Hitting Cancer in the Gut
Intestine Cultures Provide Valuable Tool to Study Cancer

We now know that cancer cells contain dozens and even hundreds of genetic mutations. But simply identifying the mutations doesn’t tell us which ones cause the cancer. It’s like apprehending someone at the scene of a crime, but not knowing whether they are the perpetrator, an accomplice or an innocent by-stander.

Individual or groups of mutations can be tested by recreating them in cells grown in the lab, or in the tissues of animals (usually mice), and determining if cancer results. But cells in petri dishes tend to be poor replicas of living tissues, and it is painfully slow, costly and difficult to assess hundreds of individual genetic mutations, and combinations, in mice.

“More accurate and efficient systems are needed to determine the function of mutations, and whether they are causing the cancer, or are just irrelevant flaws,” says Institute member Calvin Kuo, MD, PhD, professor of hematology.

Kuo and his collaborators have developed just such a system specifically for studying the mouse intestinal tract. Combining the strengths of the two testing methods mentioned above, they have effectively grown, or “cultured,” mouse intestinal organs in the lab, and done so on a scale so small that they are able to grow hundreds at a time, thus dramatically accelerating the process of discovering and testing cancer-causing mutations.

“These cultures are like mini-organs,” said Kuo. “They completely recapitulate all the different cell types with exquisite precision, and look like what you find in the intact animal.”

Despite their biological accuracy, the mini-organs look like tiny balls of cells, about the size of a pin-head. Their research potential, however, is enormous.

Tinkering With Tiny Intestines
The origin of the intestine cultures began in 2004 when a Japanese postdoctoral researcher named Akifumi Ootani invented a way to grow mouse intestine cells in a test

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The Campaign for Stanford Medicine is an ambitious effort to secure resources to complete the new Stanford University Hospital and pursue new research opportunities. The Stanford Cancer Institute’s research priorities are a major part of the campaign:

**Cancer Prevention:** Some broad risk factors have been identified (smoking cessation and radiation exposure), but we need to assess how other exposures impact select demographic groups. Population-based genetics will enable identification of new risk factors and help determine who should avoid them.

**Early Detection:** Imaging technologies can detect some tumors at an early stage, but many, such as pancreatic cancer, evade detection until they have become lethal. Engineers and biologists are now working together to develop special molecules that adhere to microscopic cancers and illuminate them for imaging devices.

**Treatment:** A new generation of more effective and less toxic therapeutics will target specific subtypes of cancers based on their individual molecular characteristics. We will convert many lethal forms of cancer to chronic conditions.

**Survivorship:** More people are surviving cancer and coping with long-term physical and psycho-social issues. We commonly treat symptoms as they emerge, but new predictive models based on tumor biology will help identify side effects early enough to allow constructive intervention.

Achieving these goals means bringing together clinical researchers and basic scientists to rapidly translate laboratory findings into treatments. Building on a superb foundation of basic science and engineering, the Stanford Cancer Institute has identified the “translational resources” needed to do so. We hope you will help us by supporting the Campaign for Stanford Medicine.

**Beverly S. Mitchell, MD**  
Director

This and previous editions of SCI News can be viewed online at: cancer.stanford.edu/news by clicking “Newsletter” in the left column.

If you would prefer to receive the electronic version of SCI News via email, please email your request to scinewsletter@stanford.edu.
tube. This was quite a feat since researchers had been trying to culture healthy intestine tissues for decades, but could never coax the cells to survive for more than a few days.

Ootani’s novel technique used minute pieces of intestine tissue to start the culture, rather than the common method of using a small number of purified cells. After much trial and error, he got the tissue fragments to grow by suspending them in a porous scaffold-like gel that allowed them exposure to the liquid nutrients in the tube as well as to the air. Nourished by “food” and oxygen, the fragments grew into three-dimensional ball-like clusters, with the different intestinal cell types organized just as they are in the body.

It turns out that Ootani’s use of tissue chunks rather than pristine cells preserved the cellular micro-environment and the all-important stem cells. Intestinal stem cells give rise to the more specialized cells of the entire system, and must constantly replenish the uniquely short-lived cell populations of the intestine.

It was a huge breakthrough, but the cultures remained fragile and difficult to work with.

Looking for ways to enhance them, Ootani came across a research paper describing how activating a specific network of proteins stimulates the stem cells of the intestinal tract. The protein network was called Wnt, and the paper’s author was Calvin Kuo.

From Wnt It Came
Kuo earned his MD/PhD at Stanford in 1994, then left to do his internship and residency at Brigham and Women’s Hospital in Boston. He went on to become an oncology fellow at the Dana Farber Cancer Institute, before returning to Stanford in 2001 to start his own lab, and to rejoin what he described as “a highly collaborative research environment.”

A blood expert, Kuo was studying ways to contain cancer by cutting off the blood flow to tumor cells. In the course of his experiments he had an unexpected—and completely unrelated—observation: suppressing the function of “Wnt” proteins selectively killed the stem cells of the intestinal tract.

This powerful response told Kuo that Wnt is critical for intestinal stem cells. If the absence of Wnt caused death, would more Wnt promote health or stimulate growth in these important cells? Kuo was eager to find out.

But stem cells in the intestinal system are a long way from blood and cancer, so Kuo sought out specialists for advice. He didn’t have to go far.

“It was very easy to find colleagues at Stanford who could help us pursue these new research avenues in which we ourselves were not expert,” Kuo said.

Before long, Kuo was expert enough to be describing Wnt’s influence on intestinal tissues in scholarly medical journals, like the one read by Ootani.

Ootani contacted Kuo, who coincidentally was planning a trip to Japan to give a presentation. The two met in Tokyo, and after learning about the intestine cultures Kuo invited Ootani to join his lab at Stanford.

As hoped, the amplification of Wnt signals in the cultures caused them to grow larger and replicate faster. Kuo recognized that they now had a robust living model with which to study many aspects of the intestinal system. While he shared the cultures with colleagues doing a variety of research, Kuo, the oncologist, was focused on their applications to cancer.

Designating the Driver
As mentioned previously, cancer cells tend to be riddled with mutations. The challenge is to determine which of them cause cancer.

“There is the concept of the ‘driver’ mutation versus the ‘passenger’ mutations,” explained Kuo. “We want to identify those minority of drivers—the ones that are truly causing the cancer—from the vast majority of ‘passengers’ that are just randomly mutating and have nothing to do with the cancer.”
In January the Cancer Prevention Institute of California (CPIC) welcomed Ann W. Hsing, PhD, as its new director of research. Hsing, an expert in the epidemiology and etiology of prostate and biliary tract cancers, joins CPIC after 22 years with the National Cancer Institute (NCI) in Maryland. CPIC is part of the Stanford Cancer Institute, and Hsing’s position includes an appointment as an SCI member.

The Fremont-based CPIC is dedicated to preventing cancer and to reducing its burden where it cannot yet be prevented. It manages extensive cancer databases, and is recognized for its work in social, behavioral and nutritional epidemiology. In addition to Hsing, several CPIC scientists are SCI members, sharing key resources and collaborating on many research initiatives.

“To me, CPIC is like heaven for cancer epidemiologists,” said Hsing. “With our internal capabilities and our partnership with Stanford, we have everything we need to carry out cancer research, prevention and control.”

While assessing CPIC’s current capacities, Hsing is also charting a course for future growth, including an expanded effort in molecular epidemiology. This burgeoning area of research evaluates the genes, molecules and chemical pathways that influence an individual’s chances of developing cancer, and surviving it. Stanford possesses the laboratory resources and technical expertise to partner with CPIC in these types of high-impact studies.

Another area of opportunity is the dissemination of cancer-related information and services to survivors, at-risk populations and the general public. Hsing supports enhancing CPIC’s and SCI’s communications and service components, particularly to underserved communities.

“We combine the intellectual pursuit of research with the on-the-ground interaction with the community,” said Hsing.

Well-rounded Leadership

As research director Hsing is responsible for helping achieve CPIC’s organizational goals, building synergies with Stanford researchers, and nurturing the growth of junior scientists and faculty. It takes skilled leadership to support and mentor the young investigators, and meld their individual efforts into a coherent research program. While at NCI, Hsing received numerous awards for her leadership and mentoring.

“I am fortunate to have had very good mentors at every stage of my career,” she said. “With experience comes the responsibility to help the next generation of scientists.”

Hsing earned an MPH in biostatistics from the University of California, Los Angeles, in 1981 and a PhD in epidemiology from the Johns Hopkins Bloomberg School of Public Health in Baltimore, Maryland, in 1988. She conducted postdoctoral research at Johns Hopkins before joining NCI in 1989 as a cancer epidemiology and biostatistics fellow.

Hsing recently relocated from her longtime home in Maryland, and is quick to emphasize the benefits of the Bay Area, from its moderate climate to the cultural melting pot of its communities.

“There is such diversity of population here,” said Hsing. “It gives us great opportunities to learn lessons and develop models that we can apply globally.”

Global Vision

Hsing is eager to expand CPIC’s and SCI’s research globally. She has extensive experience with molecular epidemiology and with population-based studies in international settings, including China, Africa, Chile and India. She notes that the incidence of many cancers is increasing around the world, and that much of the cancer burden will soon be found in underdeveloped regions, particularly Africa and Asia.

Hsing is working with collaborators in Ghana on the possibility of establishing a registry there to collect much needed cancer surveillance data. While such a registry could be a boon to epidemiological research in the area, its data would also be used to benefit at-risk groups everywhere, including African Americans, who have the highest prostate cancer incidence and mortality in the world.

Hsing is also conducting a study of gallbladder cancer in Chile, where incidence rates are among the highest in the world. Along with researchers at the Pontifical Catholic University of Chile, she is planning to investigate gallbladder cancer’s causes, as well as potential treatments. The multinational team hopes to turn their findings into improved public health policies and practices.

“We don’t want to go to a population and study their problems for merely a scientific discovery,” said Hsing. “Whatever we learn is shared, so the people will benefit from our research and hopefully the burden of cancer will be lower in the future.”
SCI Community Partnership Program

Breast Cancer & African Americans Conference

The SCI Community Partnership Program (CPP) held its first annual Breast Cancer & African Americans Conference on May 5. More than 400 attendees gathered in downtown Oakland; some coming from as far as Nevada, Georgia and even Ethiopia.

The event provides breast cancer information and resources to address the cultural, social, and educational needs of African Americans, to reduce breast cancer disparities and the burden of cancer among this population. The program included practical strategies to incorporate positive and sustainable behavior changes (e.g., healthy eating, maintaining a healthy weight, and stress reduction) in order to improve health outcomes.

“It is important to have this unique cancer education program that is centered on community engagement, and that is culturally relevant and tailored to African Americans,” said Pamela Ratliff, Senior Community Partnership Manager and organizer of the event.

The Breast Cancer & African Americans Conference—formerly called “Each One, Reach One”—will take place annually on the first Saturday in May, and is one of many CPP-sponsored events to address cancer disparities and increase minority engagement in community-based research and cancer clinical studies. The program was co-sponsored by the Cancer Prevention Institute of California.

For more information, please contact Pamela Ratliff at pratliff@stanford.edu or 800.383.0941.

CPP members wish to honor Ms. Wanna Wright, a dedicated health care professional and community advocate, who passed away following this year’s conference.

Teaming Up for Cancer Research

Seventeen members of Team Stanford competed in four different Leukemia & Lymphoma Society (LLS) “Team in Training” endurance events this summer and raised over $48,000 for blood cancer research.

SCI is a proud sponsor of the inaugural Stanford team. Each member completed one of the challenging runs, rides and/or swims.

“Having been associated with LLS for over 30 years, I know that the work they support to improve research and patient outcomes in the blood cancer field has made a huge difference,” said SCI Director Beverly Mitchell, MD. “It is truly a great organization.”

In addition to Dr. Mitchell, the LLS supports the work of many other SCI members, including Helen Blau, PhD, Susan Knox, MD, PhD, Ron Levy, MD, David Miklos, MD, PhD, Robert Negrin, MD, and Sam Strober, MD.

After a little rest, Team Stanford plans to participate in LLS’s 2013 “Team in Training” events.
SCI Member Jean Tang, MD, PhD, is the lead author on one of three recent papers showing that the drug vismodegib was effective in treating and preventing basal cell carcinoma (BCC), the most common cancer in the United States.

Tang and colleagues tested vismodegib in patients with Gorlin syndrome, a rare disease in which individuals have tens to hundreds of disfiguring BCC tumors throughout their body. Currently there is no effective treatment for Gorlin syndrome. Trial participants who took one vismodegib tablet daily developed an average of two new tumors per year, compared with 29 new tumors in subjects taking a placebo. The trial was stopped early due to the vismodegib’s effectiveness.

“In most subjects, all the carcinomas disappeared. No tumors progressed while the subjects took vismodegib,” said Tang, an assistant professor of dermatology. “We were very excited about the results.”

The drug did not permanently cure patients; the BCC tumors returned, although very slowly, once treatment was stopped.

The second paper presented findings from a phase-2 clinical trial showing that vismodegib was successful 43 percent of the time in either complete or partial shrinkage of tumors in patients with advanced BCC. Based on this study, the Food & Drug Administration approved the drug for use in treating advanced forms of BCC.

The third article was a letter to the editor detailing a case study of a 41-year-old man who had skin cancers all over his body caused by a unique genetic mutation different from that of Gorlin syndrome. The cancer also responded well to vismodegib, suggesting that the drug may be successful in treating other invasive cancers with related causal mechanisms. SCI member and professor of dermatology, Anthony Oro, MD, PhD, was the letter’s senior author.

All three papers were published in the New England Journal of Medicine.

Anxiety Increases Cancer Severity in Mice

A new study found that after mice were dosed with ultraviolet rays, the nervous ones—defined as those with a demonstrated penchant for risk aversion—developed more tumors and invasive cancer.

Researchers led by SCI member Firdaus Dhabhar, PhD, exposed hairless mice to UV rays for 10-minutes, three times a week, for 10 weeks. All the mice eventually developed skin cancer, but the anxious mice had more tumors and were the only ones to develop invasive forms of cancer.

These types of tumors may be vulnerable to an immune system response, so Dhabhar’s team compared the immune responses of the low- and high-anxiety mice. They found the nervous mice had higher levels of immune system-suppressing cells and lower levels of chemicals that initiate an immune attack on tumors.

The next step is to test this research in humans.

“It’s bad enough that cancer diagnosis and treatment generates stress and anxiety, but this study shows that anxiety and stress can accelerate cancer progression, thus perpetuating a vicious cycle,” said Dhabhar, an associate professor of psychiatry and behavioral sciences.

The study was published online in the journal PLoS ONE.

Spotting Oral Cancer With a Cell Phone

Assistant bioengineering professor Manu Prakash, PhD, has developed a way to use smartphone cameras to create detailed images of the oral cavity and screen patients’ mouths for suspicious lesions. The inexpensive, portable device could make it possible for millions of people who live in remote areas to get oral cancer screening done as easily as snapping a photo.

Prakash’s oral scanner, called OScan, attaches to any smartphone’s built-in camera, and allows an operator to take a high-resolution, panoramic image of the complete mouth cavity. Illuminated in blue fluorescent light, cancer lesions stand out as dark spots. Images can be sent wirelessly to health workers, dentists or oral surgeons anywhere in the world. The device is designed for mass production, with an estimated cost of just a few dollars.

Prakash and his design team won cash awards for first and second place, respec-
I am thankful for the current support so we can continue this transition from technology development to field deployment,” said Prakash.

Genetic Diversity in Tumor Cells

Cancer tumors randomly slough off cells into the bloodstream. Referred to as circulating tumor cells (CTCs), these tiny cancer bits contain clues about the nature of the tumor from which they came. But separating CTCs from blood cells is hard; there may be as few as one or two CTCs among the billions of cells contained in a milliliter of blood.

A multidisciplinary team of Stanford researchers, led by SCI member Stefanie Jeffrey, MD, used new technologies invented at Stanford to isolate CTCs and conduct detailed genetic analysis on them. The results show an unexpected amount of genetic diversity in cells from the same tumor.

“Within a single blood draw from a single patient, we’re seeing heterogeneous populations of circulating tumor cells,” said Jeffery, a professor of surgery and chief of surgical oncology research.

Some cells have activated genes that enable them to insert themselves in new places, helping a cancer spread between organs. Others have completely different patterns of gene activation, making them less likely to survive in new tissue. Some cells may even have genetic markers that could predict their susceptibility to a specific therapy.

This discovery is an important step toward understanding the valuable information contained in CTCs and for potentially developing new targeted therapies.

This research was published in the journal PLoS ONE.

“Altruistic” Stem Cell Behavior Has Possible Link to Cancer

Stanford postdoctoral scholar Bikul Das, MBBS, PhD led a new study showing that in times of stress certain human embryonic stem cells (hESCs) produce molecules that not only help themselves survive, but also protect nearby cells. Such so-called “altruistic” behavior is observed in animal and insect species, and even some bacterial populations, but this is the first reported finding of altruism at the cellular level.

No good deed goes unpunished, however, as these same protective hESCs appear to be more prone to accumulating genetic mutations that could lead to cancer. The finding arose from Das’ research into how hESCs react to low-oxygen environments, which is relevant because many cancerous tumors are low in oxygen. Das found that when the hESCs were deprived of oxygen, free-radical molecules were generated that began causing internal damage in some cells.

Das and his collaborators transplanted some of the mutated hESCs into mice, and cancer tumors soon formed. These findings also suggest that a better understanding of hESC altruistic behavior may provide new insights into cancer causing mutations, as well as potential therapies.

The study was published online in the journal Stem Cells.

Molecule May Help Starve Cancer

Stanford scientists have shown that a molecule, called microRNA-320a, is responsible for helping control glycolysis, the process of converting sugar into energy. Sugar is fuel for some cancers, and the research suggests that microRNA-320a may be used to cut off a tumor’s energy supply.

“We hope that this discovery will yield a new avenue of molecular treatment for cancers, particularly lung cancer, which is the number one cause of cancer deaths worldwide,” said SCI member Joseph Shrager, MD, professor of cardiothoracic surgery and chief of the Division of Thoracic Surgery.

Glycolysis is also known to contribute to the wasting of unused muscles, such as the diaphragm (the primary muscle used for breathing) when people use ventilators. Diaphragm wasting causes people to remain on ventilators for extended periods, which can lead to serious complications, including death.

Shrager and colleagues studied lung cancer tissues as well as diaphragm muscle tissues from patients who had been on a breathing machine for more than a few hours. They found that both types of tissue had increases in glycolysis, as well as reductions in microRNA-320a. Test tube experiments confirmed that microRNA-320a controls how much energy these two very different tissues have available to them.

The findings were published online in the Federation of American Societies for Experimental Biology Journal.
In Conversation

Don Listwin

Don Listwin made his mark in Silicon Valley as CEO of companies Sana Security and Openwave, and as an Executive Vice President at Cisco Systems. A native of Canada, the energetic engineer turned executive was right at home in the epicenter of high-tech creativity and entrepreneurship. But ten years ago he stepped away from the industry and established the Canary Foundation, the world’s first non-profit organization dedicated solely to the funding, discovery, and development of tests for early cancer detection. Listwin is a member of the Board of Scientific Advisors at the National Cancer Institute and this year was named a consulting professor in the Stanford School of Medicine.

SCI News recently caught up with Listwin as he took a break from preparing his Woodside home to host a dinner and research update for Canary supporters. The gourmet event featured several Bay Area “celebrity chefs,” organized and led by Traci Des Jardins, chef and co-owner of San Francisco’s renowned Jardinière restaurant.

Q: The Canary Foundation has a very specific mission. What led you to start it?

Don: My motivation stems from family involvement. I have had my mom, my uncle and, of late, my dad all die from cancer or complications of cancer. My mom passed away ten years ago from ovarian cancer, and after she died the engineer in me tried to understand what needed to be done to stop ovarian cancer. It became very clear very soon that early detection is the key to survival.

My research led me to Nobel Laureate Dr. Lee Hartwell, then the director of the Fred Hutchinson Cancer Research Center in Seattle. He felt that given the state of cancer knowledge, the most effective way to save lives in the coming decades was to invest in early detection.

The premise was that we did not understand the basic biology of cancer—we still don’t—but if you could find it early enough, you could cut it out and effectively cure it. You don’t get to use the “c” word—cure—very often with cancer.

Q: What appealed to you about this idea?

Don: What resonated with me was when Lee said, “I think that this is more of an engineering problem than a science problem.” Now, he may have been speaking to his audience (laughs), but it seemed to me that early detection was a tractable problem where we knew enough about the biology to begin to solve it.

Q: How did you get started?

Don: I initially invested in a lab at the Hutch working on ovarian cancer “biomarkers” (a specific biological substance that can be tested to identify or measure a disease state), and this was back in the early 2000’s before biomarkers were cool. (laughs)

As my relationship with Lee developed, I proposed and supported a strategic initiative, called the Canary Initiative for early detection.

Q: Why “Canary”?

Don: It’s a reference to the historic use of canaries in coalmines for the early detection of poisonous gas. For cancer, we envisioned a two-test strategy: a simple blood test for a biomarker followed by an imaging test to identify and isolate the cancer so a surgeon can cut it out.

In 2004, Lee recruited our first multi-disciplinary and “multi-omics” team. We started with surgical oncologists—all of our teams include at least one person who treats patients, so that we don’t loose track of the problems we are trying to solve—and recruited Pat Brown, MD, PhD, of Stanford to lead the genetics thinking, Peter Laird, PhD, of USC to work on methylation, Stanford’s Sam Gambhir, MD, PhD as the molecular imaging expert, and Sam Hanash, MD, PhD, of the Fred Hutchinson for proteomics.

I think this team began the first multi-omics discovery work to understand where cancer biomarkers were and how to identify them.

Q: How has the program evolved?

Don: The Canary Initiative targets all solid tumors, and to this point we have five programs, each with at least one multi-disciplinary team. Ovarian cancer was the first and we have added lung, pancreatic,
breast and prostate cancers. Next year we hope to add colon cancer, which is what ultimately killed my dad.

Q: Can philanthropy create new models for conducting medical research?
Don: Yes, I think a lot of people who come from the technology world—in particular the internet, which was a new model— tend to get involved in “directed philanthropy” where we can be very engaged. Canary is a highly directed program looking to end up with clinical products. Our model is to put together great teams, focus on specific questions, and provide seed money to increase their chances of getting additional funding from other sources.

Our long-term goal is to create a molecular diagnostics industry and then shut down Canary. I think that’s a good model: identify a problem, solve it, then shut down.

Q: Is it working?
Don: So far it is. In the last decade Canary has put between $60-70 million into this program, which we estimate has leveraged between $250-300 million in additional funding. We now have seven clinical trials ongoing, with more to come, and industry is starting to help in order to get these technologies into the marketplace.

If you really want to solve a problem like this you have to find a way to bring some substantial resources for scientists to do the extra work you need, and then to provide the leverage.

Q: Is there a role for people who don’t have substantial resources to contribute?
Don: As I am sure it is with the Stanford Cancer Institute, most of Canary supporters give modest amounts, and it is that collective group of thousands of small gifts that really makes the difference. One example is the upcoming Canary Challenge bike ride, which is a great opportunity for people to help the Institute $500 at a time. We hope to turn the Challenge into a major event that gives the Institute the unrestricted funding it so badly needs to help recruit new faculty and launch new initiatives.

Q: Describe Canary’s relationship with Stanford?
Don: The first ten years of Canary’s scientific leadership came from Lee Hartwell, and now that baton has passed to Sam Gambhir, a passionate, globally respected scientist, who understands the problem at a systems level and is willing to invest time to lead this effort.

Also critical was the support of President Hennessy, Dean Pizzo and the Stanford Cancer Institute’s Bev Mitchell to allow us to build a dedicated center. The Canary Center at Stanford (part of the SCI) is a unique national program bringing together all the technology and leadership required to solve this problem holistically.

We continue to maintain our various teams at institutions along the West Coast and in Canada, but Stanford has become the focal point from which we lead and manage them.

Q: How has your experience with the Canary Foundation affected you?
Don: It has certainly created a whole second career for me! (laughs) I am an Internet geek first and foremost, but I am now also a member of the cancer research community, and that is a wonderful thing.

We have finally stemmed the tide of the increase in cancer deaths. I think a third of that achievement is due to prevention, a third is better therapeutics, and I believe a third of it is early detection, including mammography, colonoscopy, PSA and other tests.

I hope that by the time my two-year-old is a teenager that these tests—and newer, better ones that we help create—will be routine.

Canary Center

The Canary Center at Stanford—an integrated effort of private philanthropy, the SCI and the School of Medicine—is a world-class facility dedicated to cancer early detection research programs. The mission of the Center is to foster research leading to the development of blood tests and molecular imaging approaches to detect and localize early cancers.

The Center is the first in the world to integrate research both in vivo (in the living body) and in vitro (in the test tube) to deliver these tests, and houses state-of-the-art core facilities and collaborative research programs in molecular imaging, proteomics, chemistry and bioinformatics. These initiatives are linked to the Clinical Cancer Center and form a direct pipeline for the translation of early cancer detection research into clinical trials and practice.

The Canary Center is directed by Sanjiv “Sam” Gambhir, MD, PhD, professor of radiology & bioengineering, and director of SCI’s Cancer Imaging and Early Detection Program.

Save the Date!
2012 Canary Challenge

September 29
Cyclists ride to raise $1 million for SCI’s cancer programs.

The Challenge offers fully supported 50-kilometer, 75-kilometer, 100-kilometer and 100-mile rides.

www.canarychallenge.com
experiments, thus dramatically increasing the speed and scope of their research.

As cancer-causing mutations are identified the same system can then be used to identify molecular targets for therapeutic intervention, and to efficiently screen candidate drugs for their efficacy against cancer and their toxicity to human tissue.

Kuo’s group also created a practical “behavioral” test to assess cells’ lethality. They added special semipermeable membranes to the wells in their trays. As the mutated tissue cultures grow in the wells, researchers count the number of cells that push through the membrane as a measure of their proliferation and migration—their invasiveness—as a sign of metastasis.

“Metastasis is a hallmark of cancer, and is usually what kills people,” said Kuo.

Kuo’s group has validated their methods by successfully confirming known cancer-causing mutations, assessing new ones, and deciphering which mutations are most important within some of the known combinations.

Their research has progressed farthest in colon cells—colorectal cancer is the fourth leading cause of cancer death in the US—and they have cultured other intestinal organs, like pancreas and stomach, the sites of other devastating cancers. Further, Kuo and his team are working to refine the same culture and testing protocols with human intestinal cells for pre-clinical drug screening and toxicology tests.

With new mouse mini-organs to culture, many more gene mutations to evaluate, human cultures to perfect and a host of drug compounds to screen, Kuo and his colleagues seem to have experiments planned and scheduled for years to come. The work has tremendous potential to discover and assess a plethora of gene mutations and drugs that are relevant to numerous types of cancer. As with a lot of scientific progress, though, the creation of the remarkable intestinal cultures at the center of this work could not have been scripted.

Clinical Trials Awareness Week

The Stanford Cancer Clinical Trials Office (CCTO) sponsored and organized the first Clinical Trials Awareness Week from April 23 through 27.

The week featured a daily series of presentations by patients and physicians, educational poster sessions and an information desk, all to provide clinical trials information to patients, families and staff, and to highlight some of the more than 300 trials ongoing at the Stanford Clinical Cancer Center.

This sort of education is sorely needed. Nationwide, less than five percent of adults diagnosed with cancer are enrolled in clinical trials. The participation rate plummets to less than one percent in California, with ethnic minorities significantly under-represented.

The Stanford Clinical Cancer Center fares better than many comparable providers—it has a 15 percent participation rate—but physicians and trial coordinators acknowledge the need to involve still more people in such studies.

“It’s crucially important that we get word out to the community that clinical trials are one of the critical steps required for making any progress against cancer,” said SCI member George Fisher, MD, PhD, associate professor of medicine-oncology, and the CCTO medical director.

The popularity and success of the first Clinical Trials Awareness Week has ensured that there will be more to come. Information on Stanford’s clinical trials programs can be found on the CCTO web site (http://med.stanford.edu/clinicaltrials/cancer-search.do), and phone assistance line 650.498.7061.
The Campaign for Stanford Medicine: An Investment in Hope

The Campaign for Stanford Medicine aims to improve the health and well being of humankind locally and globally. It will advance medical research and teaching, help build the new Stanford Hospital, and facilitate translating discoveries and innovations into leading-edge, integrated care. Over the next two-to-three years, the goal is to raise $700 million for the new hospital and $300 million for School of Medicine priorities. One major emphasis is to catalyze discoveries that increase our ability to prevent cancer, identify it earlier and deliver optimal, personalized care to each cancer patient.

Philip Pizzo, MD, Stanford University School of Medicine dean, says, “The Campaign is about bringing forth new ideas and leveraging them in unique ways that will transform our community.”

Amir Rubin, president and CEO of Stanford Hospital & Clinics, comments that, “The Campaign will help usher in a new era of health care, through a transformative new hospital that implements highly coordinated, patient-centered care, and through an acceleration in the pace of discovery and innovation for which Stanford is known worldwide.”

The Campaign will make essential investments in science and teaching programs to shape the next chapter of medicine, including cancer. The additional resources will enable the Stanford Cancer Institute to expand its integrated structure of multi-disciplinary research programs and shared resource cores. Here are just a few of many examples of cancer-focused research and treatment advances taking place at Stanford:

- **One example of discovery through basic research**: Innovative cell culturing techniques that mimic living organisms are helping researchers pin down the specific genetic defects that cause cancer and to test the drugs that may treat it (as detailed in “Hitting Cancer in the Gut,” page 1)

- **Translation of breakthroughs into new interventions for patients**: Research in DNA repair pathways has yielded a new drug that appears to be promising for BRCA-mutation-related breast cancers.

- **Prediction and prevention**: Minuscule nanoparticles have been engineered to home in on and highlight brain tumors precisely, greatly easing their complete removal.

- **Educating and training future leaders in medicine**: The Stanford Cancer Institute oversees a variety of advanced training programs for medical and post-doctoral fellows, and administers a renowned PhD program to train the next generation of cancer biologists.

“The additional resources provided by the Campaign for Stanford Medicine will enable us to further enhance our many exciting cancer research and patient care initiatives,” says Institute director Beverly Mitchell, MD, the George E. Becker Professor in Medicine.

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For more information or to make a gift to the Cancer Discovery Fund, please visit cancerdiscoveryfund.stanford.edu or contact Maria Burns, Director of Annual Giving, 650.562.3400 or via email, maria.burns@stanford.edu.
Stanford Partners Talk Medicine

SCI Director Beverly Mitchell, MD, was one of four Stanford luminaries to discuss the changing landscape of medical research and patient care in the 21st Century. The May 10 “Partners in Medicine” panel also included the Dean of the School of Medicine, Philip Pizzo, MD, President and CEO of Stanford Hospital & Clinics, Amir Dan Rubin, and Senior Associate Chair for the Theory and Practice of Medicine, and best-selling author, Abraham Verghese, MD, MACP.

Over 300 members of the Stanford medicine community attended this unique forum, in which the panelists spoke extemporaneously about topics both grand (what role Stanford will play in the future of medicine) and personal (what transformative lessons they have learned from patients). Paul Costello, Chief Communications Officer for the School of Medicine, moderated the thoughtful and lively discussion.

The Partners in Medicine event opened with remarks from Mariann Byerwalter, distinguished chair of the Board of Directors of Stanford Hospital & Clinics.