Collaboration

At home

In research

Treating patients

With trainees

Overseas

2017 Annual Report

Stanford MEDICINE | Department of Medicine

Department of Medicine in Numbers

15 Divisions

493 Faculty
(101 University Tenured and Nontenured Line, 101 Medical Center Line, 264 Clinical Educators, 27 Instructors)

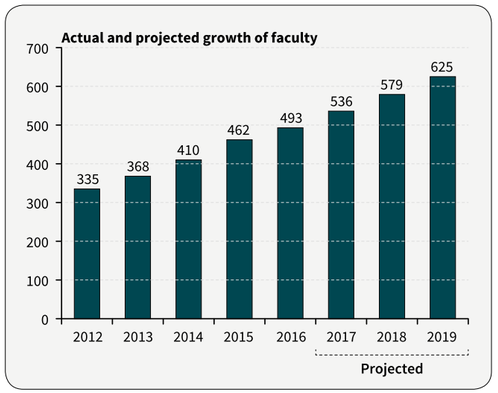
29 Endowed Professors

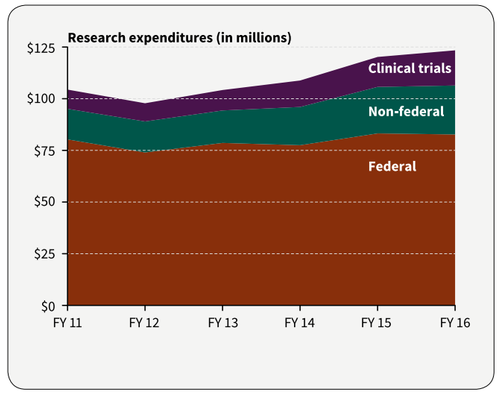
998 Staff & Research Associates
(542 Staff, 95 Research Associates, 361 Temporary Staff)

438 Trainees
(125 Residents, 154 MD Fellows, 159 Post-docs)

$124M Sponsored Research
($83 million in federal grants, $24 million in non-federal grants, $17 million in clinical grants)

477 Grants
(3 Program Projects, 58 R-01s, 35 Ks, 21 Us, 11 Training, 349 Non-Fed & Clinical Trials)





◀ On the cover: Collaboration is a key feature of the Department of Medicine. It is visible at home, in research, treating patients, with trainees, and overseas.

Welcome

Just about a year ago, you received the "2016 Report to Our Community." Because that was warmly welcomed and often complimented, we undertook another one. Now with a second report in two years, it's probably safe to refer to these as "annual reports." I'm happy, therefore, to share our 2017 annual report with you.

To select topics to include, I asked the vice chairs, division chiefs and various program heads to make nominations. This resulted in much more to write about than we had space for, so we culled until we reached a representative swath of the department, its people and the many outstanding programs.

Choosing a theme can take some time, but this year collaboration came quickly to mind. We are blessed with ideal geography, which makes it easy to find someone in another division or department or school on campus to work with. We have terrific colleagues to listen to our ideas who often find synergies between what we need and what they do. Collaboration is integral to our makeup.

Glenn Chertow proposed that we write about several members of his nephrology division who are married to Stanford physicians. This became our centerpiece article because it shows how critical continuous collaboration is to running four households, each headed by two doctors.

Several articles focus on the next generation of physicians. Faculty mentoring is one way our trainees learn the value of collaboration in academic research. Some residents take advantage of the Center for Innovation in Global Health's program to spend a rotation outside the United States. Ten residents are being trained in both internal medicine and anesthesia. The Capstone Experience is a weeklong program for senior medical students to help them make a smooth transition to residency.

Quite a few articles focus on individual researchers. Purvesh Khatri talks about how he explores potential clinical applications of his Big Data discoveries thanks to helpful colleagues with wet labs. Julie Parsonnet praises her research collaborators, while working with undergraduates in her role as a resident fellow in Robinson House – an entirely different level of collaboration. Donna Zulman describes the array of people and services she counts on to help her very high-risk VA patients. Kavitha Ramchandran talks about two different collaborative themes in palliative care.

Haruko Akatsu's writing about her U.S. medical education evolved into a well-received book and an invitation to help design an innovative medical school curriculum in Japan.

Jason Gotlib's study of idiopathic hypereosinophilic syndrome began in 2002 with a single patient and progressed through dramatic discoveries, to clinical trials, to successful treatment of patients with other diseases. Walter Park's research involves a 10-site consortium that researchers expect will help them learn much about diseases of the pancreas. Mark Genovese's research into inflammatory diseases has been improving options for patients since the 1990s. Crystal Mackall aims to make Stanford a leader in all facets of cell therapy. Mark Nicolls took advantage of the SPARK program to advance a discovery from his lab into clinical trials for pulmonary hypertension. Research from PCOR led by Jonathan Chen shows that over-prescribers of opioids are not just bad actors operating out of backroom pill mills.

Stanford Coordinated Care epitomizes team collaboration overseeing the health of university employees with multiple medical issues. A new master's degree in community health and prevention research has already stimulated collaborations among several schools and programs on campus. With Presence: The Art and Science of Human Connection, clinicians aim to collaborate among the seven schools on campus to ease the fractious relationship between physicians and technology. The new Center for Digital Health provides opportunities to collaborate with entities in Silicon Valley and elsewhere that crave creative medical input into their processes and products. And Stanford unveils its master of science program for physician assistants.

The collaborative spirit is evident across the spectrum of the Department of Medicine – in our research, when treating patients, with our trainees, overseas and at home, here in Palo Alto.

Sincerely,
Robert Harrington, MD
Chair, Department of Medicine

The Lives and Times of Two-Doctor Families

Dual doctor couples are not a novelty: A 2014 survey by AMA Insurance puts that number at 26 percent for physicians under 40 and at 18 percent for physicians 40 to 59. Nor are such couples unusual at Stanford, nor in the Department of Medicine, nor — as it turns out — in the division of nephrology. Among a faculty of 15, four members of the division are married to physicians, all at Stanford, none in nephrology.

Here are the four couples:

Fahmeedah Kamal, MD, clinical assistant professor of nephrology, and Robin Kamal, MD, assistant professor of orthopedic surgery.

Vivek Bhalla, MD, assistant professor of nephrology, and Kiran Khush, MD, MAS, associate professor of cardiovascular medicine.

Alan Pao, MD, assistant professor of nephrology, and Sun Kim, MD, MS, assistant professor of endocrinology.

Pedram Fatehi, MD, MPH, clinical assistant professor of nephrology and pulmonary and critical care medicine, and Kristina Kudelko, MD, clinical assistant professor of pulmonary and critical care medicine.

All eight individuals agreed to recent interviews, by couples, during which they answered a series of questions about their work and personal lives.

Meeting, Marrying and Having Children

Unsurprisingly, doctor couples tend to meet during medical school or post-graduate training. In the case of Pao and Kim, it happened earlier: "We actually met at Stanford," said Pao. "We were in the same undergraduate dormitory. It was my junior year, her senior year, and we were right across the hallway." The Kamals met in medical school and, as Fahmeedah Kamal says, "We were in the same group of friends, and one thing led to another." Fatehi and Kudelko were introduced by a mutual friend when both were residents in New York, at Columbia and Cornell. Bhalla and Khush met when they shared a patient in the emergency room at the University of California at San Francisco when she was a resident and he was a fellow.

These couples have been married between five and 17 years. One couple has three children, two have two and the Kamals were expecting their first just as 2016 was ending. Their children arrived between one and eight years after marriage.

▼ Sun Kim, MD, stands ready to help as Alan Pao, MD, cooks family dinner at home in Palo Alto.

The question "Is it crazy around your house in the morning?" provided the first hint at the difference children make in professionals' lives. The responses were both telling and amusing:

Khush responded, "Very; that's why we're speaking at 7 in the morning."

Kudelko said, "The answer to that is a resounding 'yes.'" Fatehi concurred: "Morning, evening…," then added: "The chunk of time after leaving work is the 'kid vortex': The hours between 6 and 10 p.m. fly by, dedicated to child maintenance, which is mostly but not always enjoyable, and no real work can reliably happen. During some of my attempts to put our 4-year-old son down for bed, he ultimately leaves his bedroom to go find Kristina to tell her that I've passed out."

Kim's response demonstrated skill at multi-tasking: "It's pretty crazy right this second. While we're talking to you I'm doing my daughter's hair." Pao extended the craziness to the other end of the day: "Pickup after school and making dinner and getting them to bed is another real crunch."

Those couples might read Fahmeedah Kamal's response with more than a little envy: "It's very peaceful. Rob's a surgeon so he gets up earlier than me most of the time. So he's pretty much ready by the time I'm getting ready."

Finding a Balance

There is much talk about the need for people to seek a balance between work and life. When both wife and husband are doctors seeing patients and doing research, the challenges are measurably greater. Here the individual responses to the question "How do you balance work and home?" were similar in tone but varied in the details.

Robin Kamal believes he and his wife succeed at finding balance "through good communication and time management. Sometimes I'm busier than she is and vice versa, so it just takes planning, most of it around who's going to make dinner." Fahmeedah Kamal reinforced her husband's sense of balance: "Right now it's all around knowing when he's busy and when I'm busy."

Humor appeared in the Pao-Kim response. Pao: "We have different roles. I am the one who focuses on the nitty-gritty, day-to-day school work, and I'm the one who cooks. And she… What do you do, Sun?" Kim's reply: "Alan has very clear roles and I try to do everything else: the cleaning, the laundry, getting everything ready for school, all the supplies, the doctors' appointments."

Khush sensed that "It's actually gotten more challenging as we've both gotten busier in our careers. At any one time one of us can be in the hospital or traveling or going to a meeting or giving a talk. The hardest part is when one of us is away." Bhalla felt that it's even more complicated: "We have to have work-life balance and work-work balance. That sometimes makes it quite hard."

Fatehi also focused on tensions that can arise. "When one of us is on service, the other knows that he or she will be the person doing the pickups and drop-offs for the kids and doing the extra stuff. That way we don't have to make the decision about whether to be with the family or the patient." Kudelko went on: "I am now super-efficient at work, meaning that I know I don't have the time I used to have at home to pick up my computer and review something. I plan my day so that work is work and home is home."

Roles Around the House

When asked if they find that they revert to traditional gender roles around the house, the universal answer was almost a resounding "no."

Kudelko said, "I will be responsible for grocery shopping and for cooking, sure. But Pedram is amazing in how much he does: laundry, garbage, diapers being changed, kids being bathed and put to bed. For sure I have a 50-50 partner." Fatehi jokingly clarified his household role a bit: "I also fix all the broken stuff, so maybe more like 51-49, with me doing more."

▲ Robin Kamal, MD, and Fahmeedah Kamal, MD, share a walk on the Stanford University campus.

Robin Kamal answered for both of them: "No, we don't, because of our work schedules. We balance ourselves around 50-50 for most roles, especially the dinner part."

The fact that the man does the cooking in the Pao-Kim household does not go unnoticed. Kim said, "Whenever one of the guys does something unexpected, he gets 10 times the credit. We're a modern couple trying to share the duties." Pao observed, "My male counterparts participate more, possibly not as much as they should, but I think it's definitely different from the older generation."

The Bhalla-Khush approach is different. Khush says that they "outsource a fair amount of housekeeping. Probably where our gender roles are most typical is that I do the cooking and Vivek does the cleaning up after meals. As far as child care I think we're pretty evenly balanced."

All four couples were then asked if they wished they had a stay-at-home spouse and, if they did, what would they have him or her do. These answers were all over the map.

The Kamals said no. Fahmeedah Kamal felt that "We've learned through communication to balance our roles. We've figured out a way to work together." Robin Kamal agreed, adding that "it makes it more difficult but more interesting to have the empowered spouses and occupations we have."

Fatehi and Kudelko also said no. Kudelko "derives a lot of joy doing the things that are very mommy oriented. I wouldn't want to hand that over to anybody."

▲ Pedram Fatehi, MD, MPH, and Kristina Kudelko, MD, catch lunch together at Tootsies near Stanford Hospital.

Fatehi sometimes feels that "I do more of those things if Kristina is busy with work or on service, and it's nice to be able to."

Bhalla and Khush don't quite agree on the answer. Khush quickly answered, "Yes, I could do with that for a while," while Bhalla said, "We need a personal family assistant. A lot has to happen between when we get home and when the kids need to go to bed. All that time is taken up by chores, sometimes including transport and homework. It would be great if we had somebody we could go to for the little things so that we could hit the high points with the kids."

Pao and Kim also had different answers from one another, although the effect of granting either of their wishes would likely be the same. Kim said, "I wish I did because it's hard to come home and have another job." Pao, on the other hand, wanted another helper. "Having a nanny would make our life much easier. For example, I get a service to drop off and pick up for soccer practice because I can't always do it and Sun can't always do it."

The Biggest Chore: Cooking

We've already learned that the cook in the Pao-Kim household is the dad, but even he was perplexed by the question, "Have you ever used Blue Apron or another service that provides ready-to-cook meal ingredients and recipes?" Pao responded that he does not use an apron and that's why he has spatters on the front of his shirt. His wife clarified, "We used a cooking service once, and we found it very limiting and very expensive."

There was no uniformity in the responses to questions about cooking.

The Kamals cook at home four or five days a week and who does the cooking depends on who gets home first. "Most of the time we try to cook together," said Fahmeedah Kamal. Her sister gave her a week of Blue Apron and she liked it but missed having leftovers. So now they "use their recipes and buy a larger quantity so we'll cook one day and then have leftovers the next day." Robin Kamal felt that Blue Apron "taught us that there were recipes that we hadn't mastered. So now we're able to create our own. The quality of the food is better."

The Fatehi-Kudelko household depends on Kudelko to do the cooking most often, usually four times a week. Kudelko really likes Blue Apron: "It makes me feel like I'm a cook when I'm really not. The most stressful part is planning and shopping; Blue Apron delivers those ingredients and just allows me to cook. That's the most fun part for me."

The Bhalla-Khush couple decided on roles around cooking early. Bhalla explained that "Before Kiran and I married she told me that she liked cooking but she never cooked because she hated cleaning up. And I don't mind the cleanup. So Kiran does 99 percent of the cooking and I do 99 percent of the cleaning." Khush said, "We try to prepare pretty much all of our meals at home. It's rare that we go out to eat, and we never order in." Nor do they use Blue Apron–like services.

Date Night

Take the busyness that any two professionals in a couple might have and layer on critical illnesses, emergency surgeries and deadlines for grant applications on which one's livelihood for the next several years depends, and a question like "How often do you go out on a date?" might fall somewhere between silly and preposterous. But married couples need "us time," just as individuals need "me time."

Once again the responses were as varied as the couples, although two couples recently hit on a clever twist on date night.

The Bhalla-Khush duo have a routine. Khush says, "We have what's called our Big Four, four nice dinners that we do every year: my birthday, Vivek's birthday, Valentine's Day and our anniversary. Other than that, the evening is really our family time, so we try not to spend the evening away from our kids." Bhalla pointed out that they recently "went out on a lunch date to a very fancy restaurant. Didn't have to get a babysitter, didn't have to take time away from the kids in the evening, and got to go to a nice restaurant when it wasn't all that crowded."

Fatehi and Kudelko take advantage of a service their day care offers: monthly parents' night out. "That's an evening date out to dinner when our kids stay late at day care," said Fatehi. "Because we have the benefit of working so close together, we meet occasionally for lunch dates and have a few quiet moments without kids."

Kim and Pao struggle to find time for themselves. Kim said, "We lack the date night aspect. We do a lot of things with other families on weekends. We have family date nights."

Robin and Fahmeedah Kamal defined date night a bit differently. Fahmeedah Kamal said, "We hang out together a lot, cooking together at night or going for a run or a hike. All those are date-like activities. Not having kids, we're together a lot and do a lot of activities that are dates in a sense."

If they had the opportunity to have a date night, what would each couple do with it?

Bhalla and Khush would go out to dinner: "Vivek and I both are kind of foodies, and we both like going out to a nice restaurant," said Khush.

Fatehi admitted to being "sleep-deprived enough that it's not as though we would want to be out at a raging party all night long." He continued, "Usually a chance to go to happy hour with friends and then have dinner and go home by 10:30 is enjoyable and satisfying."

In answering this question, Pao recalled that he and Kim actually went to a concert last month. "It was date night with another couple."

The Pluses and Minuses of Being in a Dual-Doctor Relationship

There is so much need for planning and strategizing in two-doctor families that a final question arose: What is the biggest advantage and biggest disadvantage of being part of a dual-doctor family?

Pao responded: "The greatest thing is instant empathy and shared experience. My wife always knows what it's like to have a bad clinic day or get a grant rejected. For me, the greatest drawback is time — not enough time for work, family and spouse." Kim pointed out another drawback that most of the parents mentioned at one time or another: "When you have a dual physician couple, there is not much reserve. When something unexpected happens — your child has a fever and needs to be picked up from school — it can unravel a delicate system."

Fahmeedah Kamal said the biggest advantage is that "It is fun to talk to Rob about my day because he has an understanding about what I do." Robin Kamal declared that "Being in a dual-doctor family can be awesome when you appreciate it for what it is. Our shared understanding of our professional demands makes it easy to relate to one another." About the disadvantage, Fahmeedah Kamal responded: "We both can be busy with demanding schedules especially when we are on call on nights and weekends." He responded similarly: "Time. This isn't something that can't be overcome with thoughtful planning and establishing priorities, but it requires work."

Kudelko responded: "Truthfully I never thought I was going to marry a doctor because of the potential drawbacks. I was considering the usual, you know, lead guitarist or professional tennis player," she continued jokingly. "But now I'm so happy I did. He gets it. Hard days, complex patients, unexpectedly long call days. No explanation necessary. We often talk about interesting medical stuff at home. The biggest drawback is juggling the scheduling. We miss out on a lot of time as a family because of weekend calls."

Khush said, "One of the greatest things about being married to another doctor is the intimate understanding of each other's daily lives and careers. We discuss interesting and challenging cases, hospital news and gossip, what happened in clinic or on rounds." As for the drawback, "I think a challenge particular to dual-doctor couples is how to coordinate call schedules. We have to make sure we are not on service at the same time, in case a patient emergency arises and we have to return to the hospital. Since one of us is often on call over the weekends, it becomes difficult to have weekends together as a family."

Despite the stresses of being a doctor times two, all appreciate the value of their marriage. As Bhalla pointed out: "If not for the fact that we are both physicians, I might not have found Kiran. For that I am most grateful."

▼ Family time is valuable for Vivek Bhalla, MD, and Kiran Khush MD, who play with daughters Amira (3) and Rania (7) and son Zain (9) at home.

Improving Palliative Care at Home and Abroad

> "All patients should have the best care possible throughout the trajectory of their illness from the point of diagnosis through treatment, through survivorship to the end of life."

It is not unusual to learn that such words came from a physician whose expertise is in oncology and whose interest within that specialty is palliative care. What is unusual — and really fortunate — is how Kavitha Ramchandran, MD, clinical assistant professor of oncology, has sought to improve the patient experience both institutionally and globally.

PathWell Serves Stanford Patients

Ramchandran and her team at Stanford developed PathWell. It is an access hub in the center of 26 spokes, each spoke representing a separate service available to improve all aspects of the health of cancer patients and their families. Many of the spokes are not new; some have been around for many years. Examples of these spokes include the adolescent and young adult program, spiritual care, integrative medicine survivorship, and smoking cessation. What is new is the access hub. It's a single point of contact so that, as Ramchandran says, "patients and caregivers will know what services are available, and those services can be matched to their specific needs."

Prior to PathWell, after patients with cancer met with their clinical team it really was up to them to navigate a web of services to help with additional needs such as management of symptoms or psycho-social support. This often occurred when the patients and families' ability to absorb and adjust to the reality of a serious illness was all that they could handle.

Ramchandran developed PathWell as a solution to this quandary, a way to create unique plans of care suited to each patient and family's needs. Ramchandran explains: "Being able to understand what those needs are is foundational to cancer care, whether this is a thorough financial assessment, a psychosocial assessment, an understanding of what their spiritual needs are, or what their kids are going through. It is really looking at the whole person outside the lens of his or her disease."

With the creation of PathWell, the focus for patients can again be on their illness. Likewise, clinicians no longer must refer patients to seven or eight services; now they can make one referral to PathWell. At that point, Ramchandran says, "Our nurse does an assessment of the patient and family and then recommends the additional services that will be most helpful. We then close the loop by talking with the clinician about the assessment and which referrals were placed."

The leaders of the 26 services come together for PathWell conferences, meetings similar to tumor boards where patients and their care are discussed. The focus of the conference, Ramchandran explains, "is primarily on the psychosocial health and management of the patient, not the management of the patient's disease." As a side benefit, the conferences provide an opportunity for different services to learn from one another. For example, Ramchandran mentions a case where one service might be struggling with managing a patient's pain in part because of co-existing cognitive changes. With PathWell it is simple to ask someone from neuropsychology to conduct an evaluation to figure out what resources the patient needs, which can make the treatment of the pain more feasible.

Ramchandran draws an analogy using some thoughts that Paul Kalanithi, author of *When Breath Becomes Air*, articulated before his death in 2015. Ramchandran recalls, "He talked about the little p and the big P, with the little p being palliative care as delivered by your primary care doctor and your oncologist, who ask how you are and what your goals are for the day and how your pain is. Big P is that physician saying, 'I'm a little bit outside my scope and I need some help. I want to make sure your quality of life is as good as possible and I'm going to call the expert to come in and make sure that we've got everything that we need for you.'" Big P, she says, "is these 26 organizations working in collaboration. Palliative care is one component and PathWell comprises a very complex and smart group of people who have different skills and are committed to improving the patient experience in different ways."

Ramchandran's goal? "In a perfect world," she says, "every patient will have a PathWell plan of care. It will include certain services that are right for them, and those will be incorporated automatically as they go through their process."

An Online Course for an International Audience

In addition to this focus on palliative care at Stanford, Ramchandran also enabled people around the world to learn more about the discipline through an online course that she created, Palliative Care Always. An anticipated initial audience of 500 participants ballooned to 1,250 from more than 80 countries, and the course was greeted with considerable enthusiasm. Ramchandran and her team have summarized their work in a variety of settings, including international meetings, foundations and patient forums. Now they are thinking through how the course may impact palliative care in resource-poor settings and how it might influence health care systems in a positive way via novel access to primary palliative care.

"What was profound to me," says Ramchandran, "was the excitement of a global connection around a shared common experience, thinking about health and wellness and living with dying, connecting with people around the world, having your stories heard, and feeling that there are people who want to share them."

The course was relaunched in September 2016, incorporating some of the findings from the first iteration. Ramchandran notes, "We will be doing a focus on advanced communications skills and advanced symptom management, as well as a section on support for caregivers and family members, which was lacking in the original course." The course, which is free, is also being offered for continuing education credits.

Working with Limited Resources Teaches Humility in Medicine

Throughout the academic year, many Department of Medicine residents and faculty spend time working overseas or hosting international collaborators on campus. Facilitated by the Center for Innovation in Global Health (CIGH) under the direction of Michele Barry, MD, global health programs in the department aim to equip the next generation of physicians with clinical skills, cultural sensitivity and contextual perspective to improve the health of underserved communities worldwide.

More than 60 trainees and faculty traveled to sites in 13 countries during the 2016 academic year. They extended Stanford's global impact and fostered new and old collaborations with partner institutions around the world. The following stories illustrate how each site is unique, with a range of clinical and cultural experiences:

Ecuador: Cultural Immersion through Medicine

Baldeep Singh, MD, clinical professor of medicine, traveled to Riobamba, Ecuador, in 2015 to explore training opportunities for residents at local hospitals and clinics, and a way for Stanford to bring needed clinical knowledge to the region. There, in the Andean highlands, he worked with local physicians to construct a six-week rotation in which residents split their time between providing inpatient care at local hospitals and visiting the Cacha community clinics, which serve a vast area of indigenous groups. Residents also take medical Spanish classes and live with local host families.

"Participating in the CIGH Ecuador rotation was one of my most fulfilling experiences in residency," said gastroenterology fellow Aarti Rao, MD. "With limited resources and large hearts, the physicians in Riobamba treated their patients like family. They reminded me of the importance of the art of medicine and the patient-doctor relationship as an integral part in treating a patient."

Borneo: Health for People and the Planet

Along the Western coast of Borneo lies Sukadana, a rural village neighboring the largest and most diverse orangutan park in the world. Poor health and poverty in the region push villagers into illegal logging and rainforest destruction to pay for basic needs.

Each year, a select number of residents spend six weeks working at the Alam Sehat Lestari Clinic in Sukadana, which was founded by a former trainee of Barry. The clinic provides health care to local residents in exchange for their commitment to conservation. Jessie Kittle, MD, clinical instructor of medicine, visited the clinic as a resident in March 2016.

At first, Kittle felt uncomfortable being without her usual tools and interventions, fearful that her "digital-doctoring skills" had replaced her human ones. As the days passed, she gained confidence.

"I felt deep satisfaction in facing a patient, both of us barefoot, using hands, eyes and ears to peel through layers of medical and human knowledge to craft a diagnosis and treatment plan that worked for the patient," said Kittle. "This was health care not just of people but of the earth, and has provided me with endless inspiration for working toward a better planet as a physician."

Zimbabwe: Deep Rooted and Ever Growing

Collaborations between Stanford and the University of Zimbabwe College of Health Sciences date back more than two decades. More recently, the NIH Medical Education Program Initiative aimed to strengthen medical capacity at Zimbabwe. That initiative has given Stanford residents the opportunity to spend clinical rotations at Zimbabwe helping fill gaps in the medical curriculum.

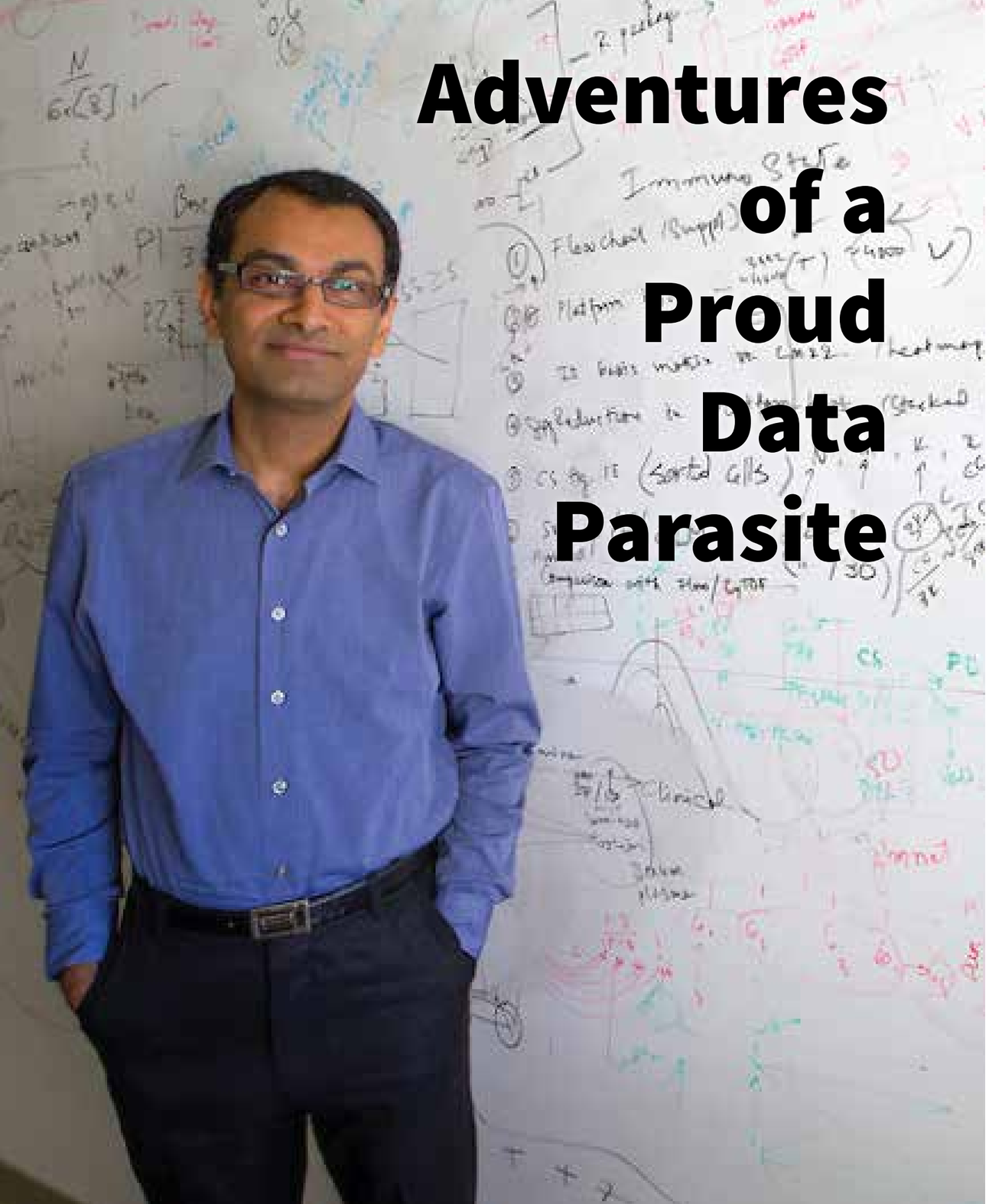
"Our partnerships in Zimbabwe draw on Stanford's interdisciplinary strengths and resources. We're not just approaching medical education from a clinical perspective, but tackling the interrelated challenges of providing internet access, libraries and e-learning resources. Real impact does not happen overnight, but is made possible through long-standing relationships and bilateral collaboration," said Barry.

Stanford Coordinated Care Illustrates What Comes from Collaboration

In 2012 Alan Glaseroff, MD, and Ann Lindsay, MD, were recruited to Stanford to develop Stanford Coordinated Care, a clinic for university employees and dependents with multiple medical issues. The clinic has achieved astonishingly good results: above the 90th percentile for primary care quality measures, 99th percentile for patient satisfaction, a 59 percent reduction in emergency visits, a 29 percent reduction in hospitalizations, and a 13 percent reduction in cost of care. They list 10 ways that the successful program epitomizes the benefits of collaboration:

1. The most critical collaboration is with the patients themselves. There is contact between the clinic and every patient on average once a week. The focus is on promoting people's self-management, not just taking care of their problem. Shared decision making with the patient is the norm.
2. The clinic team consists of four physicians, a clinical nurse specialist, a licensed clinical social worker, a physical therapist who's a specialist in chronic pain, a dietician, a pharmacist who's also a diabetes educator, and four medical assistant care coordinators, serving in a new role within Stanford specifically designed to assist patients assigned to them. The team works in the same room during and between patient visits, which directly supports the communication.
3. Coordinated Care clinic staff often attend specialty visits with the patient when a big decision is at stake to make sure that the patient's overall goals are brought into the decision-making process and that the benefits and risks of interventions are fully considered.
4. Stanford Primary Care 2.0 is an initiative aimed at providing high-value patient care. Many of its primary care transformation concepts came from Stanford Coordinated Care, which takes a nonhierarchical approach to teamwork and sees itself as a research and development shop. The key transformation is empaneling care coordinators, who have responsibility for patients rather than simply performing tasks assigned to them.
5. Patient advisors helped design the structure of the clinic. The types of patients who were likely to come to the clinic were asked what worked for them and what didn't, and that input informed the ultimate design of the clinic. They continue to advise on communication and maintenance of quality.
6. Stanford Coordinated Care partners with the Stanford D-School in a Design for Health class. Postgraduate students work directly with clinic patients for 12 weeks. Students help patients improve self-management, while also working on their own health improvement projects.
7. Through work with the Institute for Healthcare Improvement and other state and national collaboratives, this clinic model has spread around the nation. Lindsay and Glaseroff have served as faculty with The University Health Consortium and the Pacific Business Group on Health to support care transformation for other university hospitals and businesses, respectively.
8. A dozen teams from all over the country have joined clinic staff in a workshop at the Stanford Coordinated Team Training Center. Participants include Bellen Health in Wisconsin, Unite Here Union from New Jersey, Group Health in Seattle, Kaiser Permanente and Intermountain Health.
9. Glaseroff and Lindsay teach in the School of Medicine, demonstrating the role of team care, the importance of eliciting and addressing patients' goals to engage patients in self-management, and the care of patients with complex needs.
10. The clinic is paid on a capitated basis. Patients are not charged fees for services. That frees up staff to perform many services that might not be billable in a standard primary care practice. It fosters the multidisciplinary teamwork that is the hallmark of the clinic.

▼ **Seated clockwise, from left: Ann Lindsay, MD; Natasia Poso, MD; Dina Carillo, office assistant; Nancy Cuan, MD; Ann Simos, diabetes education specialist; Jen Chand, MD; Monica Curiel, care coordinator; Carmen Lu, pharmacist.**
Standing clockwise, from left: Samantha Valcourt, clinical nurse specialist; Delila Colman, care coordinator; Coleen Travers, LCSW; Kathan Vollrath, MD; Alan Glaseroff, MD.



Adventures of a Proud Data Parasite

In an era in which analyzing other people's data has been likened to research parasitism by no less an authority than *The New England Journal of Medicine*, Purvesh Khatri, PhD, assistant professor of medicine (biomedical informatics research–Institute for Immunity, Transplantation and Infection), declares, "I'm not a research parasite, because that implies that I'm stealing somebody else's idea. I am repurposing data to ask and answer questions that are not addressable using traditional approaches. I'm a proud data parasite."

Khatri's research has asked many questions and produced many answers of significance in the past three years. That is especially unusual for someone who came to this country in the late 1990s with a degree in communications and wanting to be a software engineer. After several career turns, he finds himself a bioinformatician on a quest to improve diagnostics and therapies for infectious diseases. And, perhaps next, autoimmune diseases.

Informaticians study reams of data about diseases in hopes of recognizing patterns in the data, understanding the causes of these patterns, and designing algorithms to recognize further patterns. Using such a process, Khatri and his group recently showed that they can diagnose patients with an infection two to five days before patients could be clinically diagnosed. They do this by looking at data from gene expressions of the body in response to a given infection. This work was published in *Science Translational Medicine* in 2015. While this was a useful discovery, it lacked the specificity that Khatri sought: "The problem with that approach was that we could not differentiate between bacterial and viral infections."

The next step was to try to identify the host response specific to viral infections. *Immunity* published that study, again looking at gene expression, which demonstrated not only that there is a common host response to multiple viruses different from bacteria, but also that host responses to viruses differed from one another, so that "we could distinguish among viruses."

With this information in hand, it was natural to ask another related question, which Khatri indeed asked: "Now that we've seen this on the viral side, does the immune response recognize different bacteria?" The bacterium they studied was mycobacterium tuberculosis, and again the result was positive: "Yes, there is a very specific host response to tuberculosis that allows us to distinguish active tuberculosis patients from patients with other bacterial infectious diseases, other respiratory diseases, latent tuberculosis infection and so on."

The immediate clinical action once it's known that a patient has tuberculosis is to give curative antibiotics. But Khatri wondered if the host response might also serve as a biomarker for treatment response, and his group performed another study that was reported in *Lancet Respiratory Medicine* in 2016: "If the treatment is working, bacteria are going to die. Once there are no bacteria left in the system there will be no host response, and you will know the patient is cured. So it's not just diagnostic; it should also allow you to monitor patients upon successful treatment."

Without antibiotic-like therapies for viral infections, Khatri's lab sought to look at data from vaccinated patients for more biomarkers. "When you think about vaccination," he explains, "you are giving patients the infection without the corresponding symptoms. Knowing that there is a virus-specific host response, we wondered if that would also show up when a patient is successfully vaccinated. And the answer was yes!"

In other words, patients who respond to the vaccination they were given — "those we call successfully vaccinated" — have the same response to the vaccination as patients who get the viral infection. The importance of this finding, Khatri says, is that "this gives us the opportunity to develop new immune metrics for successful vaccination."

Influenza was the virus of choice for this research because nearly everyone is advised to get vaccinated against it every year. The actual strain of influenza in a given year turns out to be unimportant, as this study demonstrates, because Khatri's group found "the same host response to 17 different strains of influenza. It doesn't matter if it's a Vietnam strain or a California strain or an Australian strain. If you have influenza, then you are going to have this same response as long as you are successfully responding to it. Therefore, as long as a patient mounts a response to an influenza vaccine, you know that they would mount that response to all strains of the flu."

The next step in this ongoing campaign is to try to determine if it is possible to identify patients who might not need vaccination. Since 50 percent of patients who inhale live virus do not get infected, Khatri explains, "we want to know what is different about the people who literally put their nose into the virus and don't get infected. The key is to know whether an individual patient falls into the *never* or the *always* category of influenza patients." In the era of personalized medicine, Khatri says, this will help reduce the disease burden by prevention, not by treatment.

A basic question that continues to intrigue Khatri is "How do you understand the immune system? One of the things that my lab is starting to show is that there are different immune responses to different groups of diseases. Organ transplantation looks very different from infectious diseases. And autoimmune diseases look very different from organ transplant and infectious diseases. My lab is working in each one of these areas."

Khatri is someone who believes that the more heterogeneity there is in the data he has access to, the better the results he will find. Thus it is not surprising to learn that he feels that there are better ways to study diseases. He explains, "The way we have been studying autoimmune diseases may not be the best way to look at them. There are similarities among autoimmune diseases, and a better way to study them might be to look at them in groups. For example, fibrosis. Everybody looks at fibrosis differently depending on whether it is in lung, skin, heart or kidney. Madeleine Scott, a student in the Medical Scientist Training Program in our lab, is looking at fibrosis across organs, so we can narrow down what causes it. It's an important disease to study because if you have idiopathic pulmonary fibrosis, the median survival is three years."

As a researcher whose chief tool is a computer with access to volumes of publicly available data, Khatri is quick to explain that this "doesn't mean that we don't need to do experiments. We are a 100 percent dry lab, but we have been really lucky to have some fantastic collaborators here at Stanford to work with us and validate our findings. The way our collaborators believe our data and our analyses is just fantastic."

Two examples Khatri mentioned were Jason Andrews, MD, and Shirit Einav, MD, both assistant professors of infectious diseases. "Jason has essentially created two cohorts for us, one in Nepal and one in Brazil, to further test our biomarkers. Shirit is now testing the drugs we predict will work in patients in mice in her lab. She's amazing; I just have to show her our analyses, and she designs the experiments to test hypotheses from our analyses."

"Collaboration is *the* best thing about Stanford School of Medicine, especially for a data parasite like me."

▲ From left: Donna Zulman, MD, MS; Kimberly Beck, recreational therapist; Debra Hummel, RNP; and Carlos Cano, social worker, are part of the ImPACT clinical team.

Meeting the Challenge of High-Risk, Complex Patients in the VA System

Donna Zulman, MD, MS (assistant professor, general medical disciplines), is intrigued by the challenge of caring for patients with multiple medical issues, often exacerbated by mental illness or social stressors. "Developing care plans for these patients requires a solid grasp of individuals' unique circumstances and priorities," says Zulman. "However, physicians rarely have access to a comprehensive picture of the factors influencing their patients' health."

Zulman's goal is to identify interventions and approaches that support individualized care for complex patients. Her three years as a Robert Wood Johnson clinical scholar at the University of Michigan and her work in the Veterans Administration system for the past 11 years have given her the skills to design, implement, and evaluate programs that do just that.

As a Stanford undergraduate, Zulman majored in Human Biology, taking courses on health and behavior, psychology, and health policy. This diverse coursework fostered her ambition to develop holistic models of health care that address both medical needs and social and behavioral factors that influence health and access to care. Early on, she gravitated toward the VA. "The VA offered a unique opportunity to care for complicated patients in a system that has a strong social mission backed by comprehensive services."

The VA offers extensive resources. In addition to medical, mental health, and social work services, veterans have access to peer support, rehabilitation services, recreation therapy, and programs for caregivers. Many are assisted in finding employment and housing. Zulman says, "We work in a team-based fashion, so we can focus on patients' medical concerns but when social issues come up we can refer patients to a whole host of services."

Still, "some patients' needs are so intense they can overwhelm the system, especially in the time allotted for most clinic visits." Several years ago, Zulman found that five percent of patients account for nearly 50 percent of VA spending—a statistic also observed in the U.S. population. "The vast majority of high-cost patients have multiple different chronic conditions, and approximately half have a mental health diagnosis, driving a need for care coordination."

Such patients became the focus of a Palo Alto VA pilot program that Zulman is now evaluating. The program, called ImPACT (Intensive Management Patient Aligned Care Team), aims to improve high-risk veterans' health and wellbeing, and—if possible—keep them out of the hospital and emergency room. The ImPACT team includes a nurse practitioner, social worker, recreation therapist, and physician. The team has a small panel of patients and offers intensive case management and chronic disease support. As Zulman describes, "This structure allows the team to spend time getting to know their patients, visiting them in their homes if necessary, and working with their other providers to improve care coordination and discharge planning." When patients have an advanced illness, the team works hard to understand and meet their goals for end-of-life care.

Zulman believes that when it comes to supporting clinically complex patients, the promises of technology are far from achieved. "Better tools are urgently needed to improve and individualize care," she says. A Viewpoint commentary on this topic written by Zulman and coauthors Nigam Shah, MBBS, PhD (associate professor, biomedical informatics research) and Abraham Verghese, MD (professor of medicine and vice chair for the theory and practice of medicine) appeared in *JAMA* in September 2016.

What pushes Donna Zulman to work with such challenging patients? "It's the opportunity to work on a complicated problem that spans multiple disciplines." Zulman is seeing a shift from a disease-oriented paradigm to an approach that offers patients personalized care across all their needs. "It's an exciting time to be doing this type of work, and there's a lot of energy and support to do it."

Stanford Launches Master of Science Program in Physician Assistant Studies

For the first time, Stanford will offer a master of science program designed to train physician assistants as both clinicians and future leaders in health care.

"As health care access improves, we need to equip medical practitioners with the skills to meet growing demand," said Lloyd Minor, MD, dean of the School of Medicine. "This new master of science program for physician assistants helps health care teams navigate that complexity and provide precision health: personalized treatment when disease strikes and proactive and preventive care that keeps people from getting sick in the first place."

Designed for a class of 25 to 30 students, the 30-month program will emphasize training alongside medical students in coursework and clinical care. It will also require students to choose a scholarly concentration within one of four fields: community health, health services and policy research, clinical research or medical education.

"With the increasing emphasis on coordinated, team-based care as supported by the Affordable Care Act, it is critical that the School of Medicine be able to create an integrated, team-learning environment to educate the biomedical scientists and clinicians of the future," said Robert Harrington, MD, professor and chair of medicine.

The master's degree program replaces the associate degree program to train physician assistants that began in 1971 as a partnership between the School of Medicine and Foothill College, a two-year community college in Los Altos, California.

The new program is designed to meet the expanding role of PAs in today's changing health care environment, said Susan Fernandes, PA, clinical professor of pediatrics and of medicine (cardiology).

"Today's PAs practice in all areas of medicine," Fernandes said. "They are leading community health centers, front stage in the health care policy arena, leaders in the classroom and changing health care delivery through innovation and research."

The role of the PA, one of the fastest growing professions, has expanded in part due to a shortage of physicians nationwide and the need to meet the growing demands of an aging population, Fernandes said. She and Rhonda Larsen, PA, clinical assistant professor of pediatrics, helped design the new program.

"We are trying to educate the next generation of PA leaders," Larsen said. "No other program sets out to do this."

PAs treat patients as part of a health care team, collaborating with physicians and other providers, Fernandes said. They often provide a broad range of health care services that may include conducting physical exams, ordering and interpreting medical tests, diagnosing illnesses, developing treatment plans, prescribing medication and assisting in surgery.

The curriculum will emphasize training in the foundational sciences during five academic quarters, followed by a year of clinical clerkships. There will be clerkships in obstetrics and gynecology, internal medicine, ambulatory family medicine, pediatrics, surgery, psychiatry and emergency medicine. In addition, students will have several elective rotations that will allow them to specialize in their field of interest.

"This is a new direction for Stanford, which has been traditionally a very research-heavy medical school," said Andrew Nevins, MD, clinical associate professor of medicine (infectious diseases) and medical director of the new program. "There is little training of advanced practice providers such as PAs. There is no school of nursing, no pharmacy school. This is an opportunity for Stanford to make a mark on this rapidly growing field."

▼ Rhonda Larsen, PA, (left) and Susan Fernandes, PA, helped design the new program.

Sometimes Diabetes Means Cancer

Walter Park, MD, an assistant professor of gastroenterology & hepatology, acknowledges that it will be many years before he recognizes the fruits of two of his current projects. The first is a large consortium targeting chronic pancreatitis funded by the National Institutes of Health through a U01 grant; one of its goals is to examine a relationship between newly diagnosed diabetes and pancreas cancer. The second is a biobank of pancreatic cyst fluid that he started eight years ago to help unlock some of the secrets of pancreas cancer.

Chronic pancreatitis is a debilitating and painful condition about which little is known. There are few treatments; patients have chronic pain; and it is a difficult disease to manage, especially as many patients are prescribed narcotics and often develop drug dependencies. It is also a risk factor for pancreas cancer.

When the National Institutes of Health announced that two of its institutes, the National Cancer Institute (NCI) and the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDKD), would fund a U01 grant to support a discrete project in chronic pancreatitis, Park and two Stanford colleagues — Aida Habtezion, MD, MSc, assistant professor of gastroenterology & hepatology, and Seung Kim, MD, PhD, professor of developmental biology — applied and were successful, along with nine other centers. The 10 centers then formed a consortium.

Park explains that the two institutes "realized that this was a poorly understood area where new knowledge would be helpful: from the NCI perspective, particularly as a strategy to identify early cancer; from the NIDDKD perspective, to better understand the natural history of chronic pancreatitis."

The focus of the U01, therefore, is on studying the natural history of chronic pancreatitis and its complications, specifically including the development of diabetes and pancreas cancer.

Many patients with chronic pancreatitis develop diabetes as a complication. Diabetes became known as an important factor following a study at the Mayo Clinic that looked at patients with pancreas cancer and found that many of them had newly diagnosed diabetes as well. This suggested that a recent diagnosis of diabetes could be connected in some way with pancreas cancer. And interestingly, says Park, "when some of these patients went to surgery because they had local resectable cancer, their diabetes went away after they removed the tumor. This stimulated a hypothesis that for some patients, diabetes is a signal, and the diabetes may have formed as an effect of the tumor in the pancreas."

With this as background, Park describes the dual goals of the 10-center consortium: to amass a large enough sample size to make sense of the relationship between diabetes and chronic pancreatitis; and to study the natural history of chronic pancreatitis. "Two major cohorts are being developed," he explains. "One is 2,000 patients with chronic pancreatitis, who we will follow over 10 to 20 years. The other is new-onset diabetics over the age of 50 who are otherwise well, and we'll follow them with the expectation that in about one percent of the patients the diabetes is actually a reflection of cancer. We have to recruit 10,000 new-onset diabetic patients to get to 100 patients with pancreas cancer."

The two other principal investigators in the Stanford group bring expertise in immunology and candidate biomarkers. Park describes the contributions his two co-PIs anticipate making to the study: "Aida Habtezion, who is an immunologist in our division, will enable us to better define certain immune profiles to try to predict cancer as well as to predict whose chronic pancreatitis is going to be worse. Seung Kim, who is a Howard Hughes investigator in the department of developmental biology, has identified a potential biomarker called Neuromedin U that could explain this tumor effect on diabetes and could be detected in the blood. In our proposal, we highlighted his work and suggested that we have some potential candidate biomarkers that we could use to try to identify whose diabetes might be related to the early onset of cancer."

Because of the difficulty of enrolling large numbers of patients with either chronic pancreatitis or new-onset diabetes, a consortium was necessary. "Once patients are recruited," Park says, "we'll be collecting and banking biospecimens for biomarker evaluation and validation from a sample size large enough to allow us to develop some meaningful observations. This material becomes the substrate for all the different ideas each center has."

Organizing a consortium of 10 centers, each with its own principal investigators, hypotheses, and expertise, is not an exercise for the faint of heart, and it takes time. Park describes it as having "a lot of chefs in the kitchen. There's a process of consensus that takes a bit of time. But we're almost done completing the study design for the prospective cohorts. We hope to launch these cohorts in January 2017 and to recruit all the patients we need in three years, ending in 2020. Then we follow them for as long as possible."

"This study will probably take me through to the mid to end of my career."

A Clinician for Patients with Pancreas Cancer

When not tending to the U01, Park devotes his clinical and research time to early detection strategies for pancreas cancer, which is one of the few cancers that are rising in incidence, lacking much progress in either screening or prevention.

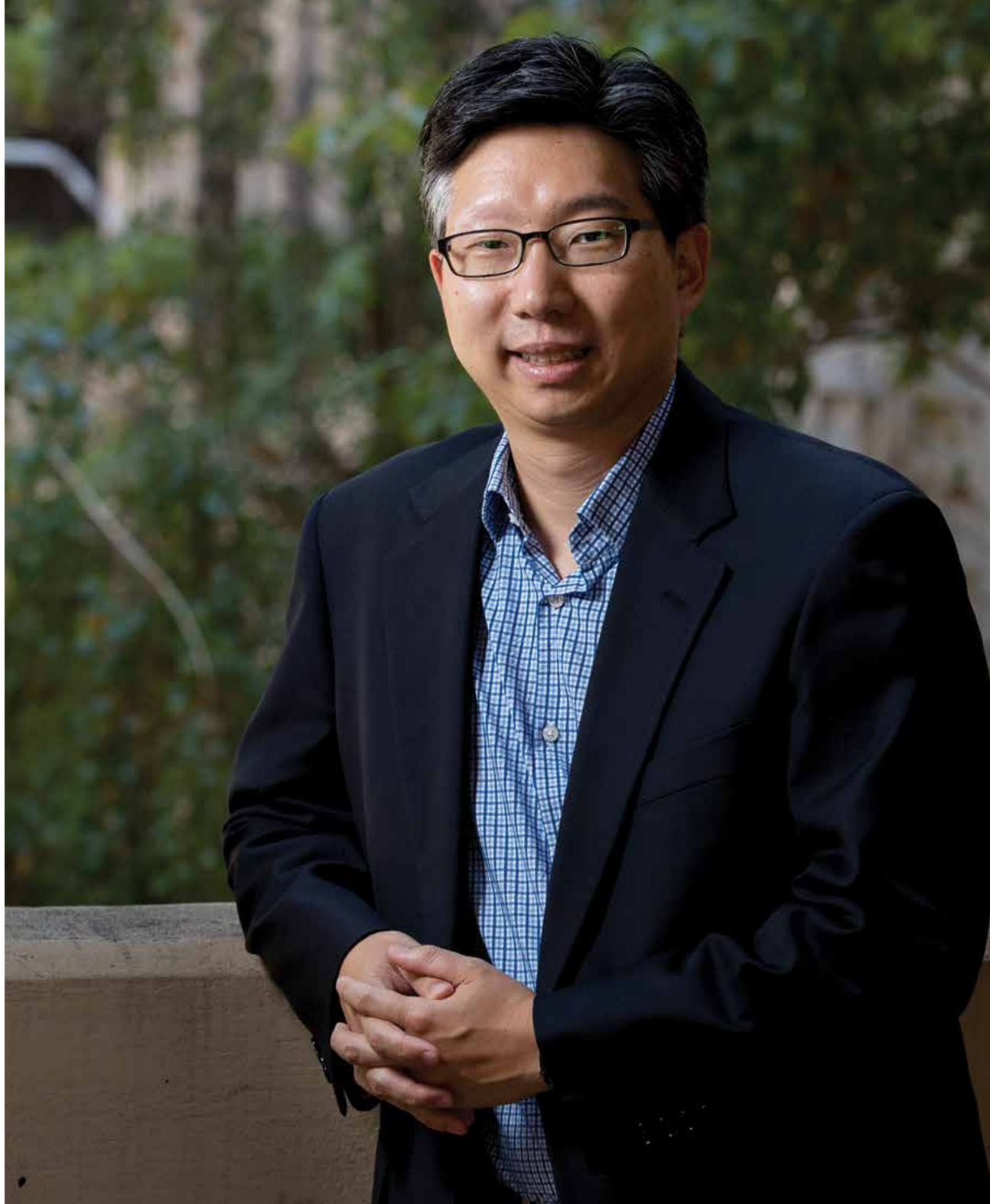
Park has been focusing on pancreatic cysts, known precursor lesions for pancreas cancer. Thanks to the use of CT and MRI in clinical practice there have been many incidental findings on the pancreas, and these include pancreatic cysts. Park points out that it is important to recognize that "not all pancreatic cysts have potential to become cancer but approximately half do. As our imaging has gotten better, we are finding these at an increasingly alarming rate. And because we can't reassure the patient that this is just a benign incidental finding, it has caused a lot of anxiety over the past 10 years."

The way to calm the anxiety is to remove the cyst, but that is not without significant risk. "It carries a mortality rate of at least two percent in the hospital, and complications are quite common, as high as 30 percent," says Park. Equally important, he continues, "what patients don't realize is that the risk of cancer from many of these cysts is actually quite low. The risk of taking them to surgery is probably higher than the chance that it would become cancer in the next year."

So, back in 2008, when he was finishing his fellowship at Stanford, he started collecting cyst fluid from patients during endoscopic procedures. "We'd send part of it for clinical care," he says, "and the other part to our freezer. Since then we've maintained a database of these samples, and we have over 300 now, which is a wonderful resource for quickly identifying and validating potential promising biomarkers."

Park also works with Stanford colleagues to try to discover new biomarkers. So far two successful collaborations have identified potentially new biomarkers which are currently being validated. One collaboration is with Gary Peltz, MD, professor of anesthesiology, perioperative and pain medicine, who is interested in metabolomics. And the other collaboration is with Anson Lowe, MD, associate professor of gastroenterology & hepatology, with whom Park is looking at another biomarker called amphiregulin.

Park is on a mission to fulfill some of the needs of patients with pancreatic cysts. "We need better biomarkers, better tools to help us discern which cysts have any potential to become cancer and then, more importantly, which of them have features that show that cancer may be imminent."



▲ Sonoo Thadaney, MBA, and Abraham C. Verghese, MD

The Doctor Is Present

It's a common complaint from contemporary patients: "During routine visits to my doctors, they never make eye contact with me. Their fingers are always on their laptop keys, and their eyes are glued to the computer. It feels like we aren't in the same room."

Health care providers feel this disconnect, too, as they find themselves in front of glowing screens rather than at the bedside; it is a situation that contributes to high rates of burnout.

It is also a subject of great interest to Abraham Verghese, MD, whose recent National Humanities Medal citation reads in part: "To Abraham Verghese, for reminding us that the patient is the center of the medical enterprise." What's often missing from today's patient-physician relationship, says Verghese, is presence, and it has become the name — as well as the driving force behind — a new Stanford center called Presence: The Art and Science of Human Connection. Presence looks to foster research, dialogue and collaboration across the Stanford campus to bring about measureable improvement in the medical experience for patients and physicians. A particular focus will be medical error.

There's a lot to learn, Verghese says — and maybe a few things to unlearn. That's where collaboration comes in. The center will work with Stanford's seven schools to discover novel ways to champion humanism in modern medicine. Executive Director Sonoo Thadaney, MBA, described several current projects: "We've partnered with the Stanford Center for the Advanced Study in the Behavioral Sciences to support one fellow, and with the Graduate School of Business to create the Innovative Health Care Leaders Program. Presence is also incubating a new global Society of Bedside Medicine, under the joint leadership of Stanford, Johns Hopkins, University of Alabama, University of Edinburgh and others."

The idea for Presence began when Verghese realized two unique things about Stanford. First, all the schools share the same campus. Second, says Verghese, "We have access to an interdisciplinary kind of research that I suspect would elude other places because they don't quite have that opportunity."

Sensing that Stanford could leverage these interdisciplinary connections into tangible projects that could improve the patient-physician experience, Verghese presented that idea to Dean Lloyd Minor because he thought it matched Minor's notion of precision health. "If we're committed to precision health," he explains, "then to me it implies we need precision at the level of the cell and the molecule; at the population level; and in the understanding of the human experience of health and wellness."

Verghese and Thadaney recently discussed their vision for the use of technology in medicine in less obtrusive ways. Verghese spoke of "harnessing the technology for the human experience, which means having the electronic medical record, for example, understand our ritual and serve us. Currently, our rituals are disrupted as we struggle to accommodate the computerization of what was a very heavy ritual-dependent field."

Thadaney concurred, adding, "One of the things we talk about is that any human experience — whether it's between a patient and physician or anyone else — is an analog experience. And by attempting digitization of it, we over-simplify it and weaken the crucial narrative. We're looking to harness existing and future technologies to enhance the human experience in medicine to be more human-centric."

While it is early to speak about legacy, Verghese finished with some hopes for the future of Presence: "I'm hoping that some years from now we might have made a particular impact on a certain kind of medical error. Perhaps we identify a critical element to be cognizant of in a particular story, or we develop a signature checklist of high-yield things to look for in the setting of a particular symptom. Or it might be that what transpires in a clinic in 2026 will be shaped by work done with our colleagues in psychology or business or anthropology."

Teaching Future Residents

Stanford's MD Capstone Experience course aims to ease the transition from medical student to resident.

Jeffrey Chi, MD, and John Kugler, MD, have been talking about medical education since they met as interns in 2005, and it's become the guiding focus of their professional lives. They spend their days in a shared office on the Stanford campus, where they bounce ideas off each other, collaborate on courses and engage in lively discussions.

They're both drawn to the idea that education — and the commitment to training the next generation — creates confident, comfortable physicians who, in Kugler's words, are "extremely resilient and well prepared."

Four years ago, Kugler and Chi, at the bequest of then-medical student Vivian Lei, began Stanford's preparatory education course for senior medical students. The course, titled MD Capstone Experience: Preparation for Residency, provides an introduction to a variety of necessary skills and prepares attendees for the precarious transition from medical student to practicing clinician. During a recent interview, Kugler and Chi, who are both in the division of hospital medicine, discussed the origins of the course and their vision for the future.

Q: You've been running the program since 2013. How has the MD Capstone Experience structure — and content — of the class changed over time?

John Kugler: When we started it, we picked three major themes: a clinical skills piece, a clinical knowledge piece and what we were calling advanced communication. Our goal from the beginning was to keep everything practical. For example, these are the things that will keep you from feeling terrible during your first four months of residency.

We made a few changes the next year: We expanded the course from three days to a full week of class — which went well — and we added in some things like making sure they practiced patient "hand-offs," which is a big issue in medical education right now.

And this year we're going to incorporate actual patient experiences. Our students will partner with an intern in the hospital and learn from that person in real time.

Q: Many medical schools have similar capstone courses. What, in your opinion, makes this course unique?

Jeffrey Chi: Other places have graduation courses, but we are lucky to have the resources that we do, which allow us to do more. For example, we wanted to teach students how to respond to pages and how to communicate with nurses, and so we actually assigned them patients that they follow throughout the course. So our students actually draw on things they did the day before and decisions they made previously to influence their future decision making. It's hard not to have lectures and didactics, but I think the amount of simulated immersion that we are doing is unique.

I would say the emphasis that we have is survival — boot camp. We know that the medical students are smart, we know they can look up almost anything, but this is geared toward your first few months in internship: What are you going to do during that first month or that second month when you are put into a situation when you don't have the time to sit down at a computer and look stuff up? You are going to call for help, obviously, but what do you do in those first 10 to 15 minutes when nobody's around, so that you don't feel like your heart rate is going faster than the patient's?

Q: As you scale up, what are your visions for the future for this program?

Jeffrey Chi: The course is being considered as a graduate requirement for Stanford School of Medicine students in the near future. So, we're going to have to scale this to the order of roughly 90 students. Right now we're getting the word out so people can plan their schedules well in advance. We'll hopefully learn enough from this year's course to scale this to an entire class in the next few years.

John Kugler: We may need to offer the class three different times, and we are probably going to cap the numbers in each cohort to about 30 students so they can have a meaningful patient simulation experience. And while we've been doing a one-week course, we'd ideally like to move to a two-week course, which we will try for 2017.

▼ John Kugler, MD, (left) and Jeffrey Chi, MD, run Stanford's MD Capstone Experience course.

I Have This ‘Research Month.’ What Should I Do with It?

▲ Mindie Nguyen, MD, MAS, is currently mentoring a third-year resident, three second-year residents, and one intern.

All residents at Stanford are guided by a core mentorship group consisting of a senior and a junior faculty member as they pass through rotations, choose a specialty, prepare a curriculum vitae (CV) and begin to make career plans. In their second and third years, residents have a research block of up to one month each year — free from clinical responsibilities — which often involves a different mentor to introduce them to academic research. Here, three faculty mentors tell how they approach this opportunity — with a few specific results their residents have achieved.

A Very Experienced Mentor

Mindie Nguyen, MD, MAS, an associate professor of gastroenterology & hepatology, is currently mentoring a third-year resident, three second-year residents and one intern.

With experience mentoring three to five residents annually for many years, Nguyen says, “I tailor it to each of them depending on their clinical and research interests and what they need the most from me, and I am always conscious of their timeline. They generally need to show results of their work by the time of fellowship application, which is usually only about a year to two after meeting me.”

Nguyen meets individually with each resident, asks them about their background and what they enjoy, and reviews their CV and prior experience. She describes for them the types of studies her lab does, examples of prior residents’ projects and the data she has available to them. Then she lets them choose a topic: liver cancer, fatty liver disease, hepatitis B or hepatitis C, and then a specific project from available options.

Nguyen’s goal for each of her mentees is to complete at least one first-authored publication. This requires a focused project that they can finish in less than two years.

Nguyen meets with her mentees individually as often as once or more a week during their research month and as needed. And she gives each of them what she describes as a “one-hour introduction to epidemiology/study design in a nutshell.”

Alina Kutsenko, MD, is the third-year resident being mentored by Nguyen. During her research period in the Nguyen lab, she found that patients with hepatocellular carcinoma differed in presentation, treatment and survival according to whether they had concurrent metabolic syndrome. She has presented these data at two major academic conferences and has a first-authored publication currently in press. She is also working on her second project, building on the niche she has developed with liver cancer and metabolic syndrome.

Transitioning from Mentee to Mentor

Sometimes a successful mentee becomes a successful mentor in just a few years. This was the case for assistant professor Mintu Turakhia, MD, a cardiac electrophysiologist; Alex Perino, MD, a cardiology fellow; and three residents who began the project as interns, during the fall of 2015.

Perino, who had been mentored by Turakhia for several years, describes the project: “This year, Mintu enabled me to assist in the mentorship of George Leef, Andrew Cluckey and Fahd Yunus on a grant-supported project we call SMASH-AF (systematic review and meta analysis of ablation strategy heterogeneity in atrial fibrillation). Published success rates of AF ablation procedures ranged from 20 to 90 percent. Our goal was to figure out what drove this significant variation in outcomes. We performed a massive systematic review, screening 9,000 articles, ultimately including 400 that met our criteria, which had more than 540 treatment arms and 65,000 patients, with over 400 unique variables abstracted per article.”

He continues: “We also utilized a research group structure and philosophy that increased mentee responsibility, resulting in greater mentee growth and project productivity.”

Leef provides an example of mentee responsibility: “Alex and Mintu wanted us to take an active part in creating the abstraction rules. Since we were the ones reviewing the articles, we were in the best position to adapt the rules as new situations arose, and it was also a valuable learning experience for us.”

The first four abstracts from this remarkable meta-analysis were submitted to the American Heart Association for its annual meeting in November 2016; two were accepted as poster presentations. Perino anticipates an additional 25 hypotheses to explore from the massive database, and “this is just the tip of the iceberg,” he says.

Perino credits Turakhia with providing a template for him to follow as a mentee. “Mintu did not just give me work to do,” he says; “he taught me how to be independently productive.” About this particular project, Turakhia says, “What’s cool here is teaching these residents about team science and collaboration early in their careers.”

Residents Delving into Residents’ Responsibilities

The final mentor-mentee project focuses on a topic of particular interest to residents: trying to find the sweet spot in balancing their inpatient responsibilities with their duty to outpatients who have problems or questions between appointments. There was a fair amount of anecdotal information among residents about finding the right balance, but there were no data.

▲ Members of Dr. Nguyen’s lab (from left: Pauline Nguyen, BA; Vincent Chen, MD; An Le, BA; Alina Kutsenko, MD; and Philip Vutien, MD) are seen during the Asian Pacific Association for the Study of the Liver in Tokyo.

The senior author and a mentor of the residents on this project, clinical associate professor of hospital medicine Jeffrey Chi, MD, had requested that data be retrieved from EPIC, Stanford’s electronic health record, in 2013. A year later he received a data set that contained information about all the things that residents did that were recorded in EPIC. It was a treasure trove.

At that point, Chi recalls, “While I could guide the research methodology, ultimately the residents know the right questions to ask. They know where the stress points are.”

The residents who took part in the project were Jason Hom, MD, Jonathan Chen, MD, PhD, and Ilana Richman, MD. Additional mentors were Baldeep Singh, MD, who is a clinical professor of general medical disciplines, and Casey Crump, MD, PhD, who at the time was director of the Center for Primary Care Research.

Chi and Hom had worked together throughout Hom’s residency and “had already established a good working relationship,” according to Chi.

He was confident that Hom and his colleagues were both accomplished and highly motivated.

Hom explains that they wanted to address “a topic relevant to house staff that has implications for how residency programs design inpatient and outpatient responsibilities. Jeff had done a great job of acquiring a difficult-to-acquire data set, and we wanted to use it to try to answer that question. It was nice to generate some solid data to help inform the discussion.”

The resulting manuscript was published in *BMC Medical Education* in May 2016. The results were not surprising: They found that at the time of the study it was difficult for residents on busy inpatient rotations to pay equivalent attention to outpatients with between-visit problems.

Hom states, “Stanford is wonderfully supportive of residents and very innovative in its approaches, and based on resident feedback, Stanford now employs a popular ‘firm system’ that uses team-based care to help with patient between-visit problems, which improves the trainee experience and also patient care.”

▲ Paolo Martin and Amia Nash are two of 25 students who are part of Stanford's newest degree program.

Newest Degree Program Combines Community Health and Prevention

Meet Paolo Martin, Amia Nash, and Vy Tran.

They're three of 29 students who are part of Stanford's newest degree program, the master of science in community health and prevention research (CHPR).

In fall 2015 the Stanford Prevention Research Center (SPRC) convened an interdisciplinary committee to create a master's degree anchored in the research and education efforts of SPRC faculty. Just six months later, the Stanford University Faculty Senate approved the master's in community health and prevention research in perpetuity. Such speedy approval was unprecedented in Stanford's history.

Martin began his career as a bench scientist, but he yearned to get to know his community beyond the walls of a research hospital, so he began a 20-year career in education and is currently a doctoral candidate in Stanford's Graduate School of Education. His research bridges CHPR with education: He is examining how pedagogies that stimulate the engagement of children's ideas affect their health and potential to thrive.

Nash received a bachelor's degree from Santa Clara University in public health with minors in biology, sociology and religious studies. After graduation, she interned with the Stanford School of Medicine and the Department of Psychiatry and Behavioral Sciences, focusing on mental health advocacy for Asian American adolescents as a Stanford Health 4 All fellow. What drew her to the CHPR program was her passion for health as a social justice issue and improving the health and wellbeing of underrepresented populations.

Tran plans to pursue a career in medicine as a community health advocate and as a family physician. Having grown up in a rural village in Vietnam, in a house built from dried mud with only natural sources of light, Tran plans to use her master's to make a difference in health care, immigration and education. Tran is currently engaged in community-based participatory research in Oaxaca, Mexico, under a Fulbright U.S. Student Award.

The aspirations of its degree candidates best speak to why the program was created.

Academic diversity

"We expect candidates to come from a diverse set of academic backgrounds — from humanities to computer science, medicine or engineering, for example," says Sonoo Thadaney, MBA, director of education programs for the SPRC.

She adds that "the curriculum is designed for graduates to work in such various activities as public health, public policy and community health, and they might start out as individual contributors in an organization and then eventually become founders or executive directors of nonprofits or leaders in government agencies. Another group of graduates might use this degree to become better-informed medical practitioners. Others might use their degree in combination with coursework in the world of performing arts — for instance to create theater aimed at inspiring healthy behaviors."

Interdepartmental teamwork

Within six months of approval by the faculty senate, the CHPR became part of dual degree programs with the Graduate School of Business and the School of Medicine. Currently, the CHPR and the master's program in science and genetics and genetic counseling are adding tracks from each other's programs into their respective curricula. Soon, the Stanford Center for Women and Sex Differences in Medicine (WSDM) will add a track with the CHPR as it relates to prevention.

"The CHPR boasts an interdisciplinary faculty representing public health, medicine, behavioral sciences, biostatistics, epidemiology and other disciplines," says faculty director and associate professor Jodi Prochaska, PhD. "In addition, the CHPR program brings the science of what's being done at Stanford out into the community. The program pairs master's candidates with community programs so students can gain hands-on experience with needs assessment, program development, evaluation and dissemination."

From Bench to Bedside for Pulmonary Hypertension

By collaborating with Stanford's SPARK program as well as those outside the university, Stanford clinician-scientist Mark Nicolls has moved a drug into clinical trials.

For 15 years, Mark Nicolls, MD — a pulmonary and critical care doctor and researcher — has been studying pulmonary arterial hypertension (PAH), a rare form of high blood pressure in the lungs. The affected arteries stiffen and thicken, making it hard for the heart to pump blood to the lungs. Today, there's no cure for the disease, and patients have a limited life expectancy. But Nicolls hopes to change that, and his basic research has led to a drug now being investigated by a publicly-traded pharmaceutical company.

By studying the blood vessels that are injured in PAH at a molecular level, Nicolls and his lab group discovered that immune cells called macrophages tended to cluster in the vessels. Coincidentally, just as they made this finding, a new member of the lab, Amy Tian, was looking for a project. Her background was in eicosanoids, a type of signaling molecule used by the immune system. That background proved valuable when she began to study the signaling involved in the immune cells congregating in PAH-affected vessels.

"By looking at macrophages around the injured blood vessels, she was pretty quickly able to discern that they were synthesizing a lot of leukotriene B4," says Nicolls. Leukotriene B4 is an eicosanoid, known to be produced in response to inflammation.

Tian and Nicolls showed that leukotriene B4 wasn't just a consequence of PAH; it was part of the cycle of inflammation and injury that keeps the disease progressing. When they blocked leukotriene B4 in rats with the disease, their symptoms lessened and blood vessels became less clogged, lowering blood pressure in the lungs. Their results were published in the August 28, 2013, issue of *Science Translational Medicine*.

Shortly afterward, the researchers turned to Stanford's SPARK program, a partnership between academia and industry that helps advance research discoveries to clinical trials and commercialization.

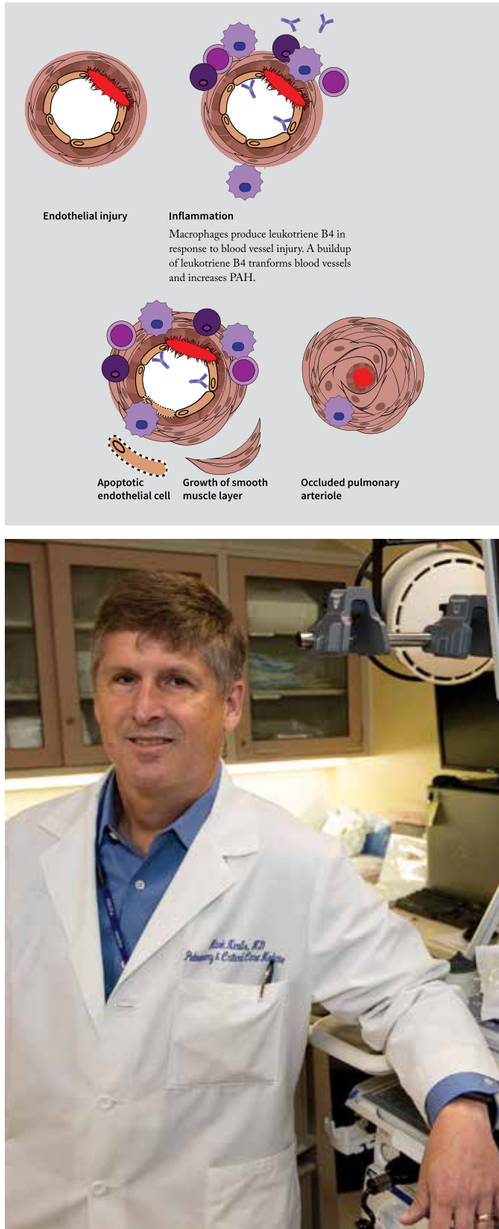
"We're a translational research program, and we work with faculty, post-docs and students who have discoveries that might be turned into drugs for unmet medical needs," explains Kevin Grimes, co-director of SPARK. "There are a lot of discoveries that never leave universities because they're considered too risky by potential commercial partners. The expense and time and know-how of getting to the point where a commercial partner would be interested is just perceived to be huge." The program provides funding, mentorship and education to bridge that gap from bench to bedside.

Blocking leukotriene B4 to treat PAH fit the bill, and Tian and Nicolls started working with Grimes. "Their work is really nice and innovative," says Grimes. One of the selling points that helped move it along: A drug already existed that blocked leukotriene B4 and had been used on patients in Japan for a different condition.

"They're repurposing a drug that has already been used in humans," says Grimes. "The fact that there was a safety track record has allowed movement into the clinic to go more rapidly." With the help of SPARK, Tian and Nicolls were able to get commercial interest in their discovery.

In mid-2016, following FDA approval, Eiger BioPharmaceuticals, Inc. launched the first clinical trial of the drug to treat patients with PAH at 45 sites throughout the United States and Canada. Nicolls is a scientific advisor for the company. "The fact that Mark has moved into the clinic so quickly is really a fantastic achievement," says Grimes.

It remains to be seen how the drug works in patients, but Nicolls has high hopes. "The main therapeutic approach right now is vasodilation, which really treats the symptoms and not the disease. We're hopeful that this therapy might actually reverse the disease," says Nicolls.



From One Patient to the World

A single case during fellowship spurred hematologist Jason Gotlib to develop a drug that's now helping patients around the world.

▼ Patient Louise Rabel visits with Jason Gotlib, MD.

January 2002

It was a winter day that began like any other in Jason Gotlib's hematology fellowship: There were patients to see, notes to write and papers to read. Then the attending in charge of the Stanford hematology clinic that day, Stanley Schrier, told Gotlib that he had one more patient to add to his schedule. The patient's records, Schrier told him, were on a table behind him.

"I turned around," Gotlib recalls, "and there was a stack of rubber-banded papers that literally was around two feet high." The patient, it turned out, was a 39-year-old man with a rare blood disease called idiopathic hypereosinophilic syndrome, characterized by a surplus of a kind of white blood cell, which can lead to inflammation, organ damage and even cancer. This patient's disease had transformed into acute myeloid leukemia. "He had gone through many treatments, including multiple rounds of chemotherapy," says Gotlib, now a professor of hematology at Stanford. "He had fluid in his lungs and abdomen, an enlarged liver and spleen, and large disease masses abutting his spine."

Gotlib and Schrier decided to try something for the patient — a course of imatinib (Gleevec), a drug that blocks a group of proteins called tyrosine kinases which some cancers need to survive. Imatinib had been formally approved by the FDA only a few months prior for treating a different type of blood cancer. Within a month, Gotlib's patient was in remission.

"We were completely astonished," says Gotlib. But when colleagues started treating other hypereosinophilic syndrome patients with imatinib, they had dramatic responses as well.

To find out exactly why imatinib had worked so well, Gotlib sent blood samples from his patient to a lab at Harvard that specialized in discovering new mutations for blood cancers.

March 2003

That Harvard team, led by physician-scientist Gary Gilliland and postdoctoral fellow Jan Cools, discovered that many patients with hypereosinophilic syndrome have two genes that have been smashed together by mutations, causing a fusion oncogene called *FIP1L1-PDGFRA*. Imatinib binds to and blocks the activity of the fusion protein. Gilliland, Cools, Gotlib and other collaborators published their findings in the March 27, 2003, issue of the *New England Journal of Medicine.*

May 2003

In the meantime, though, Gotlib's original patient relapsed and died. The Gilliland group used a new blood sample from the time of the patient's relapse to uncover a mutation that prevented imatinib from binding. Using a mouse with the same mutation, the group found that an alternative drug — midostaurin (PKC412) — treated the resulting, imatinib-resistant leukemia. Their results appeared in *Cancer Cell* in May 2003.

In the back of his mind, Gotlib kept pondering the new results. He wondered whether other diseases might also be successfully treated by midostaurin once the drug was approved by the FDA. One possibility, he thought, would be systemic mastocytosis (SM), a rare and debilitating disease caused by the accumulation of mast cells in the skin, bone marrow and internal organs. About 90 percent of SM patients have an imatinib-resistant mutation in the gene for a tyrosine kinase called *KIT*.

"I said, well, if it's resistant to imatinib, maybe midostaurin will work in these patients," remembers Gotlib. A few months later, Gotlib's hematology colleague Caroline Berube came to him asking for ideas for a patient with an advanced form of SM called mast cell leukemia who was not responding to imatinib. Gotlib called Novartis, the manufacturer of midostaurin, and asked to use the drug on a compassionate use basis.

"It took some time, and a few months went by," says Gotlib. "The patient became sicker and sicker and ultimately needed to be hospitalized." But when the clinicians finally got the OK to give her midostaurin, her mast cell disease improved immediately, although she ultimately died from separate complications of her SM.

July 2005

Based on the dramatic response that the one patient with mast cell leukemia had to midostaurin, Gotlib worked with Novartis, Tracy George of Stanford's hematopathology division, and doctors at two other institutions to launch a phase II investigator-initiated trial. They began enrolling people in July 2005 and eventually recruited 26 patients with advanced SM and evidence of mast cell–related organ damage.

November 2008

While the trial was still ongoing, Gotlib and George presented interim data from the study at a large mast cell research meeting in Budapest, generating excitement from investigators around the world. At the same meeting, Novartis, encouraged by these data, asked for researchers to help with a global trial. Gotlib and other scientists began developing a protocol and, within a year, started recruiting patients at 29 sites around the world.

June 2016

Fast forward eight years, when encouraging results of the international trial using midostaurin to treat advanced SM were published in the June 30 issue of the *New England Journal of Medicine*: Sixty percent of patients responded to the drug, with not only decreased signs of their disease based on lab tests and scans, but improvements in symptoms and quality of life as well.

"It's definitely a positive study," says Gotlib, who was the first author. Forty-five percent of patients who received the drug in the trial had a major response, with at least one type of organ damage completely resolving.

2017 and beyond

So what's next? Gotlib is ready to publish the results of the investigator-initiated trial that began in 2005, which demonstrates long-term responses with midostaurin. With more than eight years of data on some patients, it provides more evidence on how much difference midostaurin can make. The response rate in that group, he says, is similar to what was seen in the global trial — around 69 percent — and the responses often last.

Louise Rabel, the longest surviving patient in the world who's been treated with midostaurin, is in that trial; she started the drug on February 2006, and she's still on the drug now more than 10 years later," he says.

But Gotlib also wonders whether other compounds more specifically designed to target the *KIT* mutation in advanced SM could work even better than midostaurin.

"In the global trial, there were no complete remissions. Clearly whatever targets midostaurin is hitting do not yet translate into deep remissions or cures."

Gotlib indicated that a second-generation group of drugs, *KIT* D816V-selective inhibitors, are being developed. Trials have already commenced, and 2017 should be a banner year for understanding their efficacy and safety profile. But already, patients with advanced SM who previously had no treatment options have new hope.

"This really highlights the importance of a single patient observation," says Gotlib. "Fourteen years later we've gone from a single patient with a different disease to a global trial which demonstrates very encouraging results in these poor-prognosis SM patients."

A Research Career to Benefit Children and a Life Lived on Campus Among Undergraduates

◀ Julie Parsonnet, MD, is a resident fellow in Robinson House. Here, she is seen walking with Todor Markov (left) and Scott Lambert, two Robinson House undergraduates.

"What makes me excited about my research is the same sort of thing that makes me excited about living on campus: because we work closely with so many fantastically smart people."

Julie Parsonnet, MD, professor of infectious diseases and health research and policy, seems most comfortable describing herself as an "enthusiastic citizen of the university." She explains this descriptor by saying, "I've lived on campus most of my time here, and I've had neighbors who are in history and in English and in French. I've always been interested in the university as an entity, the way it works and the breadth of knowledge here. There are a lot of things going on at the university that I find appealing and interesting. And I've always wanted to be engaged."

Parsonnet has spent most of her time on her day job doing research, beginning in her fellowship at Massachusetts General Hospital when she became interested in a recently discovered organism called *Helicobacter pylori*. "Like many scientists," she says, "I started my career with a mistake. I was convinced that *Helicobacter* was an unimportant colonizer of the stomach, just an organism that lived in humans. So my first studies were designed to see if it really did anything. As I went further and further along, I found to my great surprise that this organism, which is present in about 50 percent of the world's population, was actually responsible for a lot of different things: stomach cancers, gastric lymphomas and peptic ulcers, among others. We were involved in discovering links between infection with *Helicobacter pylori* and both cancer and lymphoma, resulting in *New England Journal of Medicine* publications in 1991 and 1994."

For some researchers such results provide a line of sight to years and decades of further work elucidating mechanisms, hypothesizing therapies, grinding out hours upon hours of grant writing and manuscript preparation. Parsonnet went in a somewhat different direction. "After that," she says, "I started to think if *H. pylori* is in 50 percent of the world's population, then maybe it's not all bad. Maybe the reason it lives in so much of the world's population is because it provides some sort of survival advantage, particularly to children. And we found that it was associated with lower weights in children and might protect against tuberculosis and diarrheal disease. We learned that it protects against another form of cancer, esophageal adenocarcinoma."

These findings stimulated more thought, eventually prompting a shift away from a focus on just *H. pylori* to "looking at the totality of microorganisms. After considering that this one organism is but one of many thousands living in the human body, we started to wonder what else is in there that influences many aspects of human health. Are there other signals that might relate infections to things that we don't traditionally think of as infectious diseases, such as asthma and allergy and obesity? What we work on now is trying to understand how children acquire infection and what it means for their lifetime health."

"We" is a pronoun Parsonnet uses frequently in conversation, whether she speaks of the people with whom she collaborates in and outside the lab or the students with whom she and her husband (Dean Winslow, MD, professor of general medical disciplines) live as resident fellows in Robinson House.

"What makes me excited about my research is the same sort of thing that makes me excited about living on campus: We work closely with so many fantastically smart people. People in immunology, Scott Boyd, Mark Davis, Kari Nadeau in pediatric allergy, and the March of Dimes project with David Stevenson and Gary Shaw, and with obesity experts like Christopher Gardner and Tom Robinson. It's just really, really fun."

Parsonnet's successes in grant making have given her the opportunity to help other fantastically smart people make their way in a highly competitive world whether through support from her research grants (including her NIH Director's award) or through National Institutes of Health training grants (T32s). A T32, of which she has been principal investigator for several cycles, funds salaries and tuition for master's degrees at Stanford for three fellows in infectious diseases each year. Upinder Singh, MD, associate professor and chief of infectious diseases, describes this as "an invaluable addition to our program. Julie's success in renewing it, in these tough funding times, is a testament to her skills, effort and dedication."

For the 20 percent of her life that is not spent on research, Parsonnet can quickly provide a laundry list of campus-focused activities past and present. There have been two presidential task forces, one dealing with international global health and the other with graduate education.

Parsonnet describes the graduate education task force as "a great experience because we got to work with people from graduate education all across the campus addressing such issues as what should be the goal for graduate students here, how we increase interdisciplinary engagement across the campus, and how we support our students financially."

And then there is teaching: "I've been teaching undergraduates for 15 or 20 years. I teach epidemiology and infectious diseases, and this year I started teaching a class on how to investigate an outbreak. A lot of students are fascinated by public health and by outbreaks in particular, and we engaged a lot of people from the public health community. It was an inspiring class and I was happy to find quite a number of students begin to reshape their career aspirations toward public health."

A while back, there was a deanship: "I was the dean for medical education for five years, and I got to meet a lot of medical students as well as undergraduates applying for medical school. I love that part of the university. I just love being around smart, engaged, interested young people and seeing how they frame their careers and maybe helping them a little get where they want to go. I think that sort of explains pretty much my entire career."

And finally, in her own summary words: "It's all about being an educator. We do that in the dorm at night, and I do it on the faculty senate [she is vice chair]. It's all about how we make this the best educational institution it can be and how we foster the lives of the students who are here. That's how I've gotten engaged in all these things, and it's been a wonderful experience for me."

Julie Parsonnet is indeed a most enthusiastic citizen of the university.

Riding the Immunotherapy Wave of the Future

Crystal Mackall is joining forces with doctors and researchers who have a wide range of expertise to make Stanford a leading institution for cell therapies to treat cancer.

Today, most pills dispensed to patients — whether for diabetes, cancer or another disease — are made of synthetic proteins or other lifeless molecules. But in the future, infusions of living cells might become the go-to therapies for many conditions. Already, engineered immune cells have shown promise in treating a handful of cancers. And as the field takes off, Crystal Mackall, MD, a professor of bone and marrow transplantation, thinks Stanford has the potential to become a leader in these so-called cell therapies.

"Stanford already has a long history of being a leader in the field of cancer immunotherapy, but we're at a point in time where the whole field is really exploding in terms of new ideas, new approaches and a wider array of diseases that can be targeted," says Mackall. "So the program that I am leading will seek to really establish Stanford as a leader in all areas of cell therapy."

Mackall's goals don't just hinge on her own research success; she's bringing together researchers and clinicians from across Stanford in the effort.

Cell Therapies for Cancer

All cancers are characterized by abnormal, excessive cell growth. In most cases, these growths — which are best known as tumors — are caused by gene mutations that have accumulated in cells, keeping the cells alive and dividing when they wouldn't otherwise. Because they're rogue versions of cells from the patient's own body, these cancer cells generally can evade detection and destruction by the immune system.

With cancer immunotherapy, though, scientists aim to ramp up the activity of the immune system so that it can hunt down and destroy cancer cells. Cell therapy — a subset of immunotherapies — uses altered or synthetic versions of immune cells to accomplish this.

"Cell therapy really is an area I believe is poised for rapid growth in terms of both clinical application and developing new technologies," says Mackall. "Our ability to genetically engineer cells and use synthetic biology to direct at will the behavior of cells is in a really big growth phase right now, and Stanford's strengths lie in many of those areas: human immunology, bioengineering and technology development. And all of those strengths can be brought together."

Knowing that cell therapy works, the question is what its breadth of application will be, beyond cancers that affect B cells (cells of the immune system that are responsible for generating antibodies).

"It's absolutely clear that cell therapy for B cell malignancies is here to stay," she says. "The real question is what effect it will have on other diseases."

Parker Institute for Immunotherapy

Earlier this year, Stanford announced the creation of a new center on campus as part of the Parker Institute for Cancer Immunotherapy, a multi-institution effort established with a $250 million grant from the Parker Foundation. Mackall, armed with an initial $10 million grant from the foundation, will be leading the Stanford center.

"Joining the Parker Institute will provide access to new immunotherapeutic drugs, immune monitoring platforms and collaborative clinical trials," says Mackall. She's already identified a cadre of researchers who will join the effort and has started designating funds to build new infrastructure.

Engineering New Receptors

Mackall focuses her own research on a type of cell therapy using chimeric antigen receptors (CARs). The engineered molecules are designed to include the best aspects of two other immunotherapies: antibodies and T cells (a type of immune cell).

"Antibodies are useful because they are highly specific and can be generated to target almost any molecule," says Mackall. "And T cells are attractive because they're so potent and durable."

To treat a cancer with CARs, T cells are collected from the blood of a patient. Then the cells are engineered to have CARs on their surface that recognize the patient's tumor. Next, they are cultured so that clinicians will have many more to use for treatment. When infused back into the patient, the new cells can seek out and kill the cancer cells they recognize.

Mackall has authored numerous papers using CAR T cells, including ones designed to bind to a molecule called CD19 that's found on the surface of some tumor cells. Recently, she's been involved in clinical trials of the cells to treat acute lymphoblastic leukemia (ALL) in children and young adults; the results of a phase 1 trial were published in *The Lancet* in 2015.

"The CD19 CARs have been just spectacular against ALL," says Mackall, who is also a professor of pediatrics. "Response rates across several institutions have been in the range of 70 to 90 percent; I challenge you to find phase 1 trials of another cancer agent with that high a response."

So far, CARs have been most successful for hematologic malignancies — leukemias and lymphomas. Scientists don't know why the approach works better for blood cancers than solid tumors — like breast cancer or liver cancer — but that's one question Mackall hopes to answer. She also wants to know why the method works so well for some patients but not for others.

Answering these kinds of questions, she says, requires back-and-forth cooperative efforts between bench scientists (who study basic immunology) and clinicians (who test new approaches in patients).

Building a Foundation

With the infrastructure and collaborations in place to study cell therapy for cancer, Mackall says Stanford will be poised to be not only a leader in cell therapies for cancer, but other cell-based therapies as well.

"Giving someone living cells is completely different than giving someone a pill," she says. "And if we make a commitment now to build a program that specializes in this, we'll be in a great place to apply the approaches to a wide array of diseases in the coming years."

The lab spaces, the understanding of how to engineer cells, the experience with genetic engineering and the familiarity with collaborating can all be easily adapted to these other burgeoning research areas as cell therapies take off.

New Days for Rheumatology

Mark Genovese, MD, is one of the world's leading researchers in rheumatoid arthritis. The James W. Raitt Professor of Medicine in the division of immunology and rheumatology has also been a key player in numerous clinical trials for other diseases including psoriatic arthritis, systemic lupus erythematosus, osteoarthritis and other chronic inflammatory diseases. Over the past two decades, he's helped establish Stanford's bench-to-bedside translational medicine program for these conditions. Here is a conversation with Genovese about his progress in chronic inflammatory diseases.

What first drew you to rheumatology?

I became interested in rheumatology in 1989, as a medical student, when I became involved in research on lupus. I was drawn to the field by all the unknowns. The diseases themselves seemed so enigmatic, and there were so few treatment options for patients. It struck me that there was a great opportunity in rheumatology to take care of these patients as well as to try and advance the field through research. While the initial focus of my research was in lupus, I started working on arthritis during my fellowship at Stanford.

How has rheumatology changed since then?

The field has seen substantial changes since the 1990s with the more aggressive use of conventional anti-inflammatories and the development of biologic therapies. For rheumatoid arthritis (RA) in particular, there's been a quantum leap in what we're able to do for our patients. It's gone from a disease with few effective treatments to one in which we can make almost every patient somewhat better. I think that's really the result of years of hard work in basic immunology research that's identified new drug targets, coupled with significant efforts on the part of clinicians and clinical researchers. That being said, not all diseases have taken the same course as RA; for many rheumatologic diseases, there remain limited options even today.

What have you been able to accomplish at Stanford during that time?

At Stanford we've been able to lead cutting-edge clinical trials in inflammatory diseases that bring our patients treatment options they wouldn't have anywhere else. In the early 2000s we showed that etanercept worked better than methotrexate to decrease symptoms and slow joint damage in patients with long-standing RA. Then we went on to study how newer agents such as abatacept, rituximab and tocilizumab could help patients with refractory disease; we showed that the combination of leflunomide and methotrexate is effective and safe. More recently, we've also looked at novel small molecules like baricitinib that have the potential to change the face of the way we treat RA.

What has allowed Stanford to be a leader in this area?

I think it's the support from the institution, from the Department of Medicine and from within the division of immunology and rheumatology. The support has given me the opportunity to follow my own interests and focus on what will make the biggest impact. Along with that, the ability to collaborate with really superb clinicians and researchers throughout the university has been a boon to advancing our research.

Where is rheumatology going from here? What's next?

For RA, we could always live with where things stand now, with this idea that you can make everyone just a little bit better. But ideally, we have to figure out how to make an even bigger difference to patients, how to really eliminate symptoms and long-term joint damage. I think continuing to work on both new small molecules and novel combinations of drugs is going to be key. For other rheumatologic diseases, there's even more room for improvement, and it's just going to take a continued commitment to both bench-top basic science and clinical work.

Across the Pacific

Haruko Akatsu has spent her career strengthening ties between medical schools in the United States and Japan.

During her medical school days at Brown University and residency at Stanford, Haruko Akatsu, MD, who was born, raised and educated in Japan, got to thinking about the differences between medical education in the two countries. "I was surprised to encounter so many different ways of educating the next generation," Akatsu, a clinical associate professor of endocrinology, gerontology and metabolism, recalled thinking. "That was eye-opening for me."

She began to share and record her experiences in a Japanese medical journal and was soon approached by a publisher. Her collection of essays, entitled *Medical Education in the United States: A Medical Student Journal,* was released in 1995. To Akatsu's surprise, the book was well received. Invitations, and another book deal, soon followed: "I started to be invited to so many different grand rounds and conferences in Japan to give talks. I think people were interested in knowing more about medical education in the United States, which was not very well known to the Japanese medical community at that time."

Akatsu noted that while typical Japanese medical school curricula were more textbook- and lecture-based, American schools offered more opportunity for system-based and clinical application. She explained: "Generally, education in Japan is more dogmatic, and information is passed top-down from teachers to students. But in America, we encourage different viewpoints and opinions, and we encourage discussion. I think it's great to see how we can learn from both of these perspectives."

Though she trained and worked in the United States for the past 25 years, Akatsu's strong ties to Japan are evident and have shaped the trajectory of her career. She's sat on committees, organized education exchanges, and hosted training and faculty development workshops, including a Stanford faculty development workshop at Hiroshima University, where, she explained, "I would bring three colleagues from Stanford out to Japan to share their knowledge."

Last summer, Akatsu took a sabbatical to develop curricula for a new medical school in Japan — the country's first in roughly 35 years. "We submitted an innovative curriculum to the Ministry of Education."

The new medical school, International University of Health and Welfare, aims to be a hub for Asian medical students and will train attendees to serve the global community, Akatsu said. "When the government allowed a new medical school to be established, the condition was that this new medical school will be 'very different' from any existing medical schools in Japan. This school will invite students from other Asian countries — like Vietnam or Mongolia — and classes will be taught mostly in English, which is unheard of in Japan."

In August, Akatsu once again traveled the 5,000 miles across the Pacific Ocean to accept a new role as dean for medical education at International University of Health and Welfare School of Medicine. It's a natural fit for her, and she will oversee all aspects of education — from curriculum, to teaching, to student affairs. "There's so much to learn," she said of the opportunity. "It's like a start-up in my mind; very exciting, but very challenging."

Though she's leaving the Stanford campus, Akatsu says she would like to bring the university's innovative spirit along with her. "I'm truly grateful for the time I've had here. I'll be bringing along the Stanford attitude and spirit, including entrepreneurship and innovation. That forward-thinking spirit — where you're not afraid of failure and look for lessons in challenges — that's what I will miss, and what I'll carry with me."

The Center for Digital Health Is Open for Business

Recent conversations with architects of the School of Medicine's new Center for Digital Health painted a picture of how the center will address several questions: How useful are digital tools in today's medical arena? How can they be incorporated into clinical practice? How can patients figure out if products designed for them work or are worth the price? Those architects are Sumbul Desai, MD, a clinical associate professor of general medical disciplines; Lauren Cheung, MD, MBA, a clinical instructor of general medical disciplines; and Mintu Turakhia, MD, an assistant professor of cardiovascular medicine.

Desai described three situations that led to the creation of the center: "First, faculty were being approached by tech companies interested in health care, but there was no mechanism to track that work back to Stanford. They were working with these companies on their own, often without the resources or expertise the school offers nor working with other faculty with complementary expertise. Second, we noted a lot of interest around digital health and medical education and training: How does the next generation of physicians make a mark in this space? Third, after implementing digital health initiatives on the hospital side, Lauren and I were often called upon by startups and other health systems to explain how we did what we did. We wanted to leverage that interest and generate more opportunities for the faculty."

The center, according to Cheung, "provides an opportunity for us to build infrastructure and resources to enable collaboration between faculty and industry. At Stanford we are blessed with the School of Engineering, the School of Design and the Graduate School of Business in addition to the School of Medicine and others, and we're right here in Silicon Valley. But we've lacked a way to connect faculty to the work being done outside the academic institution, especially in digital health."

As a cardiologist with expertise in atrial fibrillation, Turakhia wants to generate data that support digital health interventions for cardiovascular disease. "We generate evidence ranging from technology assessments and implementation studies to full-scale multicenter trials working with experts across the university. My role straddles the Center for Digital Health and the Stanford Center for Clinical Research (SCCR)," he says.

Two trials that Turakhia is spearheading combine the two centers. The first is an observational study looking for undiagnosed atrial fibrillation with wearable patch ECG technology rather than a Holter monitor. The second is a randomized trial in afib patients to see whether an app plus a care team is better than usual care in improving adherence to newer anticoagulants. "My goal is to execute studies quickly and inexpensively," he says.

The center has three approaches to addressing the needs of Silicon Valley industries while engaging Stanford faculty in interesting and rewarding collaborations. Desai describes them:

1. Faculty Engagement and Consultation. We connect our faculty to companies while decreasing the burden on them to figure it out on their own. We envision the center serving as a connector joining Silicon Valley to Stanford.
2. Education. We want our faculty to become thought leaders in the precision health initiative. We will train the next generation of physicians to become leaders in digital health via fellowships, internship opportunities, conferences and traditional education methods. And we will offer educational programs to startups and other outside companies.
3. Research. We answer simple questions about digital health tools and interventions: "Does it work?" "Does it improve value?" And we validate digital health tools by creating a research validation method, leveraging the SCCR.

Look for exciting results from the new center.

▼ From left: Lauren Cheung, MD, MBA; Mintu Turakhia, MD; and Sumbul Desai, MD.

Research Refutes Common Belief about Overprescribing

Though some research has suggested the opioid epidemic is being stoked by a small group of bad actors operating out of backroom pill mills, researchers with the Center for Primary Care and Outcomes Research (PCOR) have found that prescribing painkillers is widespread among general practitioners.

Despite public policy efforts, overdoses from prescribed narcotics such as morphine, oxycodone and hydrocodone have reached record highs. The Centers for Disease Control and Prevention reports opioid overdoses have quadrupled since 2000.

The PCOR study, which examined Medicare prescription drug claims data for 2013, appeared in a research letter published in *JAMA Internal Medicine*.

"The bulk of opioid prescriptions are distributed by the large population of general practitioners," said lead author Jonathan Chen, MD, PhD, an instructor of medicine and former Stanford Health Policy VA Medical Informatics fellow.

The researchers found that the top 10 percent of opioid prescribers account for 57 percent of opioid prescriptions. This prescribing pattern is comparable to that found in the Medicare data for prescribers of all drugs: The top 10 percent of all drug prescribers account for 63 percent of all drug prescriptions.

The specialties of family practice and internal medicine prescribed the most Schedule II opioids approved by the Food and Drug Administration in 2013, followed by nurse practitioners and physician assistants, according to the study.

"These findings indicate law enforcement efforts to shut down pill-mill prescribers are insufficient to address the widespread overprescribing of opioids," Chen said. "Efforts to curtail national opioid overprescribing must address a broad swath of prescribers to be effective."

He noted in a subsequent *JAMA* essay that, "While many clinical topics compete for education priority, prescription drug misuse and addiction is one that an inadequately trained medical community will routinely contribute to, if not overtly cause. Facing this is challenging, but I recall one of my medical school attending's teachings: The patient you least want to see is probably the one who needs you the most."

A study by the California Workers' Compensation Institute in 2011 found that one percent of prescribers accounted for one-third of opioid prescriptions, and that the top 10 percent accounted for 80 percent of prescriptions.

The newer PCOR study used a different data set. Instead of California Workers' Compensation prescriptions, it looked at prescriber data from the 2013 Medicare prescription drug coverage claims and investigated whether such disproportionate prescribing of opioids occurs in the national Medicare population.

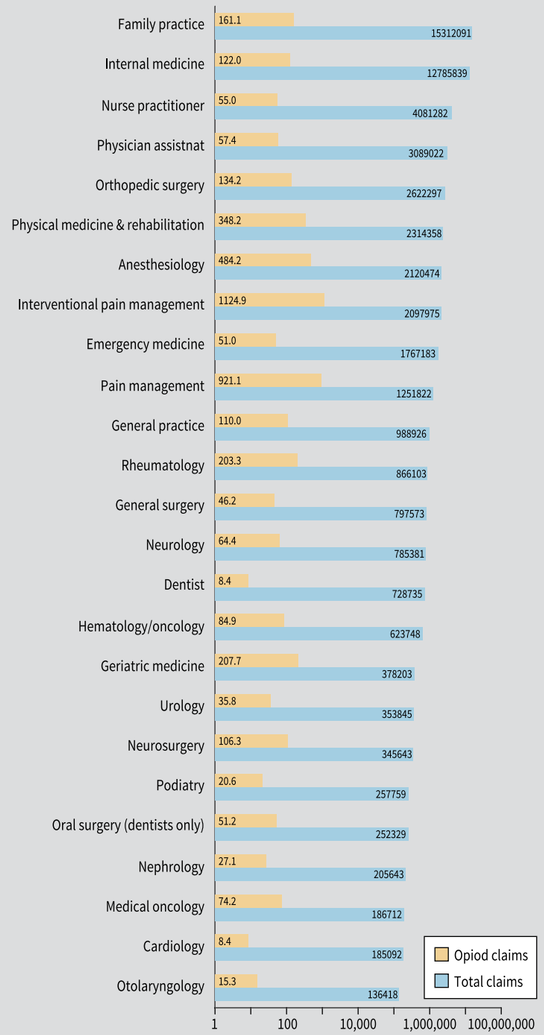
Both studies looked at Schedule II opioids, which include the commonly abused drugs hydrocodone, codeine and fentanyl, the drug responsible for the recent accidental overdose death of legendary musician Prince.

The data set created by the Centers for Medicare and Medicaid Services included all prescribers and represented all Medicare prescription drug coverage claims for 2013. The researchers focused on the data for Schedule II opioids: 381,575 prescribers and 56.5 million claims.

"The earlier study suggests potentially aberrant behavior among those extreme outlier prescribers, while implying the remaining majority do not contribute much to the problem," said Chen. "And now we know this is not the case."

Associate professor of medicine Nigam Shah, MBBS, PhD, was a co-author; assistant professor of psychiatry and behavioral sciences Anna Lembke, MD, was the study's senior author; and professor of psychiatry and behavioral sciences Keith Humphreys, PhD, was a co-author.

Distribution of opiods by Medicare prescriber type



Stanford Program Trains Half the Nation's Med-Anesthesia Residents

▲ Michael Lin, MD, will be the first person to complete the combined residency program.

Stanford offers a unique five-year combined residency training program in internal medicine and anesthesia.

Michael Lin, MD's daily schedule mirrors that of a normal, busy anesthesia resident: early call times, long hours in the operating room and a flurry of patients and cases.

Once a month, however, Lin's schedule deviates from the norm.

On these days, Lin will start early — around 6 a.m. — when he arrives at Stanford Hospital to begin preparations for his first anesthesia case of the day. By the time he gets himself prepped and situated it's about 7 a.m. — the typical time when cases begin. He'll spend the next five hours standing in the operating room anesthetizing patients.

At noon, he'll leave his fellow anesthesiology residents behind in the OR, change out of his scrubs and walk over to the Stanford Internal Medicine clinic, where he'll spend the rest of his day treating outpatients as a medicine resident.

Lin's hybridized schedule is a hallmark of Stanford's combined Internal Medicine-Anesthesia Residency, a unique five-year training program for residents interested in both specialties. Medicine-anesthesia graduates are board certified in both fields, and are poised to pursue careers focused in critical care, but they might choose another field where combined training would make sense, such as pain management or cardiac anesthesia.

The Critical Care Component

Lin says that "one thing that has really drawn residents into this program is the critical care component. The ICU is really the intersection of medicine and anesthesia. You're encountering critically ill patients with severe pathologies, so you need skills in acute resuscitation and advanced medical support that anesthesiologists are accustomed to providing in the OR, but you also need to treat the underlying pathology that landed them there in the first place, which is more aligned with the work of internal medicine physicians."

The Internal Medicine-Anesthesia Residency is structured as a five-year combined program, which basically saves a year for the person who wants training in both specialties. Residents spend their first postgraduate year in internal medicine, their second year in anesthesia and years three to five split equally between the two disciplines. Because of the parallel skills that are being acquired from both departments, the resident can cut out about six months of training in each discipline.

A Natural Fit for Stanford

"For us, this combined program makes perfect sense," says Ron Witteles, MD, director of the Internal Medicine Residency Training Program. "We have very strong departments in both internal medicine and anesthesia at Stanford. Those two departments have historically been close. In fact, we're one of the relatively few academic institutions whose ICUs are run jointly by the departments of medicine and anesthesia."

With 10 residents currently participating in the combined program, Stanford is the largest of only four such programs in the United States. "Not only are we the largest, but more than half of all the U.S. medical graduates who are training in med-anesthesia in the nation are currently in our training program," Witteles adds.

Lin, who will be the first person to complete the combined residency program — in June 2017 — sees many benefits of incorporating into his practice his training as an anesthesiologist and his training as an internist.

"It does give me a little bit more perspective that I think is helpful in counseling patients and in my own management of those patients both on the medicine side and on the anesthesia side."

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March 2

Georgette Stratos and Kelley Skeff change the way teachers at Stanford and around the world think about teaching -- and they've been at it for 30 years. http://stanford.io/1Ro0ave

Stephanie Harman
@DrSteph_H

@StanfordMedRes @cuttingforstone discussing the importance of presence, Samaritan aspect of medicine to new interns

11:49 AM - 20 Jun 2016

Stanford Department of Medicine
June 30

What does it mean to be a great doctor, diplomat and economist? Through a children's nutrition project in rural Guatemala, Stanford Health Policy's Paul Wise inspires aspiring physicians to consider how they can make a difference serving the needs of people around the globe. http://stan.md/28QxXMQ

David Svec
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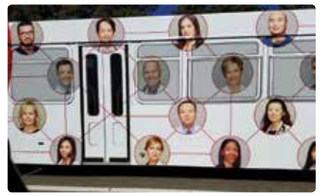
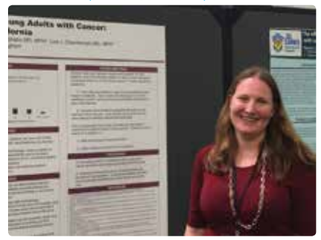
Livermore Bus - Stanford Valleycare hospitalist team



9:38 PM - 30 Aug 2016

Steven Asch
@steveaschmd

Disparities paradox:Afr Amer &Hisp adolescents get more aggressive endoflife care @StanfordDeptMed -Johnson #pallonc



6:17 PM - 9 Sep 2016

Joy Wu
@JoyYWu

Congrats to @StanfordDeptMed #endocrine fellow Rodrigo Valderrabano on winning an @ASBMR Young Investigator award

10:39 PM - 18 Sep 2016

Robert Harrington
@HeartBobH

Congratulations Abraham @cuttingforstone @ StanfordDeptMed. National Humanities Medal for "...keeping the patient in the center..."

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Andre Kumar
@AndreKumarMD

Proud of our resident Andrew Gilman for presenting today's grand rounds! @ StanfordDeptMed @StanfordMedRes

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Cathy Garzio
@cgarzio

Really proud of our women faculty

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Stanford Dept Med
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Ronald Witteles
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