African Americans have the highest cancer death rates and the worst survival of any population, a fact that hasn’t changed since 1970. The reasons behind these racial disparities are unclear and controversial.

Stanford surgeon Kim Rhoads, MD, MS, MPH, has spent the past 15 years trying to figure out why. Rhoads’s research aims to identify root causes of racial and ethnic disparities in cancer outcomes. She hypothesizes that clustering of minority patients in under-resourced hospitals may explain stark differences in cancer outcomes. She may be right. Studies have found that being black and poor with cancer increases the risk of not receiving preventive services, not receiving a diagnosis or appropriate treatment or not being treated at all. In one of her recent studies, Rhoads showed that early mortality (30-day and one-year) after colon surgery was higher in hospitals that served a high proportion (more than 40 percent) of patients with Medicaid or no insurance. It just so happened that the majority of patients treated in these hospitals were black.

A MISSION BASED ON LOVE
A pivotal event in Rhoads’s career occurred during her second year of medical school: Her beloved aunt Jeannette was diagnosed with a late-stage (III), locally advanced breast cancer in 1993.

“My aunt and uncle and seven cousins were poor and lived in public housing. I spent a fair amount of time with them during the year I was applying to medical school,” she recalled. “My aunt remarked that she felt uncomfortable in certain health care settings and preferred to use neighborhood clinics, where people would not judge her because of her social situation.”

“Then, two years later, she presented the same way we see in many of our minority patients with cancer. She had a late-stage, erosive tumor. She hadn’t sought care because was ashamed of having breast cancer and terrified about the potential cost of care,” Rhoads said.

Her aunt was admitted to and treated in the local safety-net hospital, where Rhoads was told by the general surgeon in charge of her case that her aunt’s tumor was too large to be removed because the tissue defect in the chest wall would be too large to close. The hospital did not have a surgeon who was skilled enough to reconstruct the chest wall.

“It was a real revelation,” Rhoads said. “I was a junior medical student at the time, and the hospital where I was training had all of these resources. I was shocked to learn that health care could vary so much from institution to institution.”

“This point was driven home during my surgical...”
Cancer is not a problem that can be solved by a single individual or a single approach or a single institution. However, a group of talented and creative people working in concert can make a big difference.

One of the most important and rewarding activities of our senior faculty, and I include myself among this number, is to assist in developing the full potential of these young investigators. The concept of “mentoring” junior faculty is not a new one, but it has gained increasing attention in recent years as the demands of making new discoveries and devising new treatments for cancer are balanced against the needs of family and the individual. We have many exceptional mentors at Stanford, one of whom is highlighted in this issue, but they cannot carry the burden alone. It is incumbent on us to provide young faculty with the resources and time that they need to be effective.

The Stanford Cancer Center has been fortunate to receive a number of donations that assist us in helping young faculty develop their careers. We are able to give out small ($50,000) “seed” grants to develop new ideas and we contribute to their research efforts by providing research assistants or data managers. It is sometimes remarkable to see what such support can do to generate enthusiasm for their work, and, most importantly, results that contribute to the field. We thank all those who have helped us in this endeavor and look forward to bragging about the achievements of these and other young faculty for years to come.

SINCERELY,
Beverly S. Mitchell, MD
Director
Since then, she has concentrated her research on identifying system-level approaches to eliminating disparities in cancer and equitable delivery of high-quality care to patients, regardless of their race or ability to pay.

In 2009 Rhoads received a Har- old Amos Medical Faculty Develop- ment Award from The Robert Wood Johnson Foundation for a research project titled: “Disparities in Cancer Outcomes: Do Institutional Inequities Explain Individual Health Inequalities?” The research for this four-year, $410,000 grant will build on Rhoads’s experience as a California Endowment Scholar in Minority Health Policy at Harvard in 2005 to 2006.

Since joining the Stanford faculty in 2008, Rhoads has given several national presentations on cancer disparities and the impact of poor hospital quality. Her future plans include strengthening existing relationships between physician scientists at the Stanford Cancer Center and the community outreach and education staff at the Northern California Cancer Center. The goal is to devise research-based community programs that engage the Bay Area’s underserved communities and clinical practitioners in building collaborations for cancer care excellence. Dr. Rhoads hopes to achieve this goal by working to promote prevention, early detection and participation in clinical studies.

Armed with new insights, Rhoads began to investigate the breast cancer treatment experiences of black women using public hospitals, a project she completed for her master’s thesis.

“Surgical practice is critical for developing realistic and relevant solutions to outcome disparities, as well as for maintaining the clinical credibility to argue the necessity for change,” she said.

“The mission takes hold

Armed with new insights, Rhoads began to investigate the breast cancer treatment experiences of black women using public hospitals, a project she completed for her master’s thesis.

Part of the project involved designing and administering a survey about breast cancer beliefs in multi-cultural and ethnic women, as well as interviewing these women about their experiences with their surgeons and their interactions within the health care system.

“As a result of this work – and my aunt Jeannette’s story – I became extremely politicized about the financial underpinnings that maintain disparities within our health care system,” she said.

Since then, she has concentrated her research on identifying system-level approaches to eliminating disparities in cancer and equitable delivery of high-quality care to patients, regardless of their race or ability to pay.

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Women with hormone receptor-negative (HR-) first tumors have twice the risk for developing a second primary tumor in the other breast as women with hormone receptor-positive (HR+) tumors, according to a study recently published in the Journal of the National Cancer Institute (JNCI).

Working together, Christina A. Clarke, PhD, MPH, an epidemiologist at the Northern California Cancer Center, and Allison Kurian, MD, MSc, an oncologist and researcher at the Stanford Cancer Center, led a team of investigators in an analysis of data from the National Cancer Institute’s Surveillance, Epidemiology and End Results (SEER) database to determine whether a first tumor’s estrogen receptor and progesterone receptor content, as well as the age or race of the woman, potentiate risk for a second primary tumor.

This was the first large, population-based study of contralateral second primary breast cancers for hormone receptor status.

Results of the study additionally raised important issues relevant to an understudied aspect of cancer care – survivorship.

“After a woman is diagnosed with breast cancer, one of her most pressing concerns is whether or not she will get it again,” Clarke said.

“Patients fear being diagnosed with breast cancer once again – they will accept adjuvant therapies with small anticipated benefits, and choose secondary prevention strategies like double mastectomy, to reduce the chance of a recurrence or a second primary breast cancer,” Kurian added.

It’s estimated that in 2010, about two percent of the U.S. female population, or 2.9 million women, will be breast cancer survivors.

Based on the results of their study, Kurian and Clarke believe there is an unmet need for initiatives that will address the medical and psychosocial issues of breast cancer survivorship and second cancer risk facing the growing numbers of breast cancer survivors. They recently applied for a research grant to further pursue answers to questions that were raised by the JNCI study.

**ROLE OF HORMONE RECEPTORS**

A hormone receptor is a protein that acts like a lock on the surface of the cell. The hormone acts like the key. Receptors for the female hormones estrogen and progesterone are a major feature of breast cancer. When estrogen or progesterone fits into
those with metastatic breast cancer (cancer that has spread to other parts of the body). Hormone therapy with an aromatase inhibitor is given to some postmenopausal women who have ER+ breast cancer. Aromatase inhibitors block an enzyme called aromatase that is critical to the production of estrogen in postmenopausal women.

RISK FACTORS IDENTIFIED
In the JNCI study, the researchers identified several additional important risk factors for development of second primary breast tumors. They found that women who have had breast cancer of any HR status have more than twice the risk for a second primary breast cancer, compared with that in the general population.

Women who were under 50 when first diagnosed with a primary HR+ breast tumor were four times more likely to develop a second primary breast cancer than women who were 50 or older at first diagnosis of a HR+ breast cancer.

Strikingly, women whose first tumors were HR-, compared with those whose tumors were HR+, had almost twice the risk for any second breast cancer, and a 10-fold increase in risk of a second HR- breast cancer. Risks for a second HR- cancer were also significantly higher in women who were younger than 50 when initially diagnosed and even higher in women who received their first diagnosis before age 30.

Risk for a second primary breast tumor varied by patients’ race. Non-Hispanic blacks, Hispanics and non-Hispanic Asian or Pacific Islander patients had a slightly increased risk for developing a second primary tumor than non-Hispanic whites, regardless of the HR status of the first tumor. Non-Hispanic blacks and Hispanics with a first HR- tumor also had substantially higher risks for a second HR- primary tumor than non-Hispanic whites.

These findings have important implications for the treatment and management of HR- breast cancers, the researchers noted.

“This future research should focus on identifying genetic factors that predispose women to multiple HR- tumors to target screening, prevention and treatment strategies more effectively,” they said.

Other scientists from the Stanford Cancer Center and the Northern California Cancer Center who collaborated on this project included: Laura A. McClure, Esther M. John, PhD; Pamela L. Horn-Ross, PhD; and James M. Ford, MD.
A True Tale of Mentoring

Profile of Sarah S. Donaldson, MD, FACR

Of the many stellar achievements in Dr. Sarah Donaldson’s career, perhaps none puts a brighter sparkle in her eye than her experiences mentoring medical students and residents.

“It’s incredibly rewarding to see talented, bright young people enter the field and be able to give them advice and open doors for them,” she said.

Dr. Donaldson feels strongly about mentoring because of her own experience with it.

“It’s a little bit of pay back,” she said. “Without having someone open doors for me and encourage me to take a step, I wouldn’t have gone to medical school and I wouldn’t be where I am today.”

That “someone” is William S. Fletcher, MD, who was a young surgical oncologist at the University of Oregon Medical School when he met Donaldson, a recent nursing school graduate, in 1961. Fletcher hired the bright and intellectually curious Donaldson to be his research nurse and assistant. Over the next few years, they worked closely together.

“My job was to organize the tumor board and work as a clinical research associate, keeping the flow sheets and data sheets of the investigational drugs,” Donaldson recalled. “I also worked with Dr. Fletcher in the outpatient clinic and in the operating room. I often worked as his circulating nurse. I assisted him in his lab projects and ultimately had my own lab project.”

Fletcher became her mentor and counselor, and encouraged her to apply to medical school.

“He had the idea that perhaps my future should go beyond simply working as his research assistant,” Donaldson said.

She took a bit of convincing.

Donaldson had four major reasons why she couldn’t attend medical school: “I’m a girl; I’m too old; I don’t have enough money; and I’m not smart enough.”

Fletcher countered that Dartmouth Medical School (his alma mater) was recruiting women; second, he said: “Ten years from now you’ll be 10 years older, whether or not you go to medical school.” He assured her she could apply for scholarships and loans. And, as for her not being smart enough, Fletcher said: “If you think you are more qualified than the admissions committee to determine one’s suitability as a student, you probably shouldn’t be one.”

FLEDGLING LEAVES THE NEST

Donaldson entered Dartmouth in 1964, the fourth woman to study at the medical school. She received an MD from Harvard Medical School (also Fletcher’s alma mater) in 1968. Although she initially considered surgery for her cancer patients, she opted instead to pursue a career in radiation oncology and became the first female radiologist at Stanford University School of Medicine.
Donaldson chose a residency in radiation therapy at Stanford, one of the first institutions to offer a training program in the new specialty.

residency, Fletcher encouraged her to pursue a career in the nascent specialty of radiation oncology because he felt that the field needed surgically oriented people. He ignited her enthusiasm as well as her competitive nature by pointing out that there were few women working in radiation oncology at that time.

“At that time – 1969 – Hodgkin’s disease was uniformly fatal. But with the linear accelerator, we could define and irradiate large areas of the body at high doses and kill Hodgkin’s disease. The cure rate started to increase,” Donaldson said. “Then chemotherapy was developed and treatment became a combined modality: combining radiation and chemotherapy.”

During Donaldson’s first year of residency, Dr. Kaplan, who had become another of her mentors, asked her to write a protocol using low-dose involved-field radiation and chemotherapy for children with Hodgkin’s disease. That treatment was amazingly successful because it not only spared children the toxicity associated with adult doses of radiation but also increased their survival. Today, the overall survival rate for Hodgkin’s disease is over 90 percent in most children.

BACK TO PALO ALTO

Donaldson chose a residency in radiation therapy at Stanford, one of the first institutions to offer a training program in the new specialty. Dr. Henry Kaplan, a giant in the field of radiology, was chair of the department. Dr. Kaplan was instrumental in the development of the linear accelerator. His specialty was lymphomas, and he was a pioneer in clinical trials in Hodgkin’s disease.

“At that time – 1969 – Hodgkin’s disease was uniformly fatal. But with the linear accelerator, we could define and irradiate large areas of the body at high doses and kill Hodgkin’s disease. The cure rate started to increase,” Donaldson said. “Then chemotherapy was developed and treatment became a combined modality: combining radiation and chemotherapy.”

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“It was a character-building experience. I barely spoke enough French to survive,” Donaldson reminisced. “In fact, I ate chicken every day for six months because I didn’t know how to ask for anything other than ‘poulet,’ the French word for chicken.”

After completing a post-doctoral fellowship at M.D. Anderson Cancer Center in Houston, Donaldson returned to Stanford in 1973 as assistant professor of radiology and helped establish one of the nation’s first pediatric oncology programs. In 1988 she was named professor of radiation oncology.

A REMARKABLE LIFE

In her 40-year career, Donaldson has contributed to the radiation oncology program’s national prominence and is internationally recognized for developing cutting-edge approaches for treating Hodgkin’s disease, orbital lymphoma and rhabdomyosarcoma, among other diseases. With her colleague Charlotte Jacobs, MD, professor of medical oncology, she played a major role in conceptualizing and planning the Stanford Cancer Center, which just celebrated its fifth anniversary.

Currently, Donaldson is associate chair of the...
Many cancer survivors cherish opportunities to help other patients; supporting young researchers can be one of the best investments in future cancer breakthroughs. A gift of $150,000 from the Lerner Family has helped foster the work of just such a person at Stanford.

Twenty-five years ago, Karen Lerner was treated for a rare cancer by radiation oncologist Sarah Donaldson, MD, FACR, The Catharine and Howard Avery Professor in the School of Medicine. Afterward, Lerner, and her husband Stuart Lerner, decided they wanted to support Donaldson’s work. At Donaldson’s suggestion, the couple broadened their interest and agreed that their donation would be best served if directed toward helping a young investigator launch his or her research.

PERSONALIZING THERAPY
On reviewing potential projects from young researchers in radiation oncology, the Lerners chose one that focused on developing a molecular imaging probe to help physicians personalize therapy for each patient based on the specific properties of the individual’s tumor. The method targets epidermal growth factor receptor (EGFR), a protein that is overexpressed on the surface of cancer cells and facilitates tumor progression. Developing an accurate way to measure the EGFR protein will reveal key biological functions within the body related to cancer progression and response to treatment.

“It seemed as if this research had the most potential to help patients with cancers of all types,” Karen Lerner said.

Edward “Ted” Graves, PhD, assistant professor of radiation oncology (radiation physics), leads the project. His laboratory develops molecular imaging tools to improve ways to detect, evaluate and treat cancer.

“Our initial hope was to create an imaging agent based on an antibody that binds to EGFR by labeling the antibody with a radioactive molecule,” Graves said. “In preclinical models, the compound was largely successful in measuring levels of EGFR in tumors. We are currently pursuing the compound’s introduction into clinical trials and have also begun investigating how PET imaging with other agents may be incorporated into treatment strategies, first for gastrointestinal tumors and then, we hope, for many other cancers.”

The Lerners’ gift made it possible for Graves and Albert Koong, MD, PhD, assistant professor of radiation oncology, to hire talented research fellows and to investigate clinical, PET-based treatment strategies – one of the most important elements of the project.

ENCOURAGING TALENT
Graves joined the radiation oncology faculty as an assistant professor in 2003.

“As a junior faculty member, I am especially grateful to the Lerners,” he said. “Building a lab and establishing yourself as an independent investigator requires a certain momentum, and it’s very difficult for young faculty to obtain the funding needed.”

Karen Lerner noted: “It never dawned on me that it was a struggle for young investigators to find funds. You always hear of people donating millions of dollars to cancer research. We can’t match that, but we still have something to contribute.”

Having joined the department of radiation oncology 40 years ago, Donaldson has helped many researchers launch careers. She says, “An initial grant or gift to fund an investigator’s first work is the best gift in the world. Obtaining pilot data with this opportunity then gives you the ability and security to apply for a large grant from a source such as the National Cancer Institute or the American Cancer Society. A small investment early on often turns into a huge investment in the future.”

“As long as this research contributes to detecting, treating or curing any type of cancer, somebody’s going to benefit,” Karen Lerner said. “It’s been really great to be able to give back to the institution that helped me.”
‘These gifts will allow other patients to have a better shot at surviving their cancers.’

A Debt of the Heart

Estate gift to support head and neck cancer research

S

ome 20 years ago, Kathy Knudsen was moved to make provisions in her estate for a bequest to Stanford out of gratitude for the kindness her brother, Terrence Smith, received when he was treated for a lymphoma of the neck. Her husband, Peder Knudsen, was later treated for head and neck cancer by Stanford’s Michael Kaplan, MD, professor of otolaryngology/head & neck surgery, and A. Dimitrios Colevas, MD, associate professor of medicine-oncology.

After Peder Knudsen passed away last year, Kathy Knudsen thought about the fact that head and neck cancers do not get the emphasis more prevalent cancers receive and how much she wanted to leave something important to Stanford in her husband’s name. Her confidence in the caliber of head and neck cancer research conducted at Stanford University School of Medicine led her to enquire about opportunities to support this work.

After thoughtfully considering the programs of investigation under way, she decided to support the work of John Sunwoo, MD, a young investigator leading Stanford’s interdisciplinary effort to elucidate the role of cancer stem cells in head and neck malignancies.

“It is my hope that the work in my lab and through the Head and Neck Oncology Program at Stanford will lead to the development of more targeted therapies and to improved care for patients after treatment,” Sunwoo said. “Mrs. Knudsen’s generosity in the area of head and neck cancer research will most certainly benefit future patients afflicted with this disease.”

In addition to her current gifts, Kathy Knudsen decided to provide further support through her estate plan. Her bequest is expected to provide several million dollars for an endowed professorship and program support in head and neck cancer stem cell research.

“This is a debt of the heart for Peder and me,” says Kathy Knudsen. “I’m so happy to be able to leave the majority of my estate to Stanford. It would delight both my brother and my husband to know that these gifts will allow other patients to have a better shot at surviving their cancers.”

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Philanthropy plays a critical role in supporting advances in research and treatment at the Stanford Cancer Center. Many breakthroughs in cancer care have been made possible thanks to past support, while today’s donors help to foster new discoveries and innovations that are transforming the future of cancer diagnosis, treatment and prevention.

For the fiscal year ending August 31, 2009, private and foundation support to the Stanford Cancer Center and cancer-related programs at Stanford University Medical Center totaled $18.8 million. To our donors and supporters, we say thank you! Our ability to develop new therapies, pursue novel research, and expand programs in education and survivorship depends increasingly on your generosity and support.
It was hypothesized that tumors arising in these patients rely more heavily on alternate DNA repair mechanisms, such as PARP, to survive and, therefore, blocking this enzyme with a PARP inhibitor would lead to death of the tumor.

GENETICISTS INTRIGUED
James Ford, MD, associate professor of medicine-oncology and of genetics, and director of the Clinical Cancer Genetics Program at Stanford, and Allison Kurian, MD, MSc, assistant professor of medicine-oncology and of epidemiology, associate director of the Breast Cancer Genetics Clinic at Stanford, and Stanford Cancer Center researcher, were very intrigued by this approach. They lead a program for the genetic testing of women at elevated hereditary risk for breast and ovarian cancer due to BRCA1/2 mutations, and hoped that PARP inhibitors might provide benefit for their patients. Furthermore, they wondered if this class of drugs might also have an impact on a larger group of breast cancer patients, those with so-called “triple-negative” breast cancer, that make up about 15 percent of all breast cancers.

Triple-negative breast cancers lack expression of hormone receptors and a protein called HER2 and share many biologic similarities to BRCA-related tumors. Dr. Ford is an authority on the molecular mechanisms that regulate DNA repair by tumor suppressor genes, and investigators in his laboratory had recently reported that triple-negative breast tumors, like BRCA-related tumors, are defective in DNA repair and are also very sensitive to PARP inhibitors. Indeed, their results suggested that tumor shrinkage can be augmented when PARP inhibitors are combined with chemotherapy that damages DNA.

AN EXCITING DEVELOPMENT
The two studies presented at ASCO are the first clinical results examining PARP inhibitors in breast cancer patients and provide “proof of principle” that the laboratory findings were indeed
The results of these studies of PARP inhibitors are among the most exciting developments in cancer research in a decade.

correct. In the first study, women with advanced, drug-resistant, triple-negative breast cancer received DNA-damaging chemotherapy (gemcitabine and carboplatin) with or without the PARP inhibitor BSI-201 (BiPar Sciences). Tumor shrinkage tripled when BSI-201 was added to chemotherapy (49 percent versus 16 percent). The women who received BSI-201 also lived longer (median survival of 9.2 months versus 5.7 months).

These results engendered tremendous enthusiasm, since prolongation of survival is a result that is rarely seen in clinical trials of women with advanced breast cancer. Women who received BSI-201 tolerated the therapy well and did not experience increased side effects compared with the women receiving chemotherapy only.

The second clinical study, which used a different PARP inhibitor called olaparib (Astra Zeneca), involved 54 women with advanced breast cancer linked to a gene mutation in BRCA1 or BRCA2, many of whom also had the triple-negative subtype. The study found that 40 percent of the patients who took the drugs as a single agent experienced a reduction in their tumors.

“The results of these studies of PARP inhibitors are among the most exciting developments in cancer research in a decade,” said Robert W. Carlson, MD, professor of medicine-oncology at Stanford University School of Medicine, Cancer Center scientist and one of the nation’s leading clinical investigators in breast cancer.

Similarly, Dr. Ford, who has dedicated his research career to understanding the role of DNA repair mechanisms in cancer, said that he is “very excited” with these clinical results and is optimistic that this strategy will ultimately prove beneficial to patients with other types of cancer.

“The key now is to identify those cancers that are genetically defective in DNA repair as potential targets for PARP inhibitors,” Dr. Ford said.

In fact, Dr. Ford’s laboratory has developed new techniques to measure DNA repair in tumor tissues, and hopes to apply these approaches to identify patients that may respond to this type of treatment.

**STANFORD ON CUTTING EDGE**

Based on the early, promising results with the PARP inhibitor BSI-201, Stanford researchers are currently recruiting participants for two studies using BSI-201 and chemotherapy, with additional studies in development. The first study is significant in that it is the first clinical trial to examine the activity of BSI-201 in a group of women with early-stage, triple-negative breast cancer.

In this neoadjuvant clinical trial, women with newly diagnosed, stage I-IIIA triple-negative breast cancer are treated with a combination of gemcitabine, carboplatin and BSI-201 prior to surgery. This study, led by Melinda Telli, MD, instructor in medicine-oncology and a researcher at the Stanford Cancer Center, and Dr. Ford, will examine the rate of tumor shrinkage afforded by this combination. Investigators in Dr. Ford’s laboratory, in collaboration with Kristen Jensen, MD, assistant professor of pathology, will study patient tumor samples with the aim of better understanding which patients benefit from this new treatment strategy.

The second study is a large, multicenter, randomized phase III study of gemcitabine and carboplatin, with or without BSI-201, for the treatment of metastatic triple-negative breast cancer. The Stanford Cancer Center is one of over 80 participating sites for this national study, which is the follow-up study to the clinical trial presented at the ASCO meeting in June. Dr. Carlson is the principal investigator for the study at Stanford.

Though PARP inhibitors hold great promise for women with advanced triple-negative breast cancer,
RAVINDRA MAJETI, MD, PHD

Dr. Majeti, who is an assistant professor of medicine-hematology with a co-appointment in the Stanford Cancer Center, balances his clinical duties with groundbreaking cancer stem cell research. His most recent discovery has the potential to translate into a new therapy for acute myeloid leukemia (AML), a form of cancer with a particularly poor survival rate.

Majeti and colleagues have found that human leukemia cells escape detection by the immune system by co-opting a protective molecular “badge” called CD47 that is used by normal blood stem cells to migrate through the body and evade macrophages, scavenger cells whose job it is to clear pathogens and damaged or aging cells from the blood stream.

Weissman had previously shown that CD47 was expressed at higher levels in mouse leukemia cells, but, at that time, he hadn’t learned the role of CD47 in leukemia.

Results of Majeti’s study, published in the journal Cell earlier this year, indicate that CD47 may serve as both a

Stanford Cancer Center Welcomes New Faculty

Building on an incredible and growing knowledge base

Stanford has recruited three outstanding translational cancer researchers who will be among the first occupants of the new Lorry I. Lokey Stem Cell Research Building (SIM 1). The new faculty members and their laboratories will be located in the Stanford Cancer Center’s new home, on the second floor of the Lokey Building.

“We are delighted to have attracted a group of the best young physician scientists and clinical investigators to the Cancer Center,” said Beverly S. Mitchell, MD, George E. Becker Professor in Medicine and director of the Stanford Cancer Center.

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Dr. Majeti’s most recent discovery has the potential to translate into a new therapy for acute myeloid leukemia (AML), a form of cancer with a particularly poor survival rate.
prognostic factor and a valuable therapeutic target for patients with cancer. The study showed that CD47 is more highly expressed on human AML stem cells than on their normal stem cell counterparts. Among adult patients with AML, higher CD47 predicted worse overall survival. Anti-CD47 antibody treatment allowed leukemia stem cells to be eaten by macrophages and prevented them from taking hold in mice. The antibody treatment of mice with human leukemia also cleared the animals of the disease.

Majeti and his new laboratory group are now moving ahead with plans to test a similar antibody for use in human clinical trials and have filed for a patent for the potential therapy.

RAJAT ROHATGI, MD, PHD
Dr. Rohatgi is an assistant professor of medicine-oncology who also holds an appointment in the Stanford Cancer Center. He works closely with Heather Wakelee, MD, assistant professor of medicine-oncology, whom he calls his clinical mentor.

Rohatgi was a post-doctoral fellow in the laboratory of Matthew P. Scott, PhD, professor of development biology. His laboratory research focuses on elucidating the biochemical and cell biological principles that govern signaling pathways “sitting at the intersection of developmental biology and cancer.” His goal is to develop novel strategies to manipulate these pathways for cancer diagnostics and therapies.

Rohatgi studies primary cilia, tiny, yet elaborate structures that project from the surface of most mammalian cells. Only a few microns in length, cilia are marvelously complex machines that play a central role in the detection and interpretation of signals from the environment. Primary cilia coordinate multiple signaling pathways that are important for embryo and organ development, as well as sensory function. Defects in cilia lead to many human pathologies, including cancer.

Roghati uses the hedgehog signaling pathway as a model to decipher fundamental principles of ciliary signal transduction. Hedgehog is one of a handful of molecular pathways that control the development of most organs.

Scott’s lab discovered that mutations in components of the hedgehog signaling pathway lead to a number of rare hereditary cancers. Stanford researcher Philip A. Beachy, PhD, the Ernest and Amelia Gallo Professor in the School of Medicine, showed that hedgehog signaling is involved in the development of certain sporadic cancers.

Rohatgi wants to derive a detailed biochemical

The study showed that CD47 is more highly expressed on human AML stem cells than on their normal stem cell counterparts.
Currently, Diehn’s laboratory is investigating the molecular signaling pathways and genes important for cell proliferation and self-renewal.

understanding of the hedgehog signal, find its Achilles heel and develop therapies that target the defects in this signaling pathway that may be involved in cancer development.

MAXIMILIAN DIEHN, MD, PHD
Dr. Diehn is a radiation oncologist who also has an appointment in the Stanford Cancer Center. He will divide his time between treating patients and conducting research on cancer stem cell biology.

While working in the laboratory of Patrick Brown, MD, PhD, professor of biochemistry, Diehn used DNA microarrays to study patterns of gene expression in Glioblastoma multiforme, an aggressive type of brain tumor, to develop assays that could assess patient prognosis.

Currently, Diehn’s laboratory is investigating the molecular signaling pathways and genes important for cancer stem cell proliferation and self-renewal. His laboratory studies these processes in normal adult stem cells and cancer stem cells to identify differences that could be exploited therapeutically. Further, Diehn wants to analyze and overcome resistance mechanisms to radiotherapy and chemotherapy in cancer stem cells.

In early 2009, Diehn, with Robert W. Cho, MD, instructor in pediatrics, Michael F. Clarke, MD, Karel H. and Avice N. Beekhuis Professor in Cancer Biology, and colleagues, discovered a protective pathway that renders cancer stem cells resistant to radiation. The protection occurs through increased expression of proteins that can bind and deactivate reactive oxygen species (ROS), small, unstable molecules that wreak havoc on a cell’s DNA and proteins. Although occurring naturally in cells, ROS are also important mediators of cellular damage caused by therapeutic radiation and some chemotherapies. This discovery could lead to a new approach to treating cancer by inactivating the protective mechanisms in cancer stem cells while protecting normal cells.
Donaldson has received numerous national awards and honors, including the American Medical Women’s Association Elizabeth Blackwell Medal, and was the first female president of the American Society for Therapeutic Radiology and Oncology (ASTRO) and the American Board of Radiology (ABR).

She also is a recipient of an ASTRO gold medal, the W.W. Sutow Medal and the del Regato gold medal. She is a fellow of the American College of Radiology and was inducted into the Institute of Medicine of the National Academies. She currently serves on the Board of Directors of the Radiological Society of North America and is in line to become its president in 2014.

Donaldson has presented more than 200 major scientific papers and authored two books, 72 book chapters and nearly 200 scientific articles. She serves on many editorial boards, including the International Journal of Radiation Oncology, Biology, Physics.

Not bad for someone who thought she couldn’t make it at medical school.

A LEGACY OF MENTORSHIP

Inspired by Dr. Fletcher’s example, Donaldson has mentored countless medical students, residents and fellows, which she considers an act of love.

“They need to have someone give them opportunities or ideas for research projects,” Donaldson said. “You care about them, counsel them and help them network. I love to do that! What could be more gratifying than having one of your residents become a chair at a leading institution?”

“Having a supportive and successful mentor was my good fortune. Dr. Fletcher gave me my first job after I graduated from nursing school. He became my mentor, soul mate and enduring friend,” she mused. “Recognizing that he was behind my own successes every step of the way influenced me to do the same for those students and junior faculty I might encounter along my journey.”

cancer, it is expected that this treatment strategy will ultimately prove most beneficial for women with earlier forms of the disease with the potential to increase the likelihood of achieving a cure. As such, Stanford investigators are developing a third study in collaboration with the Eastern Cooperative Oncology Group (ECOG) and BiPar Sciences to examine the activity of BSI-201 in combination with standard adjuvant chemotherapy (AC followed by Taxol) in early-stage patients who have had their tumors surgically removed.

Dr. Telli will be the study chair and Dr. Carlson the co-chair of this study. Their ultimate goal is to develop a randomized phase III study that will directly compare standard chemotherapy (AC followed by Taxol) to DNA-damaging chemotherapy (gemcitabine and carboplatin), with or without BSI-201, in newly diagnosed triple-negative breast cancer patients.

For information on the PARP inhibitor study for early-stage, triple-negative breast cancer, call 650-724-5223 or email bluett@stanford.edu. For information on the PARP inhibitor study for advanced triple-negative breast cancer, call 650-498-7977 or email ckranc@stanford.edu.
The Stanford Cancer Center was the venue for a very special evening last spring, commemorating the center’s fifth anniversary as a state-of-the-art environment for cancer research and patient care, and thanking donors who support its pioneering work.