Blocking a metabolic pathway may shrink type of kidney cancer

By Krista Conger

The first mouse model of an aggressive form of kidney cancer has identified an Achilles’ heel in the disease that could lead to new treatment approaches in humans, according to a joint study by researchers at the School of Medicine and the School of Humanities and Sciences.

Specifically, the cancer cells appear to rely primarily on the metabolism of an amino acid called glutamine for their energy. Blocking glutamine metabolism in mice caused the tumors to grow more slowly.

"In the future, we hope to use this model to categorize different types of kidney cancer and identify those patients who might respond favorably to specific therapies," said Dean Felsher, MD, PhD, professor of medicine. "In the near term, we can test whether blocking glutamine metabolism is a viable approach for people with Myc-dependent liver cancer."

Feldser shares senior authorship of the study, which was published online May 11 in the Proceedings of the National Academy of Sciences, with Richard Zare, PhD, the Marguerite Blake Wilbur Professor in Natural Science and a professor of chemistry. Postdoctoral scholar Emelyn Shroff, PhD, is the lead author.

A new strain of mice

Renal cell adenocarcinoma is the most common type of kidney cancer in adults. It develops in the lining of small tubes in the kidney that transport waste from the blood to the urine. It can be difficult to diagnose, and people with advanced cases often have a poor prognosis.

The researchers genetically engineered a strain of mice to make either Myc or another cancer-associated protein called Ras in the proximal tubules of the kidney when a compound called doxycycline, which had been added to their drinking water, was removed from it. (Myc and Ras are not normally produced at high levels by these cells.) Ras-producing mice did not get cancer. But within just a few weeks, the mice that made Myc developed kidney cancer.

Genetic signature may enable early, accurate sepsis diagnosis

By Bruce Goldman

Investigators at the School of Medicine have identified a pattern of gene activity that could help scientists create a blood test for quickly and accurately detecting whether patients are experiencing a deadly immune-system panic attack.

Sepsis is a whole-body inflammation syndrome set off when the immune system wildly overreacts to the presence of infectious pathogens. It is the leading cause of hospital deaths in the United States, accounting for nearly half of the total number, and is tied to the early deaths of at least 750,000 Americans each year. Its estimated annual cost to the health-care system exceeds $24 billion.

The great majority of sepsis cases are caused by bacterial rather than viral infections and are best treated with antibiotics. But antibiotics are unhelpful — and can be counterproductive — when a patient has an outwardly similar but infection-free syndrome called sterile inflammation, an intense, systemic inflammatory response.

Drug could be effective against deadliest childhood brain tumor

By Erin Digitale

For the first time, scientists have identified an existing drug that slows the growth of the deadliest childhood brain tumor.

The drug restricted the tumor’s growth in a lab dish and improved the survival time of mice that had the tumor implanted into their brains, according to researchers at the School of Medicine, in collaboration with colleagues at other institutions. The work is noteworthy because the disease, a brain stem cancer called diffuse intrinsic pontine glioma, is nearly always fatal and lacks an effective treatment.

"There have been over 200 clinical trials of chemotherapy drugs for DIPG, and none have shown any survival benefit," said Michelle Monje, MD, PhD, assistant professor of neurology at Stanford and a senior author of the paper. "But those trials were conducted before we knew anything about the unique biology of this tumor."

While the preclinical data in the new study are encouraging, Monje cautioned that the drug, panobionstat, needs further testing in a closely monitored human clinical study.

Nurses, doctor are honored for advances in cardiac care

By Sara Wykes

In 1966, Stanford Hospital joined the handful of hospitals worldwide with a dedicated nursing unit for coronary care. That specialized unit, with only four patient beds, was advanced for its time and so, too, was what followed for the nurses who worked there.

"Nurses then couldn’t start IVs," said Joan Fair, PhD, RN, MSN, NP, one of the unit’s original nurses and the unit’s founding director, wasn’t a fan of that kind of work. "Some doctors were totally against nurses doing these kinds of things," Fair said. "It also took time for some doctors to accept our opinions about how their patients were doing, or if we saw a problem and called them and asked them to take a different line of treatment."

The coronary care unit is now approaching its 50th anniversary. In April, Spivack, now a professor emeritus of medicine at Stanford, and many of the nurses who worked in the unit over the decades were honored at a special dinner. The occasion was the official announcement of a $2.5 million gift from Spivack to honor the nurses who pioneered the unit’s specialized critical care for cardiac patients. The gift will fund the nursing station when the unit is relocated to the new adult hospital.

Patricia Ballard, a longtime secretary in the coronary care unit, Joan Mersch, a former nurse coordinator, and Joy Oeth Paris, a former nurse, attended a celebration marking the official announcement of a gift to the unit, which was among only a few of its kind when it was established.

See NURSES, page 6
Edward Sheen on being a White House Fellow

By Kris Newby

The Stanford Healthy Neighborhood Discovery Tool has won an award for excellence from the Center for Active Design, a nonprofit organization that promotes health and vitality through urban projects that can improve public health.

The software tool allows community advocates and city planners to model the impact of a neighborhood’s walkability, safety and access to healthy food by using tablet computers. It was among six projects to win this award.

First tested in 2011, the software was designed by researchers from the Healthy Ageing Research and Technology Solutions Laboratory at the Stanford Prevention Research Center. The project was directed by Abby King, PhD, professor of health research and policy and of medicine.

Using the built-in capabilities of mobile devices, the tool tracks users’ walking routes and allows residents to geographically tag hazardous locations, linking them with the users’ audio narratives and photographs. This crowd-sourced information can then be used to notify city planners about things that need to be fixed and improved, such as poorly lit walkways and unsafe crosswalks.

In addition to the tool, the researchers have created guidelines for teaching residents and grassroots organizations how to persuasively communicate these community needs to city planners.

The Healthy Neighborhood Discovery Tool is a wonderful tool to help identify what’s important to them, said King. “By putting a human face to these problems and challenges, it is easier to identify an urgency to the changes that need to be made.”

The benefits of these changes in the built environment—the man-made environment—go well beyond aesthetics: Research shows that people who live in places that promote walking, socializing and eating fresh foods are physically and mentally healthier than those who do not.

Feliciana Jimenez, a resident of Redwood City, documents hazards in her neighborhood using a tablet computer with the software tool.

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By Kris Newby
Ulcer-causing bacteria induce stomach stem cell growth

By Kim Smuga-Otto

The ulcer-causing bacterium Helicobacter pylori can directly interact with stomach stem cells, causing them to divide more rapidly, according to a new study by researchers at the School of Medicine.

The increased cell division was observed in mice, but the findings could explain why H. pylori is a risk factor for gastric cancer in humans, the researchers said.

They used 3-D microscopy to identify epithelial cells that replenish the stomach lining. The bacteria can directly interact with stomach stem cells, causing them to divide more rapidly.
By Ruth Scheechter

Lloyd Minor, MD, dean of the School of Medicine, has announced the winners of the annual Spirit Award and Inspiring Change Leadership Award.

Spirit Award winners are selected for their outstanding dedication, initiative, motivation, positive attitude and customer service. This year’s recipients are ELIAS GODDY, a necropsy technician in the Department of Comparative Medicine; JESSICA METZGER, a lab manager in the Department of Biochemistry; and DEBRA SCHEUCHE, associate controller in the Office of Fiscal Affairs.

The Inspiring Change Leadership Award, which goes to staff members who have implemented processes that improve the school, was given to LYNN DENED, associate director of curriculum in the Stanford Biodesign Program, and ROHIT GUPTA, director of theBiobank in the Institute of Immunology, Transplantation and Infection.

The winners will each receive $3,000.

Elias Goddy

As a student at Menlo-Atherton High School, Goddy knew he wanted to work with animals. He started volunteering over the weekends, washing down cages in Stanford’s Veterinary Service Center. Twelve years later, he has held almost every position that involves working with the center’s collection of rodents, fish and large mammals.

“I am an animal lover. It’s important to me that we provide humane care and secure the well-being of the animals we work with,” Goddy said.

The center is used by faculty, fellows, lab technicians and students from a wide range of Stanford departments and divisions, as well as veterinary training programs from throughout the Bay Area, who require animal models for diagnosing and treating diseases that affect both humans and animals. Most of them are taught by Goddy on how to care for their animals and the proper method of collecting samples. He estimates he teaches an average of five new users each week.

“[I] work from the bottom and work my way up, so I probably know the center better than anyone,” said Goddy, who now collects tissue and cell samples and maintains the equipment in the necropsy lab. “I like to share what I know. Plus, the people who come here are working to find cures for cancer and other diseases, so it makes me proud to be helping them just a little in my own way.”

He is known for his initiative and works directly with investigators to meet their requests, and he has made crucial decisions about necropsy equipment and supplies. Elias is a tremendous asset to the department. He is dedicated, open and friendly, and works tirelessly with a smile and a joke on hand at any time,” said Sean Adams, PhD, a research fellow in comparative medicine. “He goes out of his way to help students, investigators and the veterinary staff, and spreads his infectious good attitude with whomever he interacts.”

Jessica Metzger

When Metzger makes her rounds on the fourth floor of the Beckman Center, very little escapes her notice. From checking freezer temperatures and how chemicals are stored to mandated health and safety regulations, she is responsible for the Biochemistry Department’s 25 research labs, equipment, maintenance and training, and for addressing the concerns of more than 250 faculty, students and staff.

Metzger started her Stanford career 17 years ago as an administrative assistant in the Department of Pediatrics and quickly took on responsibilities as a facilities coordinator. A colleague suggested she apply for the position of lab manager for biochemistry, where she has remained for the past 14 years. Aside from ensuring best practices and training all new students, staff and faculty, Metzger — an expert on space planning and on finding the best sources for furniture and equipment — must manage a complicated system of upgrades and laboratory renovations.

The biggest challenge is coordinating project schedules with researchers to have the least impact on their work,” she said. “I’ve had to re-arrange the space in several areas within the department to accommodate the influx of faculty and students and into newly renovated lab areas. There has been an enormous amount of planning and scheduling of construction and crews. Her impact extends beyond the Biochemistry Department’s walls. She helped another department prepare for a major electrical upgrade and arranged for the repair of the building’s elevator. She established a website that provides user instructions on all major pieces of the department’s equipment and manages a shared spreadsheet of students and supplies.

“This award is such an honor and a complete surprise,” Metzger said. “I am so humbled to have been nominated.”

Debra Scheuch

After 38 years at Stanford, Scheuch has gone from typewriters to databases and interdepartmental envelopes to e-mail. But what hasn’t changed is her love of numbers and her willingness to find solutions when the answer is not quite what was expected.

“The technology has changed and made information more accessible and more responsive,” said Scheuch, who started at the school’s Office of Fiscal Affairs in 1977 as her first job after graduating from San Jose State. “But it’s always changing and always challenging.

Despite a short stint as an administrative assistant in the medical school’s development office and seven years as an administrator in the Department of Pathology, Scheuch knew she belonged where she could help with the medical school’s fiscal policy, budgets and financial practices and procedures. She works mostly with department administrators, helping to resolve issues and coming up with options. Her institutional knowledge, and the extensive network she has established over the years, also allows her to connect resources and point people in the right direction.

“I am an accountant by nature,” she said. “I like to figure out problems and help to resolve them.”

Her expertise is especially appreciated by her supervi- sor, Archana Mehta, the medical school’s controller of financial operations and compliance, who has been on the job for only seven months. “Her vast knowledge of the university and the School of Medicine’s financial arena — the budgeting process, understanding policies and procedures, making her the ultimate go-to person for anyone who has financial questions,” she said. “She is always willing to help and goes out of her way for any request, large or small.”

Lynn Dened

What do you do when a new academic program is introduced? You write a textbook. What do you do when technology and fresh perspectives change the field? You make a second edition.

Dened, who has been with the Stanford Biodesign Program for 1½ years, was formerly at the Graduate School of Business, where she wrote case studies and research. The symposium is designed to be less structured and formal than other research conferences to encourage students to share their work with their peers.

Some of the projects are still in progress. All have a Stanford faculty adviser. Funding comes from a variety of outside fellowship awards and internal fellowships from the School of Medicine.

“Stanford tries really hard to open doors in the area of scientific research and give students a little nudge to go through,” said Laurene Baker, PhD, director of the Scholarly Concentration INSIDE STANFORD MEDICINE

Annual symposium showcases research by medical students

By Tracie White

In a dress shirt and tie, Raymond Deng, a third-year medical student, stood next to a poster describing his research project on opioid use among veterans.

Deng explains his research project on opioid use among veterans.

For the past 32 years, Stanford medical students have participated in the symposium as a chance to share their work with their peers.

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Anjali Dixit describes her research on managing low back pain.

She was one of the 10 winners in this year’s competition.
then served as staff director for its Program in Health-care Innovation. There she worked with faculty in the GSB and the School of Medicine to “pull their vast experience and wisdom out of their heads and put it onto paper.” The result had changed the medical technology sector that we had to revise more than 50 percent of the content.” The new edition was released in Fall use after a year, perhaps indicating a new awareness that involves publishing, clinical work, research, but most do more, he said. Stanford’s medical students are required to medical students that promotes in-depth scientific research is a key element of training.”

• Christine Luhrmann, laboratory services manager, Department of Molecular and Cellular Physiology
• Michelle Ferrari, research nurse, Department of Urology
• Julian Hinojosa, life science research assistant, Department of Pathology

• John Jeang, life science research assistant, Department of Microbiology & Immunology

• Gina Jager, life science research assistant, Department of Biomedical Engineering

• Susan Johnson, administrative services manager, Department of Medicine

• Jeannie Lukas, administrative associate, Department of Structural Biology

• Carmencita Nicolas, life science research assistant, Department of Dermatology

• Linda Yasukawa, life science research assistant, Department of Medi cine

Employees who have served for 4 years are:

• Marcia Bieber, basic life science research associate, Department of Obstetrics & Gynecology

• Mary Eaton, lab research techni cian, Department of Pathology

Employees who have served for 45 years are:

• Tom Nozaki, research and develop ment engineer, Department of Ge netics

Program, a required program of study for medical students that promotes in-depth learning and scholarship. Each of Stan ford’s medical students are required to complete at least one quarter’s worth of research, but most do more, he said.

“We train the kind of doctors who become leaders,” Baker said. “Whether that involves publishing, clinical work, re search or parenting — education in sci ence research is key element of training.”

For Deng, this was a chance to explore the world of addiction medicine, something she never thought she would pursue as a career. Deng’s study in volved researching a Veterans Health Administration’s database on opioid drug prescriptions and determining possible predictors of opioid discontinuation. He looked at a year’s worth of data on 1.3 million veterans with prescriptions for opioids. Results showed that 65 percent of patients continued opioid use after one year, two years, or even longer. He noted that patients with comorbid conditions such as schizophrenia and dementia were sig nificantly associated with discontinuing opioid use. He also found, perhaps indicat ing some success with programs begun during the same time period to prevent addiction.

Thadany, the symposium judge, lis tened intently to his description, nodding her head in encouragement. “Why did you pick this study?” she said, clipboard in hand.

“Personal reasons,” Deng said, adding that someone in his life has a heroin ad diction, and that an epidemic in prescrip tion drug abuse has been shown to have contributed to an increase in heroin use. She nodded again. “The great thing with data like this is that the data itself can bring up questions that we didn’t think of,” she said. “If the Googles and the Ya hoo blogs of the world can use this data like this for research, so can we. Great work. Go crazy with it.”

Awards

Award and Inspiring Chang Leadership Award

Rohit Gupta

Researchers require a variety of biological material for trials and assays. But thanks to Gupta’s expertise in regenerative medicine, it’s not uncommon for the researchers in his lab to use his own cells. “I keep a well-stocked lab in my lab,” said Gupta, adding that he is often asked to provide tissue for research projects. “I’ve always wanted to have her.”

Gupta had the vision of a Web interface and built it pretty much on his own.”

Gupta, who studied biochemistry and mathematics at the University of California-Irvine, came to Stan ford 10 years ago, working in the labs of various faculty before joining the center five years ago.

“He’s always had a passion for programming in the life sciences, and I wanted to apply it to do it. We need to find a way to make the system more streamlined and easier to maintain,” said Gupta, who did his own coding and testing. “I was fortunate that I was given such great support and autonomy.”

I never expected such an honor at this point.”

His efforts, in collaboration with oncology re searcher Shivani Chaitanya Leng Liu, PhD, resulted in a quick and easy-to-use website that gives authorized researchers around the country immediate access to databases. The system requires no special training, and the data can be used for clinical trial reports, assay-monitoring or grant applications. “This type of system is scattered anywhere in the research world,” Maeker said.

Gupta is now leading a big data initiative among senior investigators at Stanford to link clinical and experimental data to the same system.

Ruth Schechter is a freelance writer and editor.

“Before the textbook, there really were really no comprehensive textbooks on medical device development, and that an epidemic in prescription drug abuse has been shown to have contributed to an increase in heroin use.”

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Ruth Schechter is a freelance writer and editor.
in response to infection, and after sifting through a huge amount of data we found them,” said lead author Timothy Sweeney, MD, PhD, a postdoctoral scholar now doing a residency in general surgery at Stanford.

Numerous studies have been conducted to find differences in the activation levels of immune-response genes between infection-related inflammation and sterile inflammation. But these studies have yielded conflicting or murky results. One big reason is that both infections and noninfectious tissue trauma activate many of the same immune-system components and pathways. At the gene-activation level, the overlap is staggering. More than 80 percent of a person’s roughly 25,000 genes change their activity levels substantially, and mostly in the same direction, in response to massive inflammation, whether due to sepsis or sterile causes. That overlap obscures any easily detectable changes attributable solely to infection.

Needle in a haystack

Further confounding attempts to identify patterns of increases or decreases in gene activity is the fact that someone patients are already experiencing sepsis when they’re admitted to the hospital, who then become infected during their hospital stay. So two different sepsis patients admitted at the same time may be at very different stages of a complex inflammation process.

“How do you figure out which tiny fraction of those changes was caused by infection?” Sweeney said. “You’re looking for a needle in a haystack.”

Khatri said, “The needle, it turns out, consists of a signature formed by consistent changes in the activity levels of a mere 11 genes amid the chaotic background of the other 20,000-plus genes whose activity levels fluctuate markedly over the course of systemic inflammation and recovery.”

The Stanford sleuths analyzed a number of publicly available data sets containing results of studies that had assessed activity levels for the entire human genome in sepsis cases, as well as in controls with similar systemic inflammation. In all, they looked at more than 2,900 blood samples from nearly 1,600 patients in 27 different data sets containing medical information on diverse patient groups — men and women, young and old, suffering from sepsis or inflammation or sepsis, including patients who already had sepsis when first admitted to the hospital and patients who were diagnosed with it later — in addition to healthy controls and other subgroups.

The analysis consisted of two separate steps. First, the researchers scoured the 11 genes across more than 650 patient samples. They looked for genes whose activity uniformly and substantially increased or decreased, across all nine data sets, in patients within 24 hours of a sepsis diagnosis compared with genes from those not diagnosed with the infection.

Initially, whatever signal may have been hiding in this group of samples was lost in the surrounding noise of myriad irrelevant gene-activity fluctuations. But the cacophony ceased when the scientists adjusted their analytical approach by taking into account when the patient was injured or operated on. That way, say, researchers could compare the gene changes, following a surgery or injury, in inflammation-related gene activity over time, independent of the presence or absence of infection. Blood samples were therefore time-matched according to how soon a blood sample was drawn after the initial injury or surgery.

After this adjustment, 11 genes jumped out of the haystack as likely sep-sic markers. The researchers confirmed this 11-gene signature in an additional 18 cohorts comprising in all more than 1,800 patient samples.

“We were able to identify a slight bump in activity of these 11 genes in patients two to five days prior to their clinical diagnosis,” said Khatri. That could mean getting an earlier diagnosis than can be achieved with current approaches, which is key considering the rapid rate at which sepsis mortality rises once it gets a foothold.

The gene-activation signature showed a sepsis-detecting accuracy surpassing that of methods now in use, Sweeney said. Combining the new technique with other current diagnostic methods is likely to be more accurate than using any one alone, he added.

Stanford’s Office of Technology Licens-ing has filed a patent on the method — a first step towards realizing this particular application with these findings.

Undergraduate student Aadiya Shal- diah was another Stanford co-author of the study. The study was funded by the Stanford Department of Surgery, the National Library of Medicine and the National Institute of Allergy and Infectious Diseases.

Stanford’s Department of Medicine also supported the work.

Symposium on teaching medicine at the bedside set for Sept. 28–29

Registration is now open for a two-day symposium designed to train physicians and medical educators on how to teach medicine at the bedside. The event, which is scheduled for Sept. 28–29 at the Li Ka Shing Center for Learning and Knowl-edge, is titled “Stanford Medicine iSM 2015: Best Prac-tices for the Bedside Move-ment at Your Institution.” Registration forms are available for more information or to register, visit http://stanfordmedicine25.stanford.edu.™
Glioma continued from page 1

The research team is now planning such a trial. Panobinostat was recently approved by the Food and Drug Administration for treatment of patients with DIPG.

The repair drugs a portion of the cellular machinery now known to be defective in DIPG. This knowledge is derived from research that showed “a key thing that is wrong with DIPG cancer cells gets corrected by panobinostat,” said Monje, whose lab has been examining the protein kinase Akt as a role as a pediatric neuro-oncologist at Lucile Packard Children’s Hospital Stanford. The data also showed that some DIPG cells develop resistance to the drug, which means it will likely need to be combined with other drugs to achieve the best results in humans. “I don’t think this is a cure, but I do think it will help,” she said.

A devastating diagnosis

DIPG affects 200-400 school-aged children in the United States each year and has a five-year survival rate of less than 1 percent; half of patients die within two years of diagnosis. The data gives only a temporary reprieve from the tumor’s growth. In addition, it is inoperable. DIPG is a diffuse stem cell tumor, where breathing and heartbeat are controlled, “with the healthy and diseased cells tangled like two colors of wool knitted together,” Monje said.

The tumor has also been difficult to study. Because it is not surgically removed, it is typically biopsied, for decades researchers lacked DIPG tissue to examine in a lab. That changed about six years ago, when Monje and other scientists began asking patients’ families to consider donating tumors for research after their loved one’s death. The first study led by Monje was the first in the world to report establishment of a line of DIPG cells that could be studied in a dish. Currently, researchers have determined that 80 percent of DIPG tumors have a mutation in histone 3, one of the proteins that packages DNA. The mutation damages the regulation of DNA in cells involved in the cancer — a form of epigenetic change.

In the new study, the research team screened 16 DIPG cell lines derived from patients’ tumors against 83 possible chemicals. They discovered two cell lines associated with cancer cell growth.

The team further demonstrated that, in cells of patients’ tumors implanted in their brain stems, infusing panobinostat directly into the brain stem slowed tumor growth. They also gave the drug in an intraperitoneal injection to mice with DIPG tumors, and showed that enough panobinostat reached the brain to slow growing tumors in its survival.

In a dish, DIPG cells that survived initial treatments of panobinostat developed some resistance to the drug, the study found. However, the team also found that a specific chemical pathway that had previously been shown to inhibit DIPG cells, worked synergistically with panobinostat, with the two agents counteracting the development of resistance.

“The goal is multimodal treatment,” said Monje. In addition to the planned clinical trial, she said, which will be the first with panobinostat alone to improve survival.

The researchers then turned to a new tissue analysis technique called desorption electrospray ionization mass-spectrometric imaging, or DESI-MSI, recently implemented by postdoctoral scholar and study co-author Livia Eberlin, PhD, in the Zare laboratory to compare the lipid profiles of cancerous and normal tissue.

DESI-MS creates a highly detailed, two-dimensional map of the chemical composition of a tissue sample through a process that can be loosely compared to a specialized car wash. Samples are sprayed with a thin, high-powered stream of liquid droplets that dissolve their outer surface. The resulting back spray, which contains molecules from the surface of the sample, is collected and analyzed by mass spectrometry. By moving the tissue around in a two-dimensional plane, it’s possible to make a chemical map of its composition.

Distinct chemical composition

The researchers found that the cancerous kidney tissue had a chemical composition distinct from that of non-cancerous tissue. The former had higher-than-normal levels of molecules generated as glutamine is metabolized. By analyzing the activity of the enzyme glutaminase, which is responsible for metabolizing glutamine, caused the animal tumors to grow more slowly when exosysteme was removed from their drinking water.

Finally, the researchers showed that both Myc and glutaminase levels are also high in human samples of renal cell adenocarcinoma tumors, indicating that it may be useful not to test whether blocking the glutamine pathway is a viable treatment for patients with the disease.

The researchers are now planning to create additional mouse models of other types of kidney cancer. “Using DESI-MSI combined with immunochemistry and gene analysis, we may now be able to sort many kidney cancers into discrete types. We’re also planning on using this technique to find new therapies for kidney but also liver cancers and lymphomas,” Felsher said. Felsher emphasized that the study was only possible with the concerted effort of chemists in the Zare laboratory. “This was a true cross-disciplinary effort,” Felsher said. “I am proud and excited about the outcome of this collaboration.”

Other Stanford authors are postdoctoral scholars, Arvin Gouw, PhD, Meital Gabay, PhD, and Stephanie Casey, PhD, former postdoctoral scholars, Stacey Adam, PhD, and David Belovin, PhD; and instructor Yulin Li, MD, PhD.

The research was supported by the Burroughs Welcome Fund, the Damon Runyon Foundation, the National Institutes of Health, the Leukemia and Lymphoma Society, the American Lung Association and L’Oreal for Women in Science, Stanford’s Department of Medicine also supported the work.
By Jennifer DeCoste-Lopez

Recently, the flipped classroom — a model of instruction in which didactic content is delivered outside the classroom (usually online), and in-person class time is used for active learning — has infiltrated the educational landscape from kindergarten to professional school.

As a medical student, I generally agree with advocates for using the approach in medical education. For example, Charles Prober, MD, Stanford’s senior associate dean for medical education, argues in a New England Journal of Medicine commentary that the opportunity for enhanced time efficiency, student self-paced and classroom time freed up for more interactive learning make the flipped classroom a potentially attractive approach for educating physicians. I say “potentially” because, like anything else, the flipped classroom is a good approach only if it is done well. For me as a learner — even a modern, millennial learner — I’d much rather attend an engaging lecture or study a well-written textbook than watch a lessoy online video or struggle through a poorly facilitated interactive classroom session.

So I have to admit I harbored some skepticism when, about a year ago, Prober invited me to become involved the Re-Imagining Undergraduate Medical Education Initiative, an ambitious project to create a new, flipped-classroom-based microbiology and immunology curriculum in collaboration with four other U.S. medical schools. Although I was excited to have a role in such a large-scale project, I worried that the hype of the flipped classroom trend would overshadow what I thought should be the priority: training our future doctors with the highest-quality education — not just the flashiest.

Happily, my worries have proved unfounded. I have seen the faculty and staff from the five schools work tirelessly to produce an impressively high-quality final product. In fact, I have even come to believe that the flipped classroom model intrinsically helps incentivize medical faculty members to prioritize teaching.

One of these incentives is that old favorite from middle school: peer pressure. Traditionally, in the world of academic medicine (most med students are trained in academic medical centers), peer opinion is almost exclusively based on faculty member’s research accomplishments. Academic research involves constant accountability — faculty compete for prestigious grants, promotions and awards, and routinely present their work at conferences to be directly critiqued by their peers.

By contrast, when a professor delivers a lecture to medical students, it is uncommon for any of his or her peers to be in the audience. They probably never even knew he or she was giving a lecture, much less whether it was any good. So it’s no mystery why many faculty, even those who say they enjoy and value teaching, hold themselves to a much less rigorous standard in teaching than in research.

This isn’t to say that none of our med school faculty care about teaching — in fact, we have a wonderful constellation of faculty dedicated to educating med students. But in most cases, those who focus on teaching do so in spite of strong incentives to direct their energies elsewhere.

By contrast, the faculty working on our microbiology and immunology curriculum are subjected to the scrutiny of expert peers for every online lecture they create. As a student, it has been immensely satisfying to watch these educators strive to perfect their lecture videos before showing them to their peers, only to have the reviewing faculty member doggedly insist on making it clearer, more relevant, more concise. Even fast trackers who already tend to put considerable effort into their teaching, having peers appraise their work raises it to another level. This direct peer review of teaching (at least the online component) is made possible because online educational media can be readily accessed and reviewed by peer educators.

Another way that I have seen the flipped classroom motivate faculty educators is by giving them the opportunity for more meaningful in-person interaction with students.

Traditionally, “interaction” with students meant spending an hour behind a podium, flipping through a PowerPoint deck, while a handful of nameless medical students drowsily looked on. In the flipped model, the teacher instead spends that hour sharing clinical or scientific expertise with a group of students who are engaged in problem-solving with the concepts they are learning. After experiencing this more rewarding way of teaching through our microbiology curriculum at Stanford, our faculty (all busy clinicians and/or researchers) have been begging to come back again and again as facilitators. Several have even requested more faculty development activities to proactively improve their teaching skills in that setting.

As med schools across the country and worldwide transition to flipped classrooms, these potentially attractive approaches for educating physicians and medical students are only now beginning to come fully into play. That they’ll leverage this opportunity, by implementing rigorous peer review of online material combined with meaningful student interactions in the classroom, to motivate their faculty to become better teachers, is exciting.

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