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Stanford Cancer Institute News

A PUBLICATION FOR PATIENTS AND FRIENDS OF THE STANFORD CANCER INSTITUTE



Discovery Research



SCI Designated as a
Comprehensive Cancer Center



Clinical Research



Translational Research



Population Research

SCI's multifaceted and integrated programs provide a complete approach to cancer research, treatment and prevention.

SUMMER 2016

Years of Effort Produce National Cancer Institute Recognition SCI Earns Highest Cancer Center Designation

On July 1, 2016 the National Cancer Institute (NCI) recognized the Stanford Cancer Institute as one of the top cancer research centers in the United States. Already an NCI-designated Cancer Center, the SCI's increased breadth, depth and coordination of its research programs earned the NCI's highest cancer center status: as a 'Comprehensive' Cancer Center.

Each NCI-supported cancer center undergoes a thorough review every five years, and in its most recent assessment the SCI received an outstanding score from the external review committee. The NCI's written summary noted that the SCI "is clearly poised to make significant contributions to cancer research in the next five years."

This most recent honor is the result of years of coordinated effort by SCI's leadership and

nearly 400 members from across the University, and from its partner institution the Cancer Prevention Institute of California. Individual research achievements are laudable, but it takes many multidisciplinary scientists, physicians and staff, all working in concert, to achieve the required levels of basic, translational and clinical research—along with a broad based population science program—necessary to garner the coveted comprehensive cancer center status. SCI has done so through a strategic plan of growth, innovation and commitment to excellence, all built on a tradition of groundbreaking cancer research.

The Stanford School of Medicine has a rich history of pioneering research in the field of cancer. Among other discoveries, Stanford physicians and scientists are responsible for major advancements in radiation therapy and the development of new therapies for lymphomas. Building on this legacy, in

2003 visionary leaders set about to create a formal cancer center—what is now the Stanford Cancer Institute—by bringing together faculty and capabilities from across the School of Medicine and the entire University. The effort was spearheaded by **Philip Pizzo, MD**, Dean of the School of Medicine at the time, and the late **Karl Blume, MD**, founder of Stanford's renowned bone marrow transplantation program.

In 2007, SCI was designated as a Cancer Center by the NCI, a branch of the federal National Institutes of Health and the largest cancer research organization in the world. The NCI supports a nationwide network of Cancer Centers, recognized for their ability to conduct and coordinate cancer research. (NCI designations are based on an institution's strengths in science and

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Message from the Director

Comprehensive Cancer Research and Care



It is with great pride that I announce that the Stanford Cancer Institute has received formal designation as a National Cancer Institute Comprehensive Cancer Center! The designation is recognition of SCI's robust and integrated programs encompassing laboratory research, clinical care, population science and education.

I want to acknowledge and thank SCI's fantastic leadership team, program directors, scientific and clinical members, and our staff for their years of coordinated effort to accomplish this important goal. I also want to extend our sincere gratitude for the strong and consistent support we receive from everyone in the Stanford cancer community. Our growth and success depends on your involvement, and I want to assure you that we are already working to build on this achievement, and we will continue to accelerate our understanding, treatment and prevention of cancer.

This edition of *SCI News* highlights the work of two of our stellar physician-researchers. **Eben Rosenthal, MD**, is SCI's Associate Director for Clinical Care, and a specialist in surgical treatment of head and neck cancers (Page 3). **Pamela Kunz, MD**, (Page 6) is Medical Director of the new Neuroendocrine Tumor program, and a nationally recognized leader in the treatment of these complex cancers. Their stories illustrate both the incredible expertise and the collaborative nature of SCI's cancer care. What also stands out about both is their compassionate approach to helping cancer patients through the most difficult times in their lives.

I am excited to share that SCI members **James Ford, MD**, and **Jan Liphardt, PhD**, were recently highlighted as leaders of two ambitious research projects supporting the Obama Administration's National Cancer Moonshot Initiative (Page 5).

Part of being a comprehensive cancer center is educating and training the next generation of cancer physicians and scientists. SCI has a broad portfolio of training programs, and in this issue we highlight the 2016 class of SCI Fellows (Page 8). SCI is also committed to serving the local population, and we are happy to celebrate our 5th annual public conference on breast cancer and African Americans (Back Cover).

I hope this collection of stories gives you a sense of the breadth and coordination of SCI activities. We are gratified to have our efforts acknowledged by the National Cancer Institute, but we are committed to making sure that you, our Stanford cancer community members, remain our primary focus and our partners in reducing the burden of cancer. ■

Beverly S. Mitchell, MD
Director

The Stanford Cancer Institute

The Stanford Cancer Institute provides support and coordination for the range of cancer-related activities occurring at Stanford University, Stanford Health Care, the Lucille Packard Children's Hospital Stanford and the Cancer Prevention Institute of California. Our nearly 400 faculty members belong to more than 30 academic departments in three schools, and represent the wide array of disciplines involved with comprehensive cancer research, treatment, prevention, education and training.

The Institute is a National Cancer Institute-designated Comprehensive Cancer Center, with a scientific agenda combining laboratory research, clinical study, translational programs and population science. The Institute also engages in patient care, community education, clinical trials, as well as support and training for the next generation of cancer physicians and researchers.

Simply put, all of our members and resources are focused on one goal: to reduce the occurrence and impact of cancer.

Stanford Cancer Institute News is a quarterly update for members, supporters and friends. On behalf of our members and staff, we thank you for your ongoing support and welcome your feedback and inquiries.

Beverly S. Mitchell, MD
Director

David Rubenson
Associate Director of Administration and Strategic Planning

Michael Claeys
Senior Communications Manager

Contact

Stanford Cancer Institute
Lorry Lokey Building/SIM 1
265 Campus Drive, Suite G2103
Stanford, CA 94305
650.723.1680

scinewsletter@stanford.edu
cancer.stanford.edu

In Profile

Eben Rosenthal

Eben Rosenthal, MD, sat at the desk in his warm but modest office tucked in the back corner of the administrative level of Stanford's Clinical Cancer Center. As the John and Ann Doerr Medical Director of the Center, a Professor of Otolaryngology-Head and Neck Surgery and of Radiology, as well as a researcher, he had plenty to keep him busy, but as he worked he was mindful of the clock and the cell phone sitting near his elbow. He was waiting for a call.



Eben Rosenthal, MD

For the preceding few hours that day, other surgical colleagues had been removing a cancerous tumor from the mouth

of a patient. The case was serious, and the patient's jaw had to be removed. When that process was completed, the surgery team would call Rosenthal, a facial reconstruction specialist, on his cell phone, summoning him to repair the patient's cancer-ravaged face.

To do so he would spend four or five hours in surgery, using bone from the patient's lower leg to reform their jaw, and skin grafts from their arm to patch the face and neck, trying to restore function and form so that the patient will not only survive their cancer, but be able to eat, swallow and speak normally, and live their life with dignity and confidence.

"It is enormously satisfying to see patients who have a major issue and know you can help them," said Rosenthal. "This is a fairly narrow skill set, but it really helps the people who need it."

The treatment of head and neck cancers often involves major reconstructive surgeries, and the recovery process is fraught with an array of medical and psychosocial complications. As SCI's new Associate Director for Clinical Care, Rosenthal brings his experience with these complex cases to Stanford's effort to improve the treatment

and recovery experience to all of its cancer patients.

Rosenthal grew up in Ann Arbor, and completed medical school and residency at the University of Michigan. He then earned a fellowship in head and neck reconstruction at Oregon Health & Science University, and also pursued training in ear, nose & throat medicine. His first academic position was at University of Alabama, Birmingham, where he stayed for 14 years before being recruited to Stanford.

In his new role at Stanford—he has been on faculty for about a year—he divides his time between seeing patients, his research pursuits and his administrative responsibilities. He also performs reconstructive surgery on cancer patients almost every day that he is on campus.

"My experience at Stanford has been really good," said Rosenthal. "The research environment is lively, filled with novel ideas and a lot of interdisciplinary collaboration."

Research Interests

While Rosenthal's clinical work focuses on reconstruction, his research is aimed at achieving increased precision in cancer surgery. The challenge is to extract all the malignant tissue without taking adjacent healthy tissue. Tumors tend to look and feel different than healthy tissue, but the borders are usually not distinct, so better methods are needed to distinguish cancer tissue, wherever it resides.

"Approximately 80 percent of solid tumors get surgery, so even modest improvements will positively affect large numbers of patients," said Rosenthal.

While in Alabama, Rosenthal and colleagues developed a technique for tagging and illuminating cancer cells right before the surgeons' eyes. They chemically combined a fluorescent dye with an antigen known to selectively adhere to surface

markers of certain types of head and neck cancer cells. Patients are infused with the antigen, which binds with their tumor cells, and then the surgeon can use a common imaging device to shine light on the tumor and surrounding area. The fluorescent dye glows in response to the light, and the tumor is defined in stark relief. Even previously unknown areas of cancer spread are illuminated.

This "tumor-specific fluorescently labeled antibody" enables surgeons to remove more cancer and less healthy tissue, greatly improving outcomes for patients.

"What is also great about this approach is that we just took everything off the shelf," said Rosenthal. "We didn't have to invent anything, so we are greatly lowering the threshold for the amount of work and time required to bring this new technique to patients."

Rosenthal and others launched a clinical trial at Stanford to test two similarly labeled antibodies on several tumor types, including head & neck, brain and pancreas. More clinical trials are being planned. In collaboration with basic science and clinical colleagues, Rosenthal wants to establish Stanford as a leading center for this type of surgical imaging and experimentation.

New Clinical Initiatives

Rosenthal arrived during the early stage of the Stanford Cancer Initiative, the multidimensional effort to transform the cancer patient experience and improve health outcomes. Led by SCI and Stanford Health Care, the Initiative commits people, technology and other resources to improving coordination of care for every cancer patient treated at Stanford. Rosenthal works closely with SCI Director Beverly S. Mitchell, MD, and Sridhar (Sri) Seshadri, DM, Vice President of Cancer Services, to lead the Initiative's

See **EBEN ROSENTHAL**, page 10



Comprehensive, continued from page 1

research, and do not directly reflect on the delivery of patient care or cancer clinical services at that institution.)

The NCI reserves the “Comprehensive” designation for centers with greater capacity to conduct a wide range of basic and clinical science, and to make substantive links among these different branches of research. Comprehensive centers promote interdisciplinary collaborations and team-based science to systematically address more types of cancer in more settings, and ask fundamental questions about cancer’s underlying causes and mechanisms.

“I want to recognize Dr. Beverly Mitchell, who has worked tirelessly since becoming the SCI director in 2008 to achieve this prestigious honor for Stanford Medicine,” said Lloyd Minor, MD, dean of the School of Medicine. “The combined effort of the Institute’s multidisciplinary membership exemplifies how we are applying precision health to complex diseases and improving patient outcomes.”

INSIGHTS FROM THE DIRECTOR

Institute Director Beverly S. Mitchell, MD, the George E. Becker Professor of Medicine, led the coordinated campaign to achieve comprehensive status and advance all of Stanford’s cancer research and patient care activities. She recently answered questions about the accomplishment and the future of cancer research and patient care at Stanford.

What is the meaning of this new designation?

First, I want to say that this achievement is a testament to the talent and dedication of our members. Our faculty, young investigators, technicians and staff work together every day to improve our understanding and treatment of cancer, and to reduce its burden on patients and families.

The comprehensive designation is reserved for those cancer centers with the broad ability to connect basic science and clinical research with tangible extensions to their local populations. We are expected to serve

the people in what is called our “catchment area”—the nearby counties from which the majority of our patients come—and to identify diseases within the area on which we can focus, and thereby improve the care of our patients.

Another responsibility of comprehensive centers is to prepare the next generation of cancer researchers and physicians, and we are quite committed to our outstanding training programs. (See story on Page 8)

What was required of SCI to achieve the designation?

Stanford has always had very strong basic science, so it was a matter of building our clinical research enterprise, recruiting physicians who are also superb researchers, and building our population science program. These elements combine to form our translational research effort, which is the interaction of basic science with clinical- and population-based research in order to expedite the transformation of research discoveries into improved cancer prevention, diagnosis and treatment.

SCI’s growth and accomplishments to date would not have been possible without strong institutional support from the School of Medicine and Stanford’s two hospitals. We were also very fortunate to have received significant philanthropic investments from our community members that has been invaluable in helping us recruit many talented people and to enhance our patient care initiatives.

What are SCI’s plans for the future?

Cancer’s complexity and variation offers a great many scientific and programmatic opportunities for us to pursue, but I will mention three major themes that we are currently developing. First, we are enhancing our early-phase clinical research, which refers to testing new therapies not yet approved for use by the Food & Drug Administration. Such novel drugs need rigorous evaluation to determine whether they are effective against cancer, and that requires a significant infrastructure to ensure that patients understand and agree

to the research studies that will form the basis of future cancer treatments. We currently have key people in place to build a strong program.

We are also very interested in immunotherapy, a growing field that seeks to enable the body’s immune system to better identify and eliminate cancer cells. SCI members have done pioneering work in this area, and we have recently recruited additional talented faculty. We also have a robust laboratory research effort and several active clinical trials.

A third area is genomics and precision medicine. SCI members have developed a very effective way to identify the genetic mutations that underlie tumors, and to match those mutations with specific drugs. This program is well established, and we look forward to its continued growth and impact on patient care, particularly for those patients with treatment-resistant cancers.

What are some other promising areas of cancer research?

One exciting area of study is the tumor microenvironment—specifically, what happens in the milieu around the cancer cells, how they communicate within their environment, and how this understanding can be used to develop interventions in the tumor growth process. There is interesting new information about how cancer cells communicate. One method is through tiny vesicles called “exosomes,” which cancer cells release to interact with other cells in their environment. It is a rich area of study with lots of important questions to be answered.

The Obama Administration’s Cancer Moonshot Initiative includes a goal of finding ways to bring many different types of medical data together. Stanford has a history of innovation in data management and analysis, and several SCI members are involved in data sharing projects and collaborations, so this is another area of great potential opportunity. Benefits for patients may come more quickly in this field, since so much data already exists and

better algorithms, or “mining” techniques, can be developed far more rapidly than new drugs, for example.

What makes SCI unique?

I would argue that the talent and compassion of our faculty makes SCI unique, but I suspect every cancer center director would say that about their institution. We are an academic medical center with tremendous strength in basic research, we have partnerships with adult and pediatric hospitals, and we share a small campus with an elite engineering school, bioengineering department and a world-class computer science department. In addition, we are located at the heart of innovation and entrepreneurship in Silicon Valley, and in one of the world’s great biotech clusters. As we increase our programs in early-phase cancer therapies and population sciences, I’d say our uniqueness lies in the diversity of resources that we can apply to the study and treatment of cancer.

And although the NCI’s comprehensive

designation is based primarily on our capabilities with basic, translational and clinical research, our novel Stanford Cancer Initiative to transform patient care actually applies rigorous research analysis to every aspect of patient care in order to identify which modalities improve the cancer care experience and patient outcomes. We believe that is unique.

We practice patient-centered care in which patients and family members are involved in decision-making processes and directing care choices. Another tangible way to involve people in their own care is through patient-reported outcomes, in which patients detail their concerns right into their electronic medical records prior to their appointments, so that physicians can review them in advance and be prepared to address them.

What does it take to maintain a leading edge cancer research and treatment center?

It takes the commitment of leaders and members to embrace innovation and

new ideas, while maintaining focus on research and programmatic priorities. It takes a commitment to supporting the work of our members through competitive grant awards, shared infrastructure that enables their research, and the staff and organization needed to manage cancer clinical trials.

And as I mentioned previously, we have received tremendous community support over the years, and continued investment will be incredibly important to our success going forward.

Are you optimistic about the future of cancer research?

Absolutely. We are at a true inflection point where a number of different techniques and technologies are coming together to help us to improve outcomes and the quality of life for many cancer patients. There is much more work to be done, of course, but I am truly optimistic about our prospects to better prevent, diagnose and treat many forms of cancer. ■

SCI Members’ Projects Contribute to National Cancer Initiative Obama ‘Moonshot’ Targets Cancer

This January, in his final State of the Union address, President Barack Obama announced a bold new initiative to accelerate progress on the prevention, diagnosis and treatment of cancer.

With what he dubbed the ‘Cancer Moonshot,’ Obama has proposed nearly \$1 billion in new cancer-related investments over five years, and he tapped Vice President Joe Biden—who has had tragic family experiences with cancer—to lead the effort. In June, Biden held a Cancer Moonshot Summit in Washington, DC to promote the initiative and bring together a broad group of stakeholders. Several SCI members participated in the Summit, and two were included in a published list of

research activities supporting the goals of the Moonshot.

James Ford, MD, an Associate Professor of Medicine (Oncology) and of Genetics, is Stanford’s leader in the Oncology Precision Network (OPeN), a multi-institutional effort to share genomics data in order to bring the most promising treatment insights to cancer patients and physicians. OPeN currently encompasses data and physicians across 11 states, 79 hospitals and 800 clinics, and will impact 50,000 new cancer cases per year.

Jan Liphardt, PhD, an Associate Professor of Bioengineering, is involved with ‘CancerBase,’ a grassroots collaboration

of patients, scientists and social media volunteers to connect cancer patients all around the world to share basic but critical information about their cancers, and help patients and scientists to see cancer more clearly. Additional information can be accessed at cancerbase.org.

Through these, and many other, research initiatives, SCI members are working to advance the goals of the Cancer Moonshot, whether their projects are specifically part of the federal effort, or working in parallel to reduce the incidence and impact of cancer. *SCI News* will continue to update the progress of the Cancer Moonshot. ■



Specialized Care for Rare Forms of Cancer

Stanford Launches Neuroendocrine Tumor Program

Stanford has initiated a new program to provide comprehensive care to patients with a rare form of cancer called neuroendocrine tumors (NETs). These malignancies are most often found in the GI tract and lungs, often present with advanced disease and are sometimes associated with a complicated symptom profile. For these reasons and others, NET patients usually require integrated, multidisciplinary treatment and Stanford's program offers a framework for such coordinated care.

The Neuroendocrine Tumor Program at Stanford Health Care was established to improve the standard of care for these patients and advance the study of these rare cancers.

“The program is designed to better meet patients' needs and determine what research questions we need to answer,” said **Pamela Kunz, MD**, Medical Director of the NET program, and an assistant professor of medicine (oncology).

NETs are rare, with an annual incidence rate in the U.S. of only 5 in 100,000 people on average. Though uncommon

by incidence, the prevalence (the number of patients alive at a given time) is greater than that of pancreatic and gastric cancers combined.

“It is a greater public health problem than was previously recognized, which means we can and need to conduct rigorous research in the field,” said Dr. Kunz.

NETs derive from neuroendocrine cells, which are involved in many of the body's physiological responses through the regulation of hormones and the nervous system. While NETs can arise anywhere in the body, the most common locations are the small intestine, pancreas, appendix and lungs. A relatively slow-growing form of cancer, NETs can be asymptomatic, or cause vague symptoms like abdominal pain or pressure. Without definitive symptoms, they can often go undiagnosed for years, increasing the chances that the cancer spreads beyond its site of origin.

It is estimated that between 10 and 40 percent of these tumors actively secrete hormones, including serotonin, which

cause an array of unpleasant symptoms, like skin flushing and diarrhea. While these symptoms often prompt the patient to seek the medical attention that leads to their diagnosis, they must be managed over time along with the cancer.

“Patients with NETs really need a multidisciplinary team of experts,” said Kunz. “It is a very nuanced field, so the structured program we're building makes sense and improves care.”

The Stanford NET program brings together the necessary range of physicians—medical and surgical oncologists, endocrinologists, radiologists, nuclear medicine experts, and cancer geneticists—all of whom collaborate to care for patients throughout the course of treatment. This coordinated structure consolidates care and makes it easier for patients to access needed specialists.

Among those specialists is a nurse practitioner who focuses on survivorship. Cancer survivorship is a relatively new subspecialty within oncology and has historically focused on patients who have



Stanford Neuroendocrine Tumor Program Medical Director Pamela Kunz, MD, consulting with her patient Helen Rodde.

completed cancer treatment and moved into surveillance. Due to the slow-growing nature of NETs, many patients live for years *with* their cancer, bringing unique challenges, including reframing the concept of survivorship for this patient population. These challenges include managing cancer symptoms, hormone-related symptoms and treatment side effects, often for many years. In addition, many patients suffer from stresses and associated mood changes of frequent doctor visits, imaging scans and other test, as well as the anxiety of living with a chronic illness. For this reason the NET program is partnering with the Stanford Cancer Center's new psychoncology group, currently comprised of two psychologists and a social worker.

Later this year there will also be dietitians specialized in NETs to help patients cope with the hormone-related side effects and required dietary modifications. There are a number of foods that contain serotonin in levels that can trigger symptoms.

The program also includes a multi-specialty tumor board that meets weekly to evaluate and discuss individual cases, new research findings and trends in the field.

Historic Lack of Research Interest

This level of attention is new for NETs, which due to its rarity was simply not studied much prior to around 2000. For a long time NETs were not even thought to be cancer.

Observing NETs in the early 1900's, German pathologist Siegfried Oberndorfer at the University of Munich, noted that while the masses looked like cancer they did not feature the rapid cellular division and invasive growth that are hallmarks of the disease. Oberndorfer published a paper in 1907 and is most often credited with coining the term *karzinoide*, translated as "carcinoid," or carcinoma-like, to describe the unique feature of behaving like a benign tumor despite having a malignant appearance when examined under a microscope.

Renewed interest in NETs coincided with Kunz's medical studies. She attended

Dartmouth Geisel School of Medicine in 1997, and then moved to Stanford in 2001 for her residency and fellowship. It was during this time that she received a good piece of advice from her mentor **George A. Fisher, MD**, a Professor of Oncology and the Colleen Haas Chair in the School of Medicine.

"He told me that in medicine it is a lot easier to become an expert in a rare disease," said Kunz. "So I chose gastrointestinal cancers, with a particular focus in NETs."

In hindsight her decision seems prescient, and her passion and dedication have helped position Stanford as one of just a handful of NET centers in the US. A recognized expert in the field, Kunz contributes to guidelines through the National Comprehensive Cancer Network (NCCN), serves on the National Cancer Institute's NET Task Force, is on the board of directors for the North American Neuroendocrine Tumor Society (NANETS), and was recently the Principal Investigator on a large National Institutes of Health clinical trial for patients with pancreatic NETs.

In addition to her growing administrative duties, Kunz is also a classic physician-scientist. She designs and conducts clinical trials to test new drugs or treatment protocols of drug combinations and regimens. NET patients tend to live for many years with their cancer, and it is not unusual for patients to be given each of the few available drugs over the course of their lives. Researchers like Kunz carefully monitor the order, dosage and response of every patient to each therapy, in order to decipher the optimal treatment strategies.

For Kunz, though, it is her patients that fire her passion.

"I love sitting down and talking to patients," said Kunz "It is a really privileged time in their lives, where you have to have critical life and death conversations."

Progress and Hope

Research advances are making some of those conversations easier. In just the last five years, the Food & Drug Administration has

approved four new drugs for NETs, with two more treatments expected to be approved this year. When Kunz began treating NETs there was only one available drug.

The two newest therapies involve the chemical coupling of established NET-targeting drugs with very small radioactive isotopes, called peptide receptor radionuclide therapy (PRRT). When the drug molecules home in and bind to the cancer cells, they also bring a tiny radioactive payload, which can be used to damage or kill the cancer cell. Other isotopes can illuminate the cancer cells and enable far better medical imaging of tumors. These advances are welcomed by patients and physicians alike, who often develop long and close relationships due to the slowly progressing nature of NETs.

"I have had some patients since I was a fellow, and it is very exciting to tell them that we have new treatments for them," said Kunz.

There are approximately 100,000 diagnosed Americans, and this relatively large patient pool offers research opportunities. For example, Kunz and her collaborators are starting two new clinical trials, one for lung NET patients and another testing an immunotherapy treatment. Stanford's NET program also maintains a database of 1500 patients treated at Stanford, enabling more research projects and collaborations.

In 2017 the program is planning to offer a specialized one-year neuroendocrine tumor fellowship designed to train the next generation of NET specialists.

Fifteen years ago, when Pamela Kunz entered medical school, NETs were barely an afterthought in the national cancer conversation. Now, building on the work of many talented researchers and physicians, Kunz is propelling Stanford into a leadership position in NETs research and patient care.

"I feel fortunate to be at a place like Stanford that lets me really focus on such a rare, niche field," said Kunz. "And I love serving our patients." ■

The 2016 Class of SCI-supported Oncology Trainees SCI's Good Fellows

Education is an important part of SCI's mission, and its 14 training programs provide a robust framework for connecting knowledge with inspiration. Faculty leaders challenge MD and PhD students, residents and postdoctoral fellows to pursue their scientific interests, and equip them with the skills to make significant contributions to the prevention and treatment of cancer.

In 2014, SCI started a fellowship program to help train the next generation of cancer researchers and physicians. SCI Fellowships provide salary and benefits support to individuals motivated to pursue careers in cancer research, and help bridge the gap between training and junior faculty positions.

The program is working. The previous two classes of SCI Fellows have earned faculty posts at Stanford and other institutions, garnered prestigious awards and produced high-impact research. Here is the class of 2016, with a brief description of their research and a personal statement about their motivation.

Joshua Gruber, MD, PhD

Postdoctoral medical fellow, oncology

Integrated Omics of Malignant Transformation by Breast Cancer Genes

We are working on a methodology to discover the most proximal transforming genetic and epigenetic aberrations that drive human breast carcinogenesis. This is achieved with an in vitro system in which many cancer-predisposing germline breast cancer genes that suppress tumor formation can be assayed. By starting with non-tumorigenic human breast cells that remain responsive to external growth factors, we are identifying transforming processes that bypass the need for growth factors, an essential property of malignant transformation. These growth assays are coupled to high-throughput multi-omics profiling assays designed to capture the transforming events responsible

for malignant transformation. Importantly, we also have a pre-clinical animal model to validate pathways identified by our assays. This research approach has the potential to discover and validate cancer prevention targets specific for many breast cancer predisposition single-gene disorders. One expected outcome of this research is new evidence that anti-inflammatory therapies are safe and effective in preventing BRCA2-induced cancers in our model systems. At the completion of this research, we expect that these therapies will enter clinical trials as cancer prevention agents.

In Joshua's own words: "The main motivation is that there are really few drugs that people can take to prevent cancer. I think if we worked a lot harder at finding prevention drugs everyone would be a lot better off."

Marisa Juntilla, MD, PhD

Instructor, Pathology (oncology focus)

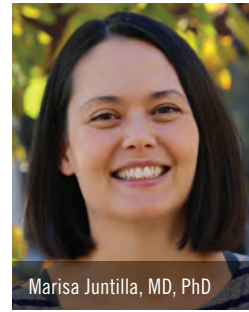
The Role of a Leukemia-specific Mutation in Nucleophosmin 1

My research seeks to identify a molecular mechanism for one of the most frequently mutated genes in acute leukemia, nucleophosmin 1 (NPM1). NPM1 mutations may promote leukemia by deregulating protein translation with downstream effects on cellular metabolism. Using a novel set of leukemia cell lines generated with CRISPR/Cas9 technology in combination with studies in primary hematopoietic stem cells, we will deconstruct the cellular pathways exploited by this unique oncogene (cancer causing gene). The successful completion of this work will suggest new pathways to target as novel treatments for patients diagnosed with AML with mutated NPM1.

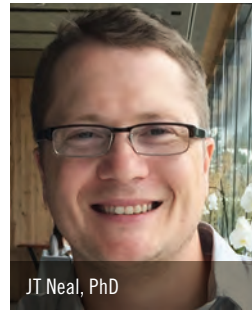
In Marisa's own words: "I developed an interest in the hematopoietic system as



Joshua Gruber, MD, PhD



Marisa Juntilla, MD, PhD



JT Neal, PhD

a graduate student in Immunology and was immediately drawn to the field of hematopathology, or the diagnosis of leukemias and lymphomas, for my clinical training. I started to work on leukemia because I saw an opportunity to address some of the big questions in the field."

JT Neal, PhD

American Cancer Society Postdoctoral Fellow

Department of Medicine, Hematology Division

Patient-Derived Tumor Organoids as a Platform for Precision Medicine

Cancer model systems strive to recapitulate the incredible diversity inherent in human tumors. A key challenge in accurate tumor modeling lies in capturing the panoply of homo- and heterotypic cellular interactions within the context of a three-dimensional tissue microenvironment. To address this challenge, we have developed a 3-dimensional culture model that allows the robust culture of a wide variety of human cancers as tumor "organoids" that recapitulate the architecture of the tumor cells within the context of the surrounding tissue, including the immune cells in this environment. We are using this system to assess tumor response to targeted and immune therapies, with the overall goal of developing predictive assays to guide patient treatment.

In JT's own words: "I study cancer because I lost my grandfather at an early age to non-smoking-related lung cancer. My goal is to improve cancer patient outcomes through the discovery of novel, clinically actionable driver alterations and the development of effective clinical diagnostic assays." ■

Stanford Introduces Web-based *PathWell*

Online Tools Help Cancer Patients Manage Their Care

Stanford Health Care has created *PathWell*, a new set of digital tools designed to improve care coordination for cancer patients, while also making it easier for them and their families to manage the challenges of the disease.

PathWell is another example of SCI's and Stanford Health Care's comprehensive approach to reducing the burden of cancer through the integration of leading-edge research, treatment and patient support services.

"Our main goal is to provide patients and their families with as much information as possible."

— Sridhar Seshadri, DM,
Vice President, Cancer Services

PathWell makes it possible for patients to take on the challenges of cancer care in a more manageable way; finding relevant information about their care, connecting with their care team, facilitating appointment planning and staying more organized. Features for cancer patients include:

- **Open Notes.** This feature makes it easy for patients, at their own convenience, to see their doctors' detailed notes about their diagnosis and treatment plan, so they can understand and evaluate their options. Open Notes also helps patients avoid the sense that they may have missed something during an appointment, by allowing them to review the doctors' notes.
- **Online Scheduling.** Helps patients schedule and manage all their appointments. Online scheduling includes a variety of options for patients to receive reminders about their upcoming appointments, simplifying what can be a complex set of steps to care.
- **Share Access.** Allows patients to name someone they know and trust to access the information in their MyHealth account. This proxy access allows the named person to see lab test results, request appointments for the patient, send non-urgent messages to the patient's care team and see approved portions of the patient's health record.
- **Update My Information.** Enables patients to make sure their information is correct and up-to-date, so they can streamline some portions of the check-in process before appointments.
- **Personalized Medical Information.** Gives patients online access to personalized content that points them to recommended information and articles that directly relates to their condition and treatment.

Ask your Stanford cancer care providers for more information about *PathWell*, or visit www.stanfordhealthcare.org. ■

"A cancer diagnosis comes with many questions, which is why we created *PathWell*, a suite of digital tools aimed at helping educate patients and their families about cancer and making what is always a difficult situation as manageable as possible," said Sridhar Seshadri, DM, Vice President, Cancer Services at Stanford Health Care. "Our main goal with *PathWell* is to provide patients and their families with as much information as possible, by giving them easy to use online tools that help them manage the logistics of their care so they can focus on life, not just their illness."

PathWell was designed with direct input and feedback from patients and their families. Research shows that patients are increasingly looking for digital services that allow them to manage and improve their health. Cancer patients are eager to get information and services online, and prefer accessing it in a central location. *PathWell* addresses these desires as well as providing more personalized and useful information to help manage the logistics of their care, before, during and after treatment.





Eben Rosenthal, *continued from page 3*

implementation, as well as set the strategy for the clinical delivery of cancer care across Stanford Medicine and its growing cancer networks.

“Part of my attraction to Stanford was the promise of working with committed partners in improving clinical care,” said Rosenthal. “Bev and Sri have been very supportive collaborators.”

Rosenthal said his first year goals were to gain an understanding of how cancer care is delivered at Stanford, study how other clinical cancer centers are run and contribute to developing new administrative initiatives. Here are three highlights:

Outreach. Stanford’s cancer care has expanded far beyond campus, with the recent opening of the Cancer Center South Bay and the acquisition of the Valley Care network in the East Bay. This growth brings opportunities and challenges pertaining to structure, staffing and logistics, and Rosenthal is working closely with other leaders to ensure that the entire Stanford cancer treatment operation remains an efficient organization while delivering the highest possible quality patient care.

Quality initiative. In partnership with Julie Porter, Stanford Health Care’s Director of Cancer Quality, they have developed new quality measures for each clinical cancer group (for example, breast cancer, bone marrow transplant, or head and neck cancer). Each group was asked to choose two specific quality control metrics from a list of American Society of Clinical Oncologist recommendations and other professional societies, and they were encouraged to select quality measures that are meaningful to them (not all groups had to adopt the same metrics). This helped create buy-in and accountability. Rosenthal describes the quality improvement process as a series of logical steps: set the standards, measure physician adherence to the standards, share the results with physicians and make adjustments as necessary. The

goal is to use relevant data to systematically improve the quality of care delivered to patients.

“Part of my attraction to Stanford was the promise of working with partners committed to improving clinical cancer care.”

— Eben Rosenthal, MD,
Medical Director, Clinical Cancer Center

Patient engagement. The volume of new and complex information related to a cancer diagnosis can overwhelm patients and family members. The accompanying stress and concern for day-to-day issues (employment, finances, logistics, etc.) inevitably mean that patients may not be able to absorb all of the material relating to their care.

Rosenthal and his team have come up with three strategies to help ensure that patients receive the information they need when they need it, and have practical ways to ask questions and provide feedback to their cancer care team.

Video resources. Working in collaboration with Marissa Duswalt, the Director of Patient Education and disease leaders, they hope to create a range of content including short videos tailored to the patient and their current stage of the treatment process, advising them on what they can expect in the near term, rather than try to give them everything all at once. Some of the content could be common for all patients at a given stage of the procedure, and some could be customized for each type of cancer and patient. For example, the patient’s own doctor could provide a quick video update with details and guidance specific to that patient regarding what to expect in the days after chemotherapy.

Videos and other educational resources will be generated when the patient leaves the hospital and transitions home. It may

include tips for managing daily activities, how to change their bandages, what is normal and not normal, and when (and not) to call for emergency services. Rosenthal noted that unnecessary trips to emergency rooms are a common problem, and that they are emotionally stressful on the patient and very expensive for the system.

Precision Education. These educational tools will be provided by a group of lay care navigators, who will each assist a number of patients throughout the course of treatment and recovery, and deliver the appropriate information at the appropriate time. For example, the patient may contact the navigator and say that they are having trouble using their feeding tube, so the navigator will send them a video on using feeding tubes, and also make a note to follow up. The navigators will be trained to look for distress signs so they can monitor patients and alert the care team if necessary.

Patient Reported Outcomes. Another element of patient engagement is establishing a method for patients to report questions or concerns to their doctors, between or in advance of, appointments. Referred to as “patient reported outcomes,” the system is built on relatively simple, but highly specific, electronic questionnaires designed for the procedure the patient has undergone. For example, the prostate cancer and leukemia treatment questionnaires will be markedly different. Importantly, patients’ comments will be reviewed and responded to by the care team in a timely fashion.

The initiatives above are examples of how Rosenthal and the other SCI leaders are working to improve the standard of care and the array of support services available to cancer patients treated at Stanford. *SCI News* will continue to provide updates as these and other programs move forward. More information is available at the SCI website: cancer.stanford.edu ■

Philanthropy in Action

Stanford Receives Share of Parker Foundation Grant

The Spring 2016 edition of *SCINews* featured a story on Stanford's growing immunotherapy program, led by SCI Associate Director of Cancer Immunotherapy **Crystal Mackall, MD**. Immunotherapy refers to techniques to help the body's immune system better recognize and eliminate cancer cells. Mackall, a professor of pediatrics and of medicine, now heads the newly established Stanford Cancer Immunotherapy Center, a growing multidisciplinary operation intent on leveraging Stanford's strengths in basic and translational research to deliver novel immune-based cancer therapies.

“Advances in cancer research and treatment are fueled by the support of generous donors.”

Since that Spring publication, cancer immunotherapy has received considerable national attention, including the cover story of the April 4 issue of *Time Magazine*. Later that month Silicon Valley entrepreneur Sean Parker—a founder of Napster and the first president of Facebook—announced a \$250 million philanthropic investment in cancer immunotherapy research at six university-based centers, including Stanford.

“Stanford has been a leading center in the field of cancer immunotherapy for many decades. Scientific and technological progress in this arena has moved the field of cancer immunotherapy to an inflection point where increased investment is poised to rapidly improve outcomes for cancer patients,” said Mackall. “Resources provided by Parker Institute will help the Stanford Cancer Institute to meet these challenges and continue to pay a leading role in this very important field.”

The Parker Institute grant, and other sources of support will help the Cancer Immunotherapy Center catalyze the work of many faculty members, including **Mark Davis, PhD**, professor of microbiology and immunology, and SCI members **Garry Nolan, PhD** and **Howard Chang, MD, PhD**, and others as they pursue a variety of immune-related strategies.

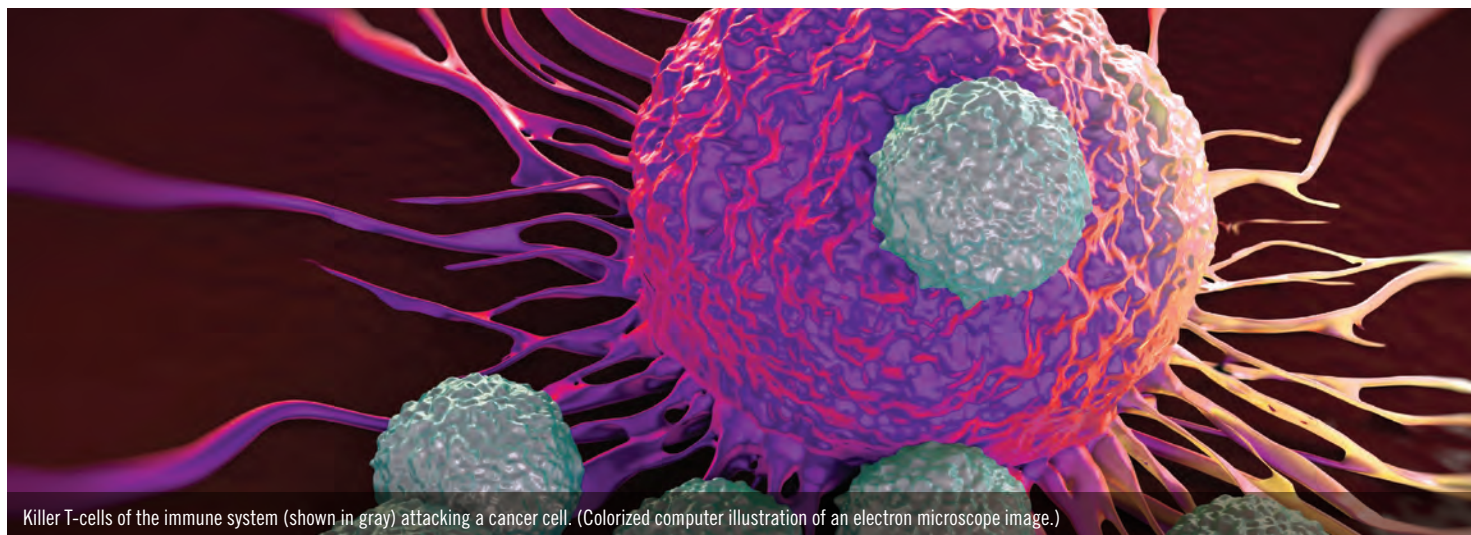
The Parker Institute for Cancer Immunotherapy will also collaborate with biotechnology and pharmaceutical companies, and with nonprofit health organizations. Parker and the other Institute's founders and investors believe that cancer immunotherapy has the promise to change cancer outcomes more

dramatically, and hopefully with fewer side effects, than advances in radiation and drug treatment of cancer.

“Immunotherapy has an innate logic to it—enhance the body's ability to fight off disease—and the potential has captivated cancer researchers for more than a hundred years,” said SCI Director Beverly S. Mitchell, MD. “With new scientific advances and this kind of targeted philanthropy, we are hopeful that immunotherapy will soon be an effective treatment for many more cancer patients.”

Advances in cancer research and treatment are fueled by the support of generous donors. Whether the gifts are large or small, they all make a difference for scientists in laboratories and patients in clinics. The hardworking members of the Stanford Cancer Institute are proud of and grateful for the support they receive from the Stanford community, and they strive every day to efficiently use these precious resources to advance the understanding, treatment and prevention of cancer.

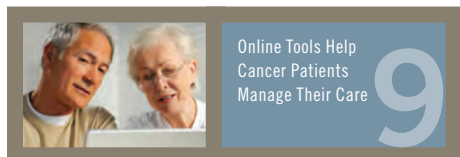
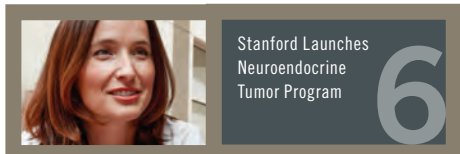
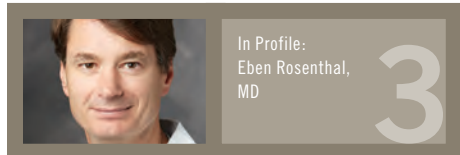
To learn more about how you can help reduce the burden of cancer, please visit: med.stanford.edu/cancer/about/help.html ■



Killer T-cells of the immune system (shown in gray) attacking a cancer cell. (Colorized computer illustration of an electron microscope image.)



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News

Stanford Cancer Institute News

SUMMER 2016

Creating Change through Education and Advocacy

Empowering a Community Response to Breast Cancer

On Saturday May 14, over 400 African American women—and a few men—congregated at the South San Francisco Conference Center to participate in the 5th Anniversary Conference: Breast Cancer & African Americans.

The SCI Community Partnership Program (CPP) conference provides culturally tailored information to raise awareness about breast cancer, promote health advocacy within the African American community and reduce cancer disparities.

The annual gathering is a unique blend of presentations by physicians and researchers

with those from inspirational speakers, faith-based leaders, poets and musicians, many of whom are cancer survivors. Part medical conference and part revival, the meeting is infused with a sense of community, shared experience and indefatigable optimism.

“We come together in an atmosphere of fellowship to create a celebration of information,” said Brenda Knight, the event’s dynamic “Mistress of Ceremonies.”

The Producer and driving force behind the conference is CPP’s Senior Manager, Pamela A. Ratliff, MPA. “We strive to provide an

environment where African American women can unite, share and discover new breast cancer and health information that can potentially save their lives,” she said.



Pamela A. Ratliff, MPA

The conference is a key component in SCI’s mission of disseminating cancer information to Bay Area minority communities and promoting minority participation in cancer clinical trials. For more information visit the CPP website at <http://med.stanford.edu/cpp> ■