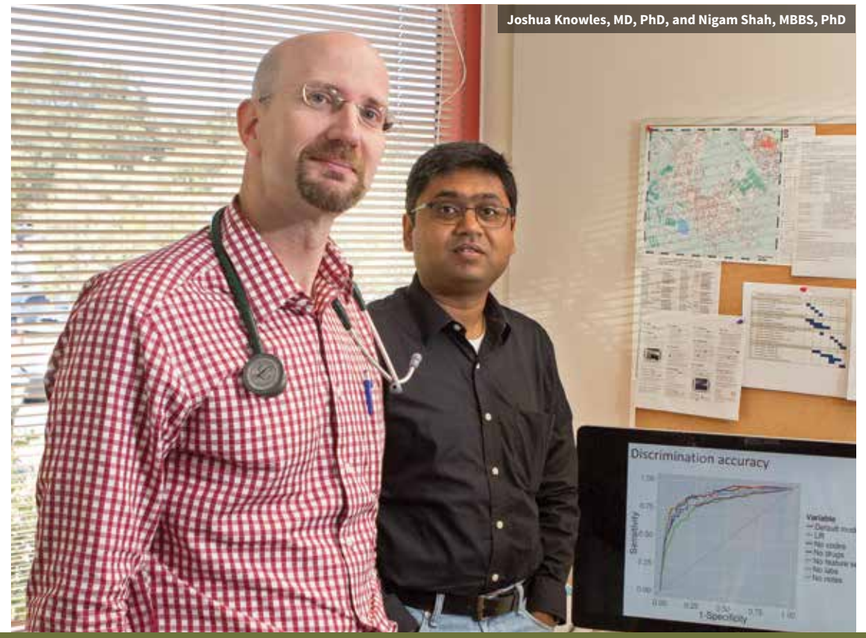
Thus far, the algorithm performs very well. According to Shah: "The preliminary algorithm works; there's no doubt about that. Now it's a matter of improving it, validating it, and figuring out where we use it."

Here the asterisk appears.

"We know that we can design an algorithm that can find most of the patients who have FH," says Shah; "the problem is with our tolerance for false positives, patients identified as possibly having FH who do not have FH. If I label somebody incorrectly, how much testing, physician visits, money,and energy are we going to waste? We also don't know physicians' and patients' tolerance level for a false positive diagnosis. These are the key issues we are working on now."

"In an ideal world the algorithm would be perfect," Shah continues, "but in the real world there are important trade-offs that need to be weighed. We hope that through a process of iteration with internal and external validation the algorithm will identify most FH patients while keeping false positives to acceptable levels."

> **Josh Knowles**
> @joshuawknowles
> Modern studies confirm Familial Hypercholesterolemia is responsible for thousands early heart attacks every year. nature.com/nature/journal…
>
> 8:54 AM - 3 Jan 2015



Joshua Knowles, MD, PhD, and Nigam Shah, MBBS, PhD

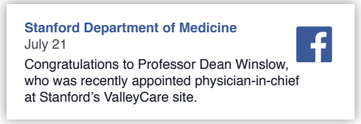
On the bright side, much progress has been made. Patients are being identified, beginning treatment, and entering a registry to follow them henceforth. Knowles comments: "The FH Foundation established a national patient registry called CASCADE FH in which Stanford is a leading participant. The registry is going like gangbusters, with over 2500 patients enrolled so far. An initial manuscript detailing the findings from the first 1400 people was recently submitted. The data are really eye opening."

Knowles explains further: "Most people are not diagnosed until their mid 40s; by that time a high percentage already have established coronary disease, so the horse is out of the barn. Even after being treated at leading lipid clinics, most people will have an LDL of about 140 mg/dl, much higher than we would like."

With the help of such compelling data, the FDA approved two drugs from a new class of cholesterol-lowering medications called PCSK9 inhibitors in August 2015. They are specifically targeted at patients with familial hypercholesterolemia, and that is a major step forward. Without an asterisk. ■

Merger of Stanford Health Care and ValleyCare Begins with the Start of a New Hospitalist Program

During a time of mergers and acquisitions in all manner of businesses, it should not surprise anyone to learn that Stanford Health Care has joined forces with a nearby community hospital. What might surprise, however, is the warmth of the merger and the excitement on both sides as the first new clinical program rolled out on August 1, introducing hospitalists from the Department of Medicine to the physicians, staff, and community served by ValleyCare, now known as Stanford Health Care - ValleyCare.



Stanford Health Care – ValleyCare's hospital of approximately 200 beds is located in Pleasanton, about an hour east of Palo Alto. According to John Yee, MD, an internist specializing in pulmonary and critical care medicine, the ValleyCare Physician Affiliate Group has had the responsibility for covering unassigned inpatients from the Emergency Department for years. During a year-long transition prior to the merger, "other health systems around us tried to grab whatever market share they could grab," he said. "We began to lose physicians, and our hiring process was frozen, so the remaining physicians not only had to cover the outpatients but also the unassigned inpatients of the physicians who left, in addition to their own outpatients and inpatients."

Yee took aggressive steps. "As CMO, I rallied the troops, pressing even older doctors who have been in practice for 20 or 30 years to help cover the ED. We basically had an all-able-body alert in our group." When the merger was completed in late May, as its first clinical program Stanford offered to introduce fulltime hospitalists. "It was a God-sent opportunity," said Yee.

Neera Ahuja, MD (clinical associate professor, General Medical Disciplines, and director, Stanford Hospitalist Program) has overall responsibility for the new program. She sees it as a win-win for both doctors and patients: "Now physicians can focus on spending time with their clinic patients and not worry about rushing to the wards early in the morning or at the end of their day to take care of sick inpatients. The patients, the nurses, and the ED physicians will now have a physician available to be at the bedside as needed throughout the day.

"Because this program falls under the Stanford Hospital Hospitalist Program, and I head that one, I asked one of our talented hospitalists, David Svec, MD, MBA (clinical instructor, General Medical Disciplines), to help lead the program at ValleyCare. I can't credit him enough," she said; "he's done an amazing job."

Svec has already found his business education to be helpful at Stanford Health Care - ValleyCare. He is a believer in workflow processes, high value care (the best quality care at the lowest cost), checklists, and growing correctly. "We intend to provide 24/7 coverage," he says. "Right now we are growing to that point, but it will take some time to ensure that we grow appropriately with both the academic and research missions of Stanford. I hope within 12 to 18 months we will be able to take care of a sizable majority if not all patients in the inpatient setting. That's our goal.

"On a day-to-day basis, we will have one hospitalist at ValleyCare all the time. We will most likely have several different teams eventually: a daytime team, a swing shift, and a nocturnist. We may also want to introduce a surgical co-management team, depending on the surgical volumes and if that is desired."

He continued: "Two hospitalists are currently onsite fulltime: Minjoung Go, MD (clinical instructor, General Medical Disciplines) and Alex Chu, MD (clinical instructor, General Medical Disciplines). Both of them went through Stanford residency, finished on June 30, and took their Boards."

One of the attractions for Go and Chu was being involved in a program that was starting from the ground up. Svec said, "Even during their Board preparation they helped out by creating templates and smoothing the workflow for the hospitalist team."

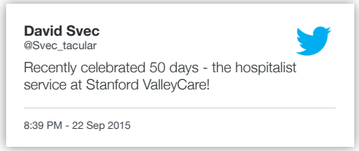
> "...the potential for continuing the educational mission of Stanford..."

For Svec, education follows right after patient care on his list of achievable goals. "One of the things about ValleyCare that excites me is the potential for continuing the educational mission of Stanford, having medical students, advanced residents, and physician assistant students train here."

Minjoung Go, MD, David Svec, MD, and Brittney Kendall, MHA, BSN,RN

After only a few weeks praises were being sung on all sides. But this successful rolling out of the hospitalists could not have occurred without additional help from Brittney Kendall, Manager of Strategic Initiatives at Stanford Health Care - ValleyCare. Kendall's role critically involves, as she says, "building out programs that add value from the perspective of our patients and driving communications among various disciplines in support of this vision."

Her role has been significant, according to Svec: "Brittney has been extremely helpful with data that we needed in order to properly plan and properly structure the hospitalist team. She's been able to find us the resources (a hospitalist workroom) and supplies (for example, a pocket ultrasound machine to enhance our physical diagnoses). She has helped us through the credentialing process, helped us understand what the current status is like, and helped us plan for the future."



Overall, the hospitalists feel totally welcomed. Svec describes it: "I have to stress how supportive everyone here has been. I can only imagine how difficult it is for them to have brand new faces as well as a new concept of care. Yet from Scott Gregerson (Stanford Health Care - ValleyCare President) on down—nurses, pharmacists, patients, physicians—everyone is willing to help, provide insights, support the team."

Given the auspicious introduction of the ValleyCare-Stanford hospitalist endeavor, it is not too early to ask how the team will define success. On their behalf, Svec responds: "When we are able to provide educational opportunities and research opportunities as well as excellent patient care in this uniquely different environment." ■

The Contemporary Approach to Managing Bone Disease

It's easy enough to take our bones for granted when everything is working correctly. In the normal course of events our bone tissue turns over regularly, with mature bone being replaced (through resorption) by new bone (through formation). Problems arise when our bone strength declines and we sustain fragility fractures.

In the Osteoporosis and Metabolic Bone Disease Clinic and in other venues, Joy Wu, MD, PhD (assistant professor, Endocrinology, Gerontology, & Metabolism) and Aimee Shu, MD (clinical assistant professor, Endocrinology, Gerontology, & Metabolism), see patients with a broad range of problems they are well equipped to manage. And they are increasingly working in a multidisciplinary fashion with colleagues in other divisions and departments.

Joy Wu, MD, PhD, and Aimee Shu, MD

Osteoporosis

Long considered a disease of aging, particularly of aging women, osteoporosis often first manifests itself as a fragility fracture sustained with minimal trauma. Particularly devastating is the elderly woman who falls and breaks a hip. Of approximately 250,000 such fractures in the US each year, only 100,000 patients return to normal life; 100,000 are thereafter bedridden and 50,000 die. It is clearly best that osteoporosis be prevented. If that is not possible, the best option is to treat it aggressively once it is diagnosed.

A history of fractures in the young increases the risk of hip fracture later in life. "Among patients who have hip fractures," Shu says, "more than half had a previous fracture, perhaps of a wrist. So taking care of early fractures and making sure that the patient's bone health is optimal may help to avoid devastating hip fractures later in life. If you want to build your bones, it's usually best around the time of your growth spurt for both men and women. We encourage our patients to be playing sports."

The best known and most used therapies for preventing and treating osteoporosis are the bisphosphonates, which reduce bone resorption. "This class of drugs has gotten a bad reputation," Wu explains, "because of two exceedingly rare occurrences associated with them: osteonecrosis of the jaw and atypical femur fractures. But osteonecrosis of the jaw occurs almost entirely in cancer patients, who are treated with much higher doses of bisphosphonates than are patients with osteoporosis, while atypical fractures are clearly associated with longer-term use of bisphosphonates. Our fear is that the rate of hip fractures, which had been declining, will rise if patients abandon these therapies, which are very effective at preventing fragility fractures."

To avoid atypical fractures from long-term use of bisphosphonates, endocrinologists today employ them with a more nuanced approach. Shu explains that "the evolving concepts are time of therapy initiation, doses used, and duration of treatment – perhaps three to five years – before we take a drug holiday. And then the question becomes: how long a drug holiday do we recommend?"

Osteoporosis is a common problem for women, but men are also at risk. About one-quarter of hip fractures occur in men. Wu says that it's easy to lose sight of how devastating hip fractures can be for men: "If anything, their mortality rates are even higher than women's. They are less likely to be treated appropriately yet more likely to die after hip fractures."

Joy Wu, MD, PhD, and Aimee Shu, MD

Multidisciplinary Interest in Bone Disease

Diseases of the bones pay no attention to specialty silos. Shu explains that this fact encourages teamwork, "including the relationships that we've built with other divisions in the Department of Medicine. For example, we have formed a 'Bones and Stones' program with the nephrologists since patients who have abnormally high levels of urine calcium are at higher risk for both kidney stones and low bone mass. We also work closely with our colleagues in rheumatology, oncology, gastroenterology, and of course primary care."

Important therapies used in rheumatology and oncology (glucocorticoids, for example) can have long-term adverse effects on patients' bones. Once these patients have survived their acute health threats, they need to attend to their compromised bone health. Shu explains, "We care for childhood survivors of systemic illnesses – leukemia patients and lupus patients, for example – and they often experience bone fragility sooner than their peers do. We strive to be proactive about protecting their bones sooner than when they are in their 80s and 90s.

> "We encourage our patients to be playing sports."

"In addition," Shu continues, "we share many patients with our surgical colleagues in orthopaedics, sports medicine, and transplant medicine. We even have a bone health clinic housed within the orthopaedics facility."

Novel bone therapies are currently in clinical studies and may debut in coming years. In the meantime, endocrinologists are making use of their current armamentarium in creative combinations and sequences. Wu explains: "There are exciting early studies about how denosumab (FDA-approved in 2010) and teriparatide (approved in 2002) can be used in combination or sequentially. We would consider the combination for patients who have very low bone density or a significant fracture history. Or perhaps for patients who are particularly young and we are concerned about their bones in the future. These are all very early studies so we are just learning."

Drs. Wu and Shu are encouraged by the many inventive ways they and their colleagues are able to optimize the care of their patients' bones. ■

Connect Science to the Clinical

Judith Graham Pool

Work leads to the discovery of cryoprecipitation allowing for the creation of blood clotting factors.

Mark Cullen, MD

Birthing the Center for Population Health Sciences

We are told to beware of moving parts, and those of us who value our digits and appendages wisely stay out of the way. In the new Center for Population Health Sciences, there are an infinite number of moving parts; standing there in the middle of them is Mark R. Cullen, MD, its director (professor, General Medical Disciplines), bringing order to this new venture.

All new academic endeavors have some similar needs: space, funds, staff, interest. The center has some of these, especially a lot of the latter. "There is incredible interest," says Cullen enthusiastically. "We are enrolling people who are interested in being affiliate members. We already have 350 from the School of Medicine, and we anticipate another few hundred from across the campus."

Together with Deputy Director Lorene Nelson, PhD (associate professor, Health Policy and Research), Cullen is creating "a place where health and other forms of data derived from large populations will be made accessible to Stanford faculty and staff supported by our curation services to assist investigators in finding collaborators and analytic support."

Working Groups

The fundamental unit of these collaborations is the working group, which Cullen describes this way: "What I imagine is that each working group will attract 10 to 12 people who are really interested in a particular project and another 10 or 20 who will be bystanders, watching everything on the intranet we are building to facilitate the work before they get engaged.

"We've got 10 working groups that we're about to spawn," Cullen continues. "Each targets a problem area or phase of the life-course where there are myriad unanswered questions about the origins of health and disease. Some examples are 'Sex Differences in Health' or 'Retirement, Disability, Cognitive Decline and Aging' or 'Immigration and Health.' It's hard to know how fast these and the others will gel, but I'll be disappointed if some don't begin to gain traction by the end of 2015.

"For every group, I'm trying to group faculty on the main campus with counterparts from the School of Medicine so that there are at least two very distinctive perspectives about what's important, and different research approaches."

Raw Materials

Some working groups have great ideas but limited access to data or populations ideal for study. Cullen has an answer: "We've already bought a big commercial claims set; we are negotiating with the Centers for Medicare and Medicaid Services to buy the Medicare set; and there are literally dozens of fabulous data sets around campus, including the Federal Research Data Center, that need only new coordination to become a researcher's dream."

Some more ambitious projects with groups both local and global are also underway. For example, Cullen points to the INDEPTH dataset, about which "we are actually sending a group to meet in Addis." INDEPTH has surveillance and demographic data on 52 discrete, large populations (10 to 300,000 people each) in 52 Southeast Asian and African countries. He continues: "A core agreement to facilitate exchange with the Danish Registries and Biobank has been executed and three pilot projects have been launched; we are having ongoing discussions with Santa Clara County to develop a health information exchange that will link electronic medical records on almost all county residents irrespective of which health care they use, and further link these to population-level data at the County Health Department. Recently we received expressions of interest from both Singapore and Taiwan about collaborating with their national health authorities, gaining access to additional data troves."

Cullen cautions that "some of these projects will take several years to mature, but that's the whole point. We want them to mature under the watchful guidance of the working groups so that people can mold what might come from them."

Cullen also has plans to support the working groups in novel ways. For instance, "When our intranet is up and going, we will start a resource exchange where people can post projects, ideas, opportunities for postdocs, requirements for a research assistant, etc. A student seeking a particular type of research experience could post that, hoping a faculty member might say, 'oh great, a student with nothing to do; just what I need for the new study.…'"

As grants are funded and donations received, Cullen will achieve another goal: "Someday I'd like to say to the leaders of the working groups, 'here is $5,000 or $10,000 to help you grow; here's a full-time staffer to help you write grants; here are two postdoc stipends; here's a stipend for a visiting scholar to come work with your group.'"

Space

For most academic centers, space is right up there with money as the biggest concern. So too for Cullen. "A lot of working group faculty have no proximity to each other. What would be truly fantastic would be if we had a building, where people in working groups could use a chunk of space; where, for example, every Friday morning the working group on 'The First 1000 Days of Life' could meet. There would be hotelling space, good coffee, and quiet group work areas."

Staffing

The center will not have a huge staff. Cullen explains: "I imagine we will eventually have 10 or 15 faculty who get some support from the center and a professional staff of another 20 people. We are shortly merging with the Office for Community Health, which already has a staff of 10. It will be the feet-on-the-ground link with the community health centers nearby, plus it will drive some of the education around population health."

Funding

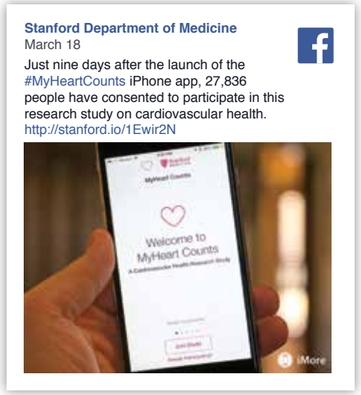
The Center received its initial operating budget from The Stanford Center for Clinical and Translational Research, Stanford Health Care, and the Dean of the School of Medicine, along with a future allocation of space and resources to attract new and promising faculty. The challenge is to develop a stream of revenue from grants, and through philanthropy raise the resources needed to become a sustainable fixture.

"We are trying to write some grants which themselves could generate immediate payback in terms of resources," says Cullen. "For example, we are responding to a request for applications from the National Institute for Minority Health and Health Disparities to develop a center focused on using tools of precision health to address health disparities. If we're successful, that would produce substantial resources to jump-start several working groups, including one on 'Health Disparities' and another on 'Gene-Environment Interactions,' as well as the Office for Community Health."

It is obvious this is a work in progress, with many moving parts and uncertainties. But the director of this center has dreams and enthusiasm and plans to make it all come true. "It's exciting precisely because it's not all pat and set in stone," he says. "There's so much opportunity for innovation, for experimentation, and for leadership and members alike to shape and mold those future dreams." ■

An App to Improve Heart Health

In March, Stanford cardiologists launched MyHeart Counts—a new mobile app that enables users to contribute to a large-scale study of heart health while learning about their own cardiovascular risk.



The public reception was overwhelming. To date, over 41,000 users have signed up for the free app and consented to participate in the study, and the number continues to climb. Apps may be a relatively new frontier of medicine, but they have the potential to reach large populations that traditional medical studies can't. "There have been larger research studies, particularly national efforts to study their populations, but we believe enrolling this many participants in such a short time frame is unprecedented," Michael McConnell, MD (professor, Cardiovascular Medicine), told *Stanford Medicine* earlier this year.

The goal of MyHeart Counts, McConnell said, is "to be the largest study of measured physical activity and cardiovascular health to date." He continued, "We want people to join in this research effort to give them personalized information about their heart health and help provide fundamental new insights into how activity helps your heart, across all ages, genders, cultures, and countries."

MyHeart Counts is one of the first five apps to use Apple's ResearchKit, an open source software framework specifically designed for medical and health research.

The app relies on questionnaires, surveys, and the iPhone's built-in motion sensors to collect data on cardiac risk factors, lifestyle behaviors, and physical activity. After an initial survey of basic health information – including age, weight, sleep patterns, daily exercise routines – users participate in a seven-day assessment of physical activity and complete a six-minute walk. Participants are then asked to check in with the app every three months.

Once users' data has been collected, it is then used for research. As McConnell explained: "There are two major elements to the study. One is collecting data as broadly as possible on physical activity, fitness, and cardiovascular risk factors, which provides important feedback to the participants and helpful research data for our study. The second is studying ways to help people enhance activity and fitness, and decrease their chances of heart disease."

Five months after its debut, researchers launched MyHeart Counts in Hong Kong and the United Kingdom. At the same time, they released a new version of the app that focuses on providing participants with more feedback about their individual behaviors and risk, and compares an individual user's fitness data to other participants.

"We are very excited to be able to take MyHeart Counts global," said Euan Ashley, MD (professor, Cardiovascular Medicine), a co-investigator for the MyHeart Counts study. "Cardiovascular disease is the number one killer worldwide, and we have an unprecedented opportunity to study risk factors such as physical activity, fitness, and sleep in countries around the world." ■


Alan Yeung, MD, and Michael McConnell, MD

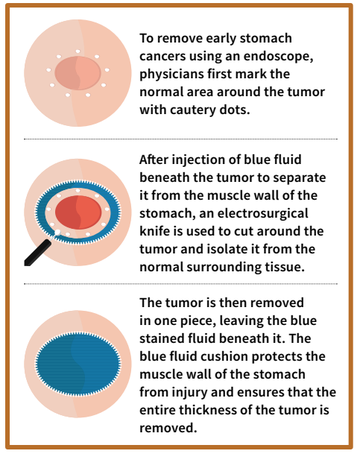
Endoscopic Submucosal Dissection

Curing Early GI Cancers Without Surgery


Shai Friedland, MD

Maybe it's the sushi, or maybe it's the Korean barbecue, but for some reason stomach cancer is more prevalent in Asia than in the United States. That's why 10 years ago doctors in Japan developed a minimally invasive technique called endoscopic submucosal dissection to overcome the technical limitations of removing early gastric (stomach) cancer with other endoscopic tools.

About two years ago Shai Friedland, MD (associate professor, Gastroenterology and Hepatology), began performing the procedure at Stanford. That was after Friedland met several Japanese and Korean pioneers of the technique, observed them perform the procedure in Korea, attended courses they had taught in the United States, and practiced the technique under their careful supervision.



To date, Friedland has performed about 50 cases, and he's currently collaborating with Dong-Hoon Yang, MD, a clinical associate professor at Asan Medical Center in Seoul, Korea, on a manuscript about a simplified endoscopic submucosal dissection technique in the colon. The two doctors are comparing the success of the technique at the two institutions, and they expect the paper to show that the technique is successful in both countries.

Because relatively few patients in the US have the stomach lesions that would merit the procedure, only a couple of doctors in this country have had an opportunity to perform endoscopic submucosal dissection, a procedure that usually takes one to two hours.

"The procedure is very challenging technically to perform, and it is relatively risky, especially for a doctor who is not very experienced in the technique," says Friedland.

However, the procedure has many advantages over standard treatment methods.

"The endoscopic technique that this replaces is known as EMR – endoscopic mucosal resection," Friedland points out. "That's a technique where you also inject fluid underneath the lesion, but you use a snare, which is like a lasso with an electric cautery, to remove one piece at a time until the whole lesion is removed. That technique is suitable for very small lesions or when you don't care about removing the lesion all in one piece. We use that technique with a lot of colon polyps because they're more benign than these stomach cancers, and it seems to work pretty well in those instances. But for earlier stomach cancer, EMR is really inferior to endoscopic submucosal dissection. In those cases it's important to remove the lesion in one piece, and those lesions are often fairly large—much larger than a snare can get."

Often when there are larger lesions in the stomach, the recommended treatment is a total gastrectomy, which is open surgery to remove the entire stomach and connect the esophagus directly to the intestine.

"While a total gastrectomy is not overly complex and takes only a few hours, it is generally very difficult for patients to live well and eat well after that kind of surgery. They've lost their entire stomach, which means they then can no longer eat large meals, they can't enjoy their food as much as they did before, and they lose a lot of weight," Friedland says.

Before development of endoscopic submucosal dissection it was only possible to remove relatively small lesions in one piece, which the Japanese found to be sub-optimal for early gastric cancers, according to the Stanford professor.

"Because we're just removing the mucosa—the inner lining of the stomach—the wound heals on its own in a few weeks, and the patient is basically left with a stomach that works as well as it did before. So that's really the great advantage of these minimally invasive treatments," Friedland says.

Endoscopic submucosal dissection is ideally suited for selected patients with pre-cancerous conditions or early cancer in their stomach, esophagus, colon, or rectum. ■

The Search for Uremic Toxins

Kidney dialysis has not changed much since it was first introduced to a broad public in the 1960s as a miraculous life-saving system to clean the blood when natural kidney function fails. Although dialysis continues to save lives, it does only about 10 percent of what a functioning kidney can do to remove toxic wastes (called "uremic toxins") from the blood stream. A patient on dialysis faces an exhausting and time-consuming process multiple times a week, with the prospect of serious health problems, from heart and bone disease to anemia, and a significantly shortened life expectancy once dialysis begins.

The problem is that after dialysis, patients continue to suffer from a previously non-existent, life-threatening disease that has been called "residual syndrome." Scientists now believe that this syndrome that strikes down dialysis patients is probably caused by as-yet unidentified toxic molecules that remain in the blood stream when they are not removed by dialysis. It is known that dialysis removes urea from the patient's blood, to alleviate symptoms after kidney failure.

What if dialysis could identify and target the remaining toxins, among the hundreds of "waste" molecules left in the bloodstream after urea has been removed, so patients could live longer, healthier lives after treatment. That has been the focus of a decade of investigations by Timothy Meyer, MD (professor, Nephrology), and new studies with his colleague, Tammy Sirich, MD (instructor, Nephrology). Both specialize in kidney research, along with the care and treatment of patients with kidney disease at Stanford and its affiliate Palo Alto Veterans Affairs (VA) Hospital.

Meyer and Sirich are determined to change the way that dialysis works.

"We think that dialysis patients still feel sick because many different substances could be removed by dialysis—but we have not yet identified which of those left in the bloodstream after treatment are the harmful ones," explains Meyer. "It is shocking that with all the technology at our disposal, we have not yet been able to identify exactly which chemicals are the ones that cause illness when the kidneys fail."

> "This is like searching for a needle in a haystack, to solve a major clinical problem in the field of kidney disease"

"This is a chemistry problem with a solution that can change the face of dialysis," Meyer says. "We were both chemistry majors in college, which predisposes you to go into nephrology to study the waste chemicals that the kidney cleans from the body." Their background in chemistry has led them to the current investigations.

It is Meyer and Sirich's goal to find new ways to establish the chemical identity of the specific molecules that make patients sick. Scientists have characterized over 200 molecules (called "solutes") that appear in high concentrations in the blood after kidney failure occurs, and there could be thousands more. It is known that certain classes of solutes are removed less well by dialysis than urea, including those that are protein-bound, relatively large ones, sequestered compounds, and substances removed by the normal kidney at rates higher than urea. But until recently, there were no good analytical tools to determine which of these were the uremic toxins—that caused patient symptoms and illness.

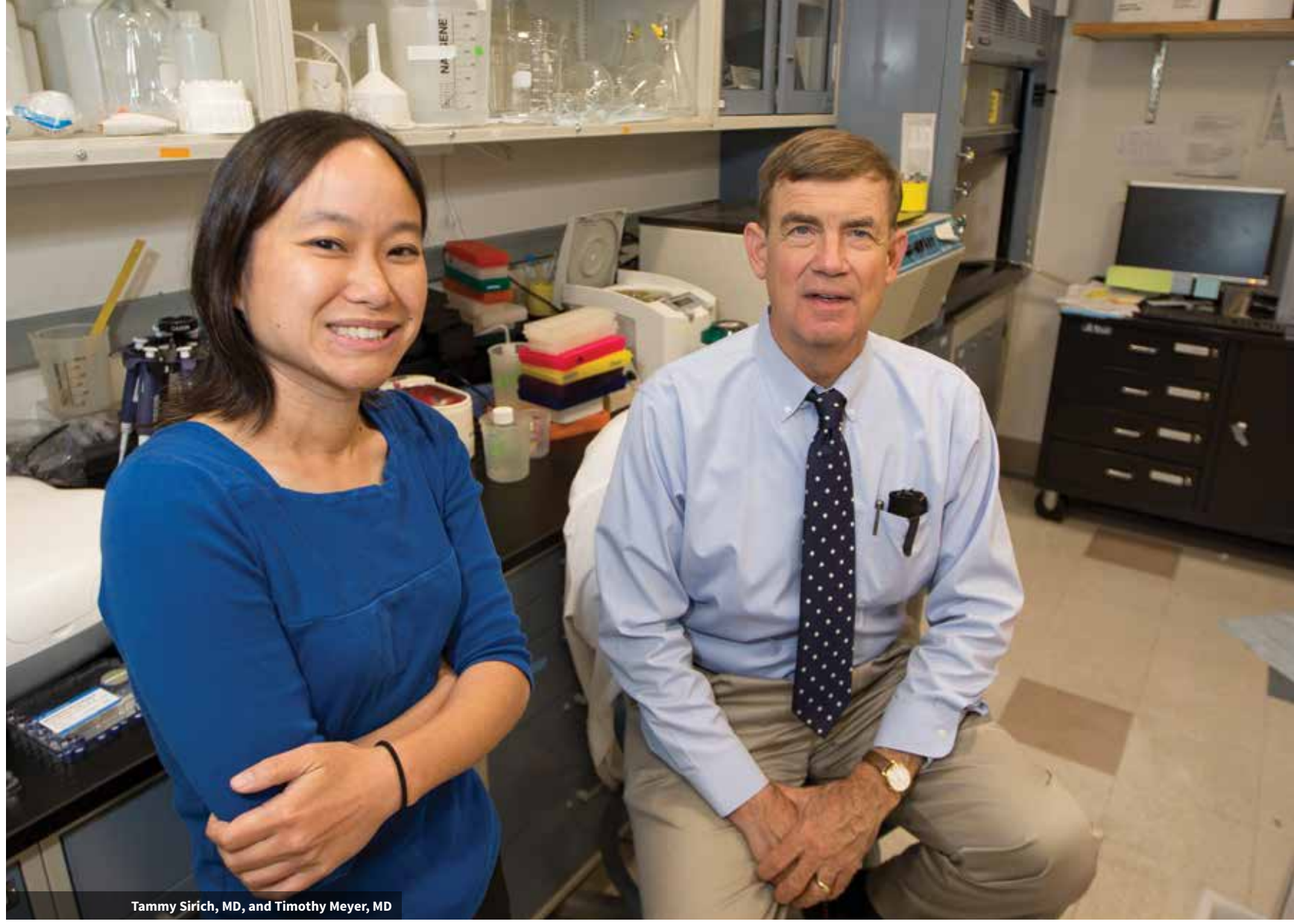
Meyer's research has focused on elucidating the cellular and pathophysiologic mechanisms responsible for the progression of kidney disease. His work includes studies of which molecules are toxic, how these are produced by the body, and how their production could be decreased or their removal could be increased.

Meyer and Sirich now want to identify the toxic substances causing harm in the bloodstream—to provide a more rational basis for prescribing dialysis to patients before they become seriously ill. Ultimately it could lead to improved treatment of patients with kidney failure.

The mass spectrometer is what first brought Meyer and Sirich together in their search for uremic toxins. Sometimes called the smallest scale in the world, the mass spectrometer is an analytical chemistry device with software and detection tools that can measure the size and volume of atoms and molecules. It can identify the specific chemicals in a sample.

"We were both interested in identifying uremic toxins, and we were both interested in using mass spectrometry to characterize the toxic solutes in the blood that were poisoning our patients," Sirich recalls.

Meyer had just acquired a mass spectrometer for his research lab when Sirich joined his team as a research fellow and chose "the search for uremic toxins" as her research focus. Together, they began to unravel the candidates for "most toxic solute" in the waste chemicals they found in samples from patients who were on dialysis, as compared with the compounds found in patients with healthy kidney function. They learned what mass spectrometry could do to identify the mass and abundance of the compounds they found. With a grant from the National Institutes of Health (NIH) in 2008 they began to study patient samples in a large dialysis cohort, and they have since received additional funding from the NIH and the Department of Veterans Affairs to continue their work in the field.



Tammy Sirich, MD, and Timothy Meyer, MD

"We use mass spectrometry to examine the biochemical garbage that is left after dialysis is done, and our goal is to sort out which streams of garbage—which solutes left in the bloodstream after dialysis—are causing so many symptoms for patients," Meyer says. They use sophisticated metabolic studies to identify and characterize small molecules in the blood, and then establish which ones appear in the highest concentrations in patients with kidney failure and disease symptoms.

Meyer and Sirich have characterized new solutes in the blood of patients after kidney failure, with their mass spectrometry studies of patient samples. The investigators have also employed untargeted mass spectrometry to identify ones that are protein-bound and that are most efficiently cleared by the kidney, and they believe that further analysis of those could indicate a route to the identification of other harmful substances.

Their studies to date have focused largely on two specific protein-bound molecules that may turn out to be uremic toxins in dialysis patients. Indoxyl sulfate and p-cresyl sulfate may contribute to cardiovascular disease in kidney failure; and indoxyl sulfate may also contribute to progression of kidney disease. These are among the large number of waste substances produced by colon microbes; and because they are made by microbes in an isolated compartment, they may prove simpler to suppress than other kidney waste.

A clinical trial that derives from this work, Dietary Maneuvers to Reduce Production of Colon-Derived Uremic Solutes, directed by Meyer, is now recruiting patients to evaluate whether dietary fiber supplements can reduce production of chemicals produced by colon bacteria that build up in the body in patients on dialysis.

Further studies and expanded clinical trials are the next steps in the search for uremic toxins. Although it is now possible to reduce the levels of some solutes by modifying the dialysis procedure or by limiting production, clinical trials must determine if these changes will clinically benefit dialysis patients.

"This is like searching for a needle in a haystack, to solve a major clinical problem in the field of kidney disease," explains Sirich. "But our studies could impact all the patients that we see every day at Stanford and the VA, and more than 350,000 kidney patients who are on dialysis in the US and beyond." ■

Educate & Train the Next Generation

Arthur L. Bloomfield

"His best teaching, and it was superb, came at the bedside where it was a memorable privilege and real pleasure to observe Dr. Bloomfield intent at his daily work."

Residents Create a New Curriculum for Future Hospitalists

Hospital medicine, whose practitioners are known as hospitalists, is a popular career choice for Stanford residents in internal medicine and also has been the fastest growing specialty across the country over the past eight years. Given the attention that such statistics can command, is it at all surprising that leaders of the residency program took it seriously when two of their residents suggested that a new curriculum be devised for those pursuing a career in hospital medicine?

Why is hospital medicine so popular?

According to Neera Ahuja, MD (clinical associate professor, General Medical Disciplines), there are several reasons; "In part I think it's because residents receive a good deal of exposure to hospital medicine during their training: through working with hospitalists in the clinical setting; with hospitalists being a part of many of the educational initiatives in the residency program (the Stanford 25, the pathways of distinction [PODs], the popular quality improvement elective led by Lisa Shieh, MD, PhD [clinical professor, General Medical Disciplines]); and as core faculty/mentors. So they know what they're getting into. And secondly, there's no additional training requirement." When residents graduate from their residency program, they are qualified to be hospitalists. As both the Director of the Stanford Hospitalist Program and associate residency program director, Ahuja is in a position to know.

Two second-year residents, Andrea Smeraglio, MD, and Andre Kumar, MD, came up with a proposal: what if we had a curriculum that residents could opt-in to, so that those who were interested in becoming hospitalists could take certain electives during residency to better prepare themselves?

Seeking data to back up their idea and to determine the amount of interest it engendered, the residents surveyed their peers, and the results of the survey helped to build the curriculum. Here are some pivotal results:

Areas of a potential hospitalist program that the residents defined as important:

90.9%	Mentorship
86.9%	Opportunities to teach
85.7%	Establishment of a hospitalist curriculum

Clinical rotations that were identified as important:

95.5%	Medicine consult
90.8%	Point-of-care ultrasound diagnostics
86.4%	Exposure to community practice

Interest was clearly keen among many residents, but balance was critical. Making mandatory changes to the internal medicine residency program to benefit future hospitalists would not benefit everyone. Out of this concern for balance came SHAPE, Stanford Hospitalist Advanced Practice & Education, a certificate-awarding program aimed at those resident colleagues of Kumar and Smeraglio who anticipate becoming career hospitalists.

"This curriculum is not the easy way out," says Ahuja. In addition to the usual rotations required of all residents, "there's an extra ICU month, some perioperative medicine which residents don't get a lot of exposure to, some neurology, and some consultative electives."

SHAPE is a three-year program, and there are expected to be five residents participating per year. After starting July 1, 2015, there are currently between eight and 12 SHAPE participants, including some interns who want to start preparing themselves now.

SHAPE has three foci. The first is clinical excellence, which will be achieved in part through the new curriculum. The second is academic advancement, which will include some targeted lectures, including a medical teaching workshop led by Kelley Skeff, MD, PhD (professor, General Medical Disciplines), and a course on the use of bedside ultrasound as suggested in the survey. The third is mentorship, also a key finding from the survey, in which hospitalist faculty will provide guidance in areas such as research, quality improvement activities, CV building and, ultimately, job applications.

The SHAPE curriculum includes a research requirement: a project and a presentation at an academic meeting. The project is designed to begin in the first year. Ahuja explains: "We will first hear what each resident is interested in; for those who are unsure about a topic, the mentors will make some suggestions and give them some options and let them choose one that suits their interests. Their mentors will help them start the project, maybe in quality improvement or medical education, maybe something a little more clinical. My hope is that in three years they'll do more than one project."

The key to SHAPE in Ahuja's mind is that it was resident-initiated. "This is a generation that is comfortable being vocal and empowering change," she says. "The housestaff have a voice and we are very open to changes that can help the residency program."

No one anticipates that SHAPE was born fully formed. As some elements fail to gain traction, they will be replaced with others of interest to the participants. It will evolve, says Ahuja, "according to the residents' voice. I really commend Ann and Andre for being creative and proactive about it."

"This is really an exciting time for hospitalists," explains Smeraglio. "The career, the training, and the opportunities are exponentially expanding. We want Stanford to be on the cutting edge of that growth, and with SHAPE I believe we will be."

Kumar adds: "We are hoping to train the best, and we have set the bar high." ■


Poonam Hosamani, MD, Andre Kumar, MD, Andrea Smeraglio, MD, and Neera Ahuja, MD

Abraham Verghese, MD, with symposium attendees

Inaugural Stanford Medicine 25 Skills Symposium

On his first day as an attending physician at Stanford, Abraham Verghese, MD, noticed something unusual. “I was struck by the fact that the house staff were spending a great deal of time wedded to their computers,” he recalled. “And it was not their doing. They didn’t sign on to do that.”

His experience reflects an increasingly common trend in modern medicine: With the introduction of new medical technologies, physicians today find themselves spending more time at the monitor and less time at the bedside.

Verghese recounted his story to a packed room of physicians and clinical educators who had traveled to Stanford from places as far flung as Brazil and Australia to attend the inaugural Stanford Medicine 25 Symposium.

The two-day event provided attendees with the tools to foster and encourage a robust bedside medicine culture at their home institutions.

The time is right, said Verghese. Today, many physicians and educators are advocating for a more hands-on approach to medicine. At the same time, an increasing number of bedside medicine programs are popping up at universities and hospitals worldwide. “I’m hoping that this is the moment when we all come together, and we stay together and connected in this effort to take what we all believe are fundamental and important skills—important to the welfare of the patient, important to practice cost-effective medicine, important in choosing wisely—and we form a community with solidarity around that theme.”

Throughout the symposium, participants learned the basics of evidence-based physical diagnosis from Steve McGee, MD, author of a textbook of the same name and a professor of medicine at the University of Washington. They learned how to schedule and program consistent teaching rounds and how to incorporate technology without losing connection with the patient. They also heard from Andrew Elder, MD, a professor of medicine at Edinburgh University and Junaid Zaman, MD, a postdoctoral researcher at Imperial College London and Stanford, about the MRCP PACES examination—a high stakes clinical exam that all medical school graduates in the UK must pass to continue their postgraduate education, an exam run and administered by Elder.

During an afternoon panel, experts from Johns Hopkins, Stanford, the Seattle VA, and the University of Alabama, Birmingham discussed ways to create a bedside medicine culture. Ideas included inviting master clinicians to teach at the bedside and hosting regular workshops. But, the panelists agreed, the support of community is critical. “It’s really hard to build a bedside medicine experience,” noted Brian Garibaldi, MD, of Johns Hopkins. “Community is key.”

> “I’m hoping that this is the moment when we all come together…in this effort”

In a series of breakout sessions, participants had the opportunity to practice exam techniques and to work together to develop their own 5 Minute Bedside Moment—a teaching vignette that includes both a narrative and a physical maneuver.

After an hour of brainstorming, they took to the stage with their stethoscopes and reflex hammers in hand. Presentations varied widely, from the gait assessment of elderly patients to pediatric oral examinations. One group chose to tackle opiate toxicity in hospice patients and also demonstrated ways to compassionately support grief-stricken family members. The audience gave each presentation their rapt attention, nodding their heads in agreement and recognition, laughing when a seasoned physician played the role of an unsure medical student, knitting their brows in concern, and furiously taking notes.

For many attendees, the symposium was a unique chance to interact and collaborate with like-minded professionals. “This meeting was a great model of what all of us should be doing,” said Ruth Berggrenn, MD, the director of the Center for Medical Humanities & Ethics at the University of Texas, San Antonio. “We should go back to our institutions, engage others, and train more facilitators.

And we should have a sense of pride and belonging in this movement.”

This feeling of connection and community lingered long after symposium co-director John Kugler, MD, offered his closing remarks. During the final reception, participants exchanged cards, contact information, and ideas about future collaborations. “You should give rounds at our institution,” one physician suggested to a new acquaintance. “I bet our residents would love to hear about the work you’re doing.” ■

John Kugler, MD, demonstrates clinical skills

Expanding Global Health Opportunities for Medicine Residents

In the last five years, the Department of Medicine has made global health education a priority by implementing a number of programs dedicated to reducing health disparities and strengthening human capital. Leading the charge is Michele Barry, MD, a pioneer in the field who was recruited to Stanford from Yale University in 2009 to assume a new position of Senior Associate Dean for Global Health at the School of Medicine and Director of Global Health Programs in the Department of Medicine.

Upon her arrival, Barry established the Center for Innovation in Global Health (CIGH), which has enabled the growth of global health educational opportunities and curriculum within the Department, and serves as a catalyst for interdisciplinary collaboration across the university.

"To have Stanford lead in global health medical education requires not just highlighting cutting-edge technologies and biomedical innovation, but also thinking about how we can implement these technologies to reduce the dramatic health inequities around the world," says Barry. "There's much we can also learn from our colleagues who provide care with limited resources while we help contribute towards building medical capacity in those settings."

> "It's an exciting time to be working in global health at Stanford"

While at Yale, Barry co-founded the country's first organized program to send physicians overseas in an effort to inspire a global vision of health care in a traditional internal medicine residency program. Known today as the Yale/Stanford Johnson & Johnson Global Health Scholars Program, or simply as the J&J Global Health Scholars Program, the program has mobilized almost 1100 physicians to underserved sites around the world. It has become a pillar of global health education in the Stanford medicine residency program, enabling physicians and trainees to work alongside their international colleagues at carefully selected sites.

Interest in global health has grown significantly within the Department; the number of residents participating in an overseas rotation has doubled within the last two years. In the 2015-2016 academic year, 23 medicine residents will participate in an overseas rotation, representing two-thirds of the PGY3 class. These residents will spend six weeks at partner sites in South Africa, Uganda, Rwanda, Indonesia, Zimbabwe and Ecuador, a new site established in 2015.

The experience provides physicians with invaluable skills training and a deep sense of cultural humility critical to practicing medicine in any setting. J&J Global Health Scholar Andrew Chang, MD, reflected on his rotation in Rwanda, which coincided with the annual commemoration of the 1994 genocide.

"I looked for signs of discontent, of division and resentment in my team. I found none. The trainees who had lost the most in the genocide were often my hardest workers, most committed to rebuilding the health

Andrew Chang, MD, during his Johnson & Johnson rotation in Rwanda

care system and caring for the underserved," wrote Chang. "Through our medication shortages, inconsistent laboratory, and inadequate procedure materials, I developed a respect for the resilience and optimism I saw in my Rwandan colleagues…I left Kigali impressed with the strength and generosity of the Rwandan spirit."

Chang is one of two physicians per year who match into the Stanford Global Health Track in the medicine residency program. Residents in the Global Health Track have up to 18 weeks of dedicated time overseas, participate in rotations and a Social Medicine elective at Santa Clara Valley Medical Center, as well as continuity clinic at Fair Oaks. Through these experiences, residents care for underserved patient populations locally and abroad.

They also have access to focused educational opportunities to build clinical and research skills applicable to global health. The flexibility of the track, along with its mentorship in developing a research career, led Chang to attend Stanford for his residency.

"We are increasingly seeing overseas rotations being incorporated into residency programs nationwide, but it can be challenging to fit a wide range of opportunities focused on caring for underserved patient populations into the rigorous rotation schedule," says Cybele Renault, MD, clinical assistant professor of medicine and Program Lead for Global Health in the Internal Medicine Residency Program. "One of the major draws of our Global Health Track is the amount of time residents are able to spend overseas and our ability to customize the program based on each individual's career aspirations."

Global Health Track residents also have the option to pursue a funded Masters degree during the year following residency, which allows them to gain a complementary skill set. Graduating residents have chosen to take a variety of career paths. For example, Global Health Track graduate Alexander Sandhu, MD, is currently pursuing a fellowship in health services research and development at Stanford's Center for Health Policy/Center for Primary Care Outcomes Research to support his interests in cardiovascular medicine, health economics, and cost-effective analysis research.

Laura Greisman, MD, is currently a PGY3 Global Health Track resident. With a passion for bedside medicine, she aspires to continue her training next year as a student in the Gorgas course in clinical tropical medicine, a nine-week diploma course taught in Peru.

The Global Health Track in medicine provides a framework for other specialties looking to establish more formalized global health opportunities in their residency programs. Through conversations with colleagues in other specialties, Renault recognized a need for increased communication and collaboration between departments. With support from CIGH, Renault helped create the Program Leadership Council, which brings together faculty representatives from each residency program on a quarterly basis to share best practices and key learnings in global health program development.

Interdisciplinary collaboration has been integral to Barry's mission since day 1. Looking ahead, she plans to build on the increasing momentum and excitement for global health within the medical school and across campus.

"It's an exciting time to be working in global health at Stanford," says Barry. "We are continuing to build on our interdisciplinary strengths, culture of disruptive innovation and commitment to research to be able to tackle some of the tough questions in achieving global health equity, but there is much more left to do." ■

Michael Mancuso, MD (second from left), with colleagues during his Johnson & Johnson rotation at the Alam Sehat Lestari clinic in Borneo

Mentoring Residents


Shriram Nallamshetty, MD, Angela Rogers, MD, MPH, Stephanie Harman, MD, Ronald Witteles, MD, and Neera Ahuja, MD

The latest class of internal medicine residents—50 of them—arrived on the Stanford campus at the end of June. They had just completed four rigorous years of medical school, and they were looking forward to the next phase of their careers.

Residency is an important time when newly minted MDs hone and develop their knowledge and skill. It's also a critical time for mentorship and guidance. Two Department of Medicine programs are specifically designed to support incoming residents and propel them into successful professional and academic careers.

Pathways of Distinction

Pathways of Distinction, or PODs, is a new initiative that allows residents to select one of several individualized pathways—clinical research, underserved populations/ global health, clinical teaching, primary care, basic/translational science, and innovation/biodesign—that best aligns with their academic and professional interests. Each POD is led by a senior faculty member in the department, and offers residents a host of opportunities, including lectures, courses, specialized rotations, and additional training. "The PODs allow residents to get extra mentorship and training, and provide a unique addition to their education that they wouldn't have the ability to receive elsewhere," explains Ronald Witteles, MD (associate professor, Cardiovascular Medicine), who directs the residency program.

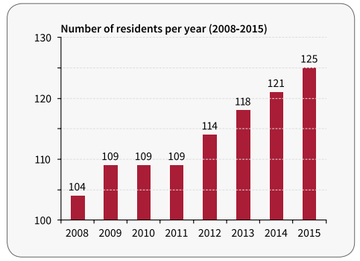
The PODs are also meant to encourage connection between residents and faculty. "As the program matures, residents can expect a growing sense of community amongst the participants as well as faculty."

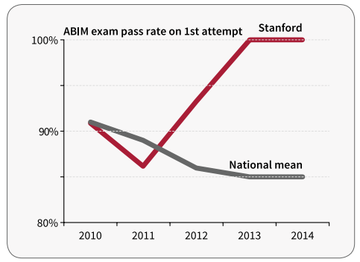
Though the program is only a few months old, Witteles says that preliminary feedback has been positive. "We've received a lot of informal, positive reviews from the residents so far. We recognize that it's a brand new program and we'll learn along the way. We'll undoubtedly make some changes, and we're extremely interested in hearing from both the residents and the faculty, but we're excited about this. I think it's going to be a great addition to the residency program."

Faculty Mentorship Program

A second opportunity is the department's core faculty mentorship program, which gives interns an additional layer of sponsorship and support. The program, which is now entering its third year, pairs first-year interns with a core faculty membership team comprised of one senior and one junior faculty advisor. This structure is valuable to residents, Witteles says, because it introduces them to a range of perspectives. "If you're a new intern, there are a lot of things you can learn from a junior faculty member and a senior faculty member. For example, one might be able to answer your questions about how to succeed on the wards, while the other might be able to offer broad, far-reaching career advice."

These mentorship groups meet quarterly throughout an intern's career, often at casual, off-hour events. "Though these meetings are meant to be informal, they provide an important opportunity for career guidance, and they create a real sense of community," says Witteles. "The faculty have really enjoyed getting to know residents in a less formal, unstructured setting."





Additionally, the mentorship program aims to encourage interns' scholarly pursuits and research interests. "One of the advantages of training at Stanford is the ability to work with faculty with the experience and enthusiasm for scholarly pursuits. It's easy for a resident to get caught up in the day-to-day of being a resident, learning clinical medicine. So we make sure to focus on linking residents with faculty members who can work with them on scholarly work early on. We believe it is our job and a key priority to make sure residents all have the opportunity to pursue and succeed in original scholarly work while they're here." ■

Department of Medicine Notable Events

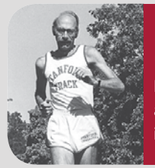
1909
First year of medical instruction begins with students to receive MD degrees in 1913

1925
Medicine Clerkship introduced for third-year medical students to provide practical ward experience

1950s
Characterization of hyperaldosteronism by John Luetscher

1964
Judith Graham Pool develops the technique of cyroprecipitation that would greatly improve care for hemophilia

1971
John Farquhar, Peter Wood, and other faculty/researchers in the department run first community-based program to use mass media to prevent heart disease/change behaviors



1975
Peter Wood and colleagues discover a link between exercise and increased HDL cholesterol levels

1987
First successful bone marrow transplant completed by Karl Blume

1914
Department of Medicine becomes the School of Medicine and includes divisions of medicine, neurology, psychiatry, jurisprudence, and dermatology

1954
Heart specialist David Rytand succeeds Arthur Bloomfield as the Department of Medicine Chair

1961
Internal Medicine residency program begins with Saul Rosenberg as the program director

1968
John Farquhar and Gerald Reaven discover that insulin resistance is the principal physiologic characteristic of mild type-II diabetes and obesity

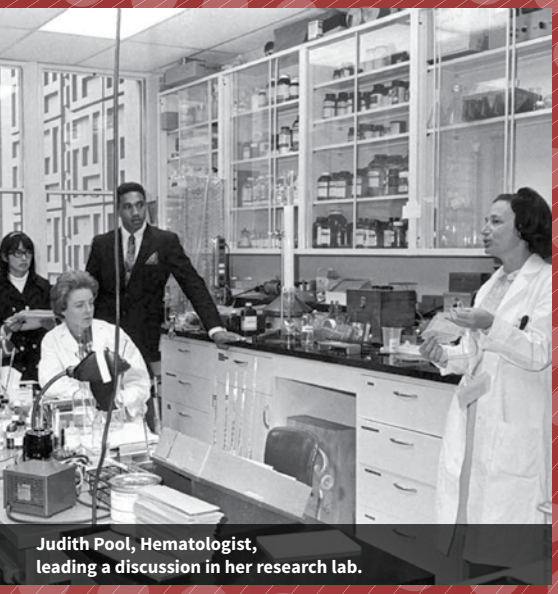
1972
Hugh McDevitt discovers regulatory genes that control the body's response to foreign proteins

1985
Kelley Skeff and Georgette Stratos first to introduce 'train the trainer' model in faculty development

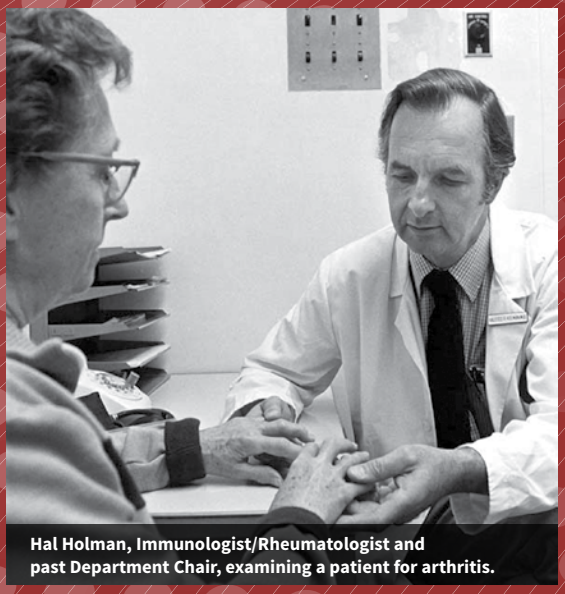
2009
Stanford holds first symposium on Bedside Medicine

Images courtesy of Stanford Medical History Center

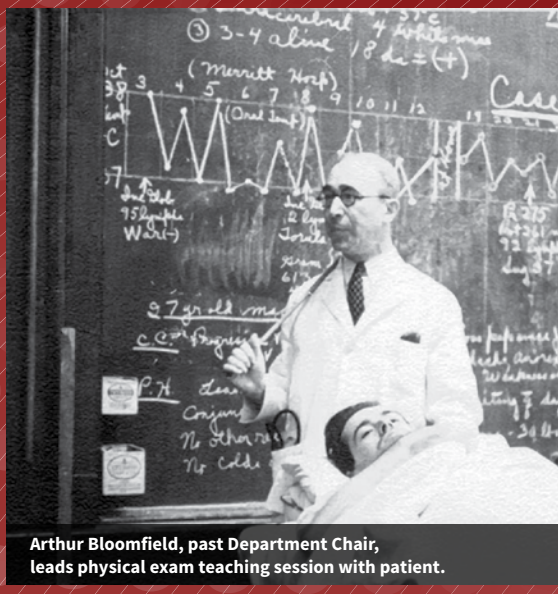
Building on Our Past



Judith Pool, Hematologist,
leading a discussion in her research lab.



Hal Holman, Immunologist/Rheumatologist and
past Department Chair, examining a patient for arthritis.



Arthur Bloomfield, past Department Chair,
leads physical exam teaching session with patient.

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