cancer center
Notes

WINTER 2008

A Publication for Friends of
Duke Comprehensive Cancer Center,
A Comprehensive Cancer Center Designated
by the National Cancer Institute

CANCER OUTCOMES WORSE FOR MINORITIES AND THE OBESE

"African American women 1.5 to 2.2 times more likely than white women to die from breast cancer"

– International Journal of Surgery

"US study found that men who are obese or overweight when diagnosed with prostate cancer have a higher risk of death after treatment"

– Cancer Journal

The headlines describe the disparity among the outcomes for cancer patients nationwide, but Gary Lyman, MD, MPH, the director of Duke's Health Services and Outcomes Research Program in Oncology, wants to know why. Lyman and his research group use a variety of large health-care databases such as SEER (Surveillance, Epidemiology, and End Results) from the National Cancer Institute to investigate patterns of care and outcomes for cancer patients in today's society. His goal is to optimize the care currently delivered to cancer patients.

"Even without new treatments, we can reduce cancer mortality substantially if we can optimize the current health system to ensure that everyone is diagnosed early, is properly evaluated, and is treated and supported appropriately," says Lyman.

In one of his previous studies, Lyman studied the racial and social differences in the selection of breast cancer treatments. He found that black women did not survive as long as white women and also had a shorter survival time after the disease recurred.

Lyman believes a variety of factors may play a part in these outcome disparities including limited access to care often related to a lack of insurance; poor compliance with screening and treatment recommendations based on fear or lack of understanding of the health system; and a number of other barriers to receiving adequate health care today.

Lyman has also studied obese cancer patients and found that this group of individuals is often under treated and may experience poorer outcomes than patients of normal weight. The amount of chemotherapy a cancer patient is prescribed is generally based on the weight of the patient. Although research has found that full doses of chemotherapy are appropriate and safe if guided by a patient's weight, Lyman says that he believes physicians may be hesitant to prescribe the very large doses of chemotherapy often required for obese patients. While physicians want to avoid potential severe and harmful side effects in their patients, his studies demonstrate that adequately treated obese patients are not at any greater risk of major toxicity than healthy weight patients. While Lyman acknowledges that obese patients often have other health issues, he argues that undertreatment of this population may, in part, account for the poorer survival observed in obese patients who develop cancer.

"We must continue our quest to understand why disparities in treatment and outcomes exist among cancer patients so that we can work to ensure that each and every person—regardless of race, socioeconomic status or weight—can have the best outcome possible with their fight against cancer." ✻

Researcher Receives International Recognition for Epigenetics Discovery

In 2007 Duke Comprehensive Cancer Center member Randy Jirtle, PhD, was nominated for *Time* magazine's "Person of the Year" award and his research was featured in *Newsweek* and on *NOVA*. Proclaimed by many as a pioneer in epigenetics and genomic imprinting, Jirtle's most recent study, published in the December issue of the journal *Genome Research*, revealed the creation of the first map of imprinted genes throughout the human genome. Jirtle and his colleagues found 156 new likely imprinted genes, four times as many imprinted genes as has been previously identified. One of them, KCNK9, is known to cause cancer and may also be linked to bipolar disorder and epilepsy. The second, DLGAP2, is a possible bladder cancer tumor suppressor gene.

"Imprinted genes have always been something of a mystery, partly because they don't follow the conventional rules of inheritance," says Jirtle, a genetics researcher in the departments of radiation oncology and pathology at Duke. "We're hoping this new roadmap will help us and others find more information about how these genes affect our health and well-being."

Many of the newly identified imprinted genes lie within genomic regions linked to the development of major diseases like cancer, diabetes, autism, and obesity. Researchers say that if some of these genes are later shown to be active in these disorders, they may offer clues to better disease prevention or management.

Randy Jirtle, PhD

"We have touched just the tip of the iceberg in epigenetics," says Jirtle. "Much more work must be done." Nonetheless, Jirtle's accomplishments thus far are thought by many to hold dramatic consequences in science and in the treatment of cancer and other diseases.

Nora Volkow, director of the National Institute on Drug Abuse, who nominated Jirtle for the Person of the Year award says, "[His] pioneering work in epigenetics and genomic imprinting, has uncovered a vast territory in which a gene represents less of an inexorable sentence and more of an access point for the environment to modify the genome. The trailblazing discoveries of Dr. Randy Jirtle have produced a far more complete and useful understanding of human development and diseases." ✻

Duke Comprehensive Cancer Center

Non-Profit Org.
U.S. Postage
PAID
Durham, NC
Permit No. 60

FROM THE

Director

Dukes Hosts International Prostate Conference

Dear Friends,

In February, the Duke Comprehensive Cancer Center and the Duke Prostate Center hosted the First International Workshop on Focal Therapy and Imaging of Prostate Cancer at the Washington Duke Inn in Durham. This conference featured international experts who provided insight into imaging and new and exciting treatment techniques for prostate cancer patients.

Prostate cancer is the most common cancer in American men. By age 50, up to one in four men may have some cancerous cells in the prostate gland. As men age, their risk of developing prostate cancer increases. However, unlike other cancers, most men don't die from prostate cancer. An American man has about a 30 percent risk of having prostate cancer, but only about a 3 percent risk of dying of the disease. This means that side effects—especially long-term side affects—of treatment for the cancer are especially of consideration.

New procedures for the treatment of prostate cancer, such as cryotherapy and focal therapy, have become options as viable alternatives to traditional radical surgery and radiation therapy. With the two latter procedures, the entire prostate gland is targeted for treatment; however, these two new minimally invasive procedures focus only on the cancerous tumor and a portion of normal tissue. This means that the patient usually experiences fewer long-term side effects such incontinence, impotence, and rectal problems.

The February workshop provided clinicians from all over the world with groundbreaking data concerning these new procedures. Duke prostate specialists Thomas Polascik, MD; Judd Moul, MD; Vladamir Mouraviev, MD, PhD; Cary Robertson, MD; Dan George, MD; Robert Lee, MD; John Madden, MD, PhD; and Zeljko Vujaskovic, MD, PhD, and imaging specialists Dan Sullivan, MD, and Warren Warren, MD, were among the speakers at this conference.

Duke is on the cutting edge of treatment in prostate cancer, and this conference highlighted the incredible work that is being done to ensure that all prostate cancer patients are provided with the most advanced treatment with the fewest side effects.

Sincerely,
H. Kim Lyerly, MD · Director

NEW DEPUTY DIRECTOR RELISHES ROLE AS SCIENTIST, TEACHER, LEADER

Professor Tony Means, PhD, instructs his graduate students in the pharmacology and cancer biology department of Duke University not to form hypotheses when conducting research. Although contrary to the scientific process taught by many other scientists, Means does not want his students to be predisposed to a particular finding. Instead, he wants them to ask questions which should allow the students to obtain less biased results.

This kind of thinking has led Means, chair of the department, to a long and distinguished career as a scientist and administrator. In 2007 Means added deputy director of the Duke Comprehensive Cancer Center to his many responsibilities.

As deputy director, Means hopes to be an advocate for basic science. More than half of the Cancer Center members are not medical doctors, but are instead esteemed basic scientists with advanced degrees. Basic science research is conducted in laboratories and focuses on understanding how the human body works including the exploration of cell signaling, genetic mutations, and molecular structure. The information gathered from basic science research is essential for translating or applying new discoveries to patient care within the medical center.

"It's wonderful that—unlike many other top medical schools—Duke's medical center is in close proximity to the main university campus," explains Means. "This is great for both entities and allows for partnerships that other schools cannot have."

Means has been chair of the pharmacology and cancer biology department since arriving at Duke in 1991. Prior to joining Duke, he held faculty and leadership positions at Vanderbilt University and Baylor College of Medicine. Means is a fellow of the American Association for the Advancement of Science, the American Academy of Arts & Sciences, and the European Academy of Sciences. He is a former president of the Endocrine Society.

"I am very proud of helping to build this department into one of the best of its kind in the world," he says. "I take a lot of pride in hiring and mentoring many of these faculty members and look forward to continuing this process in my role with the Cancer Center."

When Means isn't busy chairing his department and helping lead the Cancer Center, he spends time in his laboratory, where over a dozen researchers are investigating cell signaling cascades. "I've always been interested in how cells communicate with each other and within themselves," he says. "These signaling pathways are important in the regulation of many physiological processes within the body, and as such, can be important to better understand disease progression. For example, some of the pathways we study that involve the Pin1 protein are important for tumor growth or suppression and targeting these pathways may help treat certain cancers.

"Understanding signal transduction pathways is vital to treating cancer and has led to the development of FDA-approved targeted therapies such as Avastin and Herceptin—both of which had clinical trials at Duke," says Means. "This is a perfect example of a successful partnership between basic science and medicine." *

Cancer Center Notes is produced three times a year by
Duke Comprehensive Cancer Center;
Office of Communications,
DUMC 2714, Durham, NC 27710;
Phone: 919-684-3560;
Fax: 919-684-5653;
E-mail: jill.boy@duke.edu

H. Kim Lyerly, MD Director

Karen Cochran Executive Director of Development

Jill Boy Editor/ Writer

David Elstein Writer
Lauren Shaftel Williams Contributing Writer

DCCC is a designated Comprehensive Cancer Center by the National Cancer Institute.

Produced by the Office of Creative Services and Marketing Communications

MCOC 5485

DUKE RESEARCHERS DISCOVER MECHANISM UNDERLYING A VIRUS-INDUCED CANCER


Bryan R. Cullen, PhD

Researchers led by Duke Comprehensive Cancer Center Member Bryan R. Cullen, PhD, a professor in the department of molecular genetics and microbiology, have discovered that the virus which causes a type of cancer called Kaposi's sarcoma produces molecules known as microRNAs. These microRNAs are nearly identical to similar microRNAs found naturally in normal cells.

Scientists have discovered that some cellular microRNAs are implicated in the development of cancers. In particular, one microRNA called miR-155 has been linked to lymphoma induction. The study was published in *Nature*.

Certain viruses also produce their own microRNAs, but their function has been unclear. One such virus is Kaposi's sarcoma associated herpesvirus (KSHV), which causes both lymphomas and a rare skin cancer in humans. Cullen and his colleagues reported that a microRNA made by KSHV exploits the same cancer-causing pathway as the cellular miR-155 microRNA. This may represent the first example of a viral cancer-causing microRNA.

"The viral microRNA expressed by Kaposi's sarcoma associated herpesvirus is remarkably similar in both structure and function to miR-155, which has previously been causatively linked to lymphoma," says Cullen. "Turning off this viral microRNA could be a step toward a treatment for some virus-induced cancers." ❋

New Pathway Provides More Clues About BRCA1 Role in Breast Cancer

Women who have inherited a BRCA1 mutation have up to an 80 percent risk of developing breast cancer in their lifetime, and they are also at risk for developing the disease at much younger ages than women without the mutation, according to the American Cancer Society. A breast cancer gene's newly discovered role in repairing damaged DNA may explain why.

The discovery also could lead to more effective therapies for women with and without mutated copies of the BRCA1 gene, according to a study led by Duke Comprehensive Cancer Center Member Craig Bennett, PhD.

"Since it was discovered in 1994, BRCA1 and its role in preventing and causing cancer have been intensely studied, and our research represents an important piece of the puzzle," says Bennett. "This study has identified an important mechanism by which BRCA1 comes into play when DNA —the basis for all cell function—is damaged."

"The BRCA1 pathway we discovered is directly involved with the critical process of transcription, in which RNA acts as a messenger between DNA and the making of proteins," Bennett continues.

DNA damage is a normal result of exposure to environmental agents, such as carcinogens, and the response to this damage can be influenced by other normal human processes such as aging and hormonal changes, Bennett says. It's what happens to RNA transcription after damage occurs in DNA that is BRCA1-dependent.

"We found that BRCA1 acts together with transcription to detect DNA damage and to signal the cell to repair itself," Bennett said. "When BRCA1 does not function correctly, as when it is mutated, DNA damage remains un-repaired and cancer can occur." ❋

After Decade of Research, Duke Investigators Make Critical Discovery

For more than a decade, researchers at Duke University Medical Center and their colleagues around the world have been working to understand the role of MutLa, a key component of the DNA mismatch repair system that functions to prevent mutations. Paul Modrich, PhD, Duke Comprehensive Cancer Center member, and Farid Kadyrov, PhD, senior research associate, recently made a critical discovery concerning the biological function of MutLa and its probable role in the prevention of cancer.

DNA is the hereditary material in humans and all cellular organisms. The information in DNA is stored in a code made up of four chemical bases. The human genome consists of approximately three billion bases, and more than 99 percent of those bases are the same in all people. The order of these bases determines the information available for building and maintaining an organism.

When cells divide, highly accurate copies of the set of human chromosomes are transmitted to each daughter cell. The machinery responsible for copying the chromosomes makes approximately one mistake for every 10 million DNA bases copied. While this is satisfyingly precise, this error rate corresponds to hundreds of mistakes per cell division.

DNA mismatch repair is the molecular editor that corrects these mistakes, which take the form of incorrectly paired bases. The failure to correct these errors causes mutations which can lead to cancer. In fact, inactivation of mismatch repair is the cause of one of the most common forms of hereditary colon cancer and has also been implicated in the development of 15 to 20 percent of spontaneous tumors with no known hereditary factor.

Two proteins are essential for the initiation of DNA mismatch repair—MutSa and MutLa—the inactivation of either of which leads to cancer. The role of MutSa was discovered in Modrich's laboratory in 1995. MutSa is responsible for the recognition of the mismatch. Since then, researchers have focused their efforts on determination of the function of MutLa. After years of study, Modrich and Kadyrov have discovered that MutLa introduces breaks in the DNA strand that must be corrected. These breaks allow the entry of enzymes which remove the incorrect bases of a mismatch.

"Without this kind of basic knowledge, we can't truly understand the causes of cancer. This discovery is just one step to understanding the underlying causes of cancer and other diseases," says Modrich. ❋

"This discovery is just one step to understanding the underlying causes of cancer and other diseases."

PAUL MODRICH, PhD

EXPLORING RARE CANCERS

Just before Thanksgiving of 2006, Josh Sommer, a sophomore engineering student at Duke University, attended a lecture by Neil Spector, MD, a senior leader of the Duke Comprehensive Cancer Center and director of Translational Research in Oncology. Little did Sommer or Spector know the impact that this chance encounter would create.

Six months prior to the seminar, Sommer had been diagnosed with chordoma, a rare bone cancer that can develop in the head or spine. Only about 300 new cases are diagnosed each year in the United States, and the average survival time is seven years. In May 2006 Sommer underwent surgery to remove the tumor.

After his diagnosis, Sommer went in search of information about his disease. Unfortunately, his searches often came up empty-handed. In Sommer's Google search of the Web, only a few useful Web sites were found. He was forced to find other resources. Luckily as a Duke student, Sommer had access to all of the university's online subscriptions to medical journals, so he read every study he could find about the disease.

In his lecture that day, Spector discussed his research of the epidermal growth factor receptor, which when mutated, can cause breast cancer. Lapatinib, a drug recently approved for women with breast cancer, targets this receptor. Spector led the development of lapatinib while working at GlaxoSmithKline, prior to joining the Duke faculty. In the course of his research, Sommer had read that the same receptor may play a role in the development of chordoma. He approached Spector after the lecture and spoke with him about his diagnosis and about chordoma.

"Josh and his mother Simone are such an impressive team that it would have been impossible to say anything but 'yes' to helping them," says Spector. Along with his mother Simone Sommer, MD, PhD, a Duke-trained physician, Josh started the Chordoma Foundation to accelerate the search for a cure and promote collaboration among researchers around the world.

"Much of my research has focused on breast cancer," explains Spector. "But it's not a big leap for me to begin studying chordoma. Two cancers that occur in two locations in the body may seem to be different but may be impacted by the same pathway and thus could require similar treatment.

"The key message," says Spector, "is to look not just at the tumors, but also at the pathways." Signaling pathways allow the cell to receive, process, and respond to information. Researchers work to determine which pathways may cause a tumor to form and then find treatments that target these pathways to thus block tumor formation.

Through his literature review, Sommer had also read about Michael Kelley, MD, a Duke physician-researcher who has been investigating chordoma for close to ten years and has a similar philosophy to Spector.

"I don't refer to my research as chordoma research per se," says Kelley, an associate professor of medicine at Duke and chief of hematology/oncology at the Durham VA hospital. "I'm researching the biology of disease."

Sommer befriended Kelley and began working in his lab in October 2006. While he has a science background, Sommer had no experience with molecular biology, yet Kelley has patiently mentored Sommer.

Kelley's laboratory is studying families with multiple cases of chordoma. Through classical genetics and candidate gene analysis, they are looking for mutated genes to determine why some family members have chordoma and others do not. Kelley's lab is also examining the gene expression signatures of chordomas to find clues about which biochemical pathways are altered in chordoma.

"What we can learn from our study of a tumor that may affect only a few hundred people a year can likely be relevant to tumors that affect thousands or hundreds of thousands of people," says Kelley.

> "I am working as fast as I can to find a cure for my disease. The type of collaboration I see at Duke is really inspiring, and we need more of it."
>
> JOSH SOMMER

"There has been an unbelievable level of enthusiasm and compassion shown by the faculty at Duke," says Sommer. "I'm so happy that they're including chordoma in their research interests and are helping me discover more about this awful disease."

David Rizzieri, MD, director of the Hematologic Malignancy Program at Duke, also believes his work on rare diseases will help patients with other, more common tumors. Rizzieri and his colleagues are investigating rare cancers such as mantle cell lymphoma (3 to 5 percent of all non-Hodgkin lymphomas) and adult Burkitt lymphoma, which is even rarer at 2 percent. He recently led a national institutional study on an aggressive treatment for the condition under the auspices of the Cancer and Leukemia Group B (CALGB, a national clinical research group sponsored by the National Cancer Institute [NCI]).

The approach combines an aggressive regimen of multiple chemotherapy agents given in a compact schedule to overwhelm the cancer cells before they have a chance to develop resistance to the agents. The initial published results reveal over 50 percent of the patients remain well and in remission beyond five years with this approach, Rizzieri is leading the current CALGB strategy to minimize toxicity of the regimen using newer, improved supportive care agents.

Rizzieri also sees his research with rare cancers having broader ramifications. With blood cancers, doctors are constantly monitoring a patient's blood to see how the treatment is working.

"With these multiple tumor samples routinely assessed, we are able to determine quickly if and how a treatment is working. The knowledge of a particular drug's effectiveness for a rare tumor can provide a model to assess response that may be applicable to other types of tumors as well," he says.

The federal government defines rare cancers as those with fewer than 40,000 cases a year in the United States. Cancers of the brain (18,000 cases a year) and ovaries (25,000 cases per year) fit in that category. However, there are many other much more rare cancers that have fewer than 1,000 cases diagnosed in the United States each year. What truly sets these cancers apart from other cancers are the barriers for researching and developing treatment options.

The Challenges

One of the biggest challenges associated with studying cancers that may only affect a few hundred or thousand is funding. Federal funding for cancer research has become increasingly more difficult to obtain. The budget for the NCI has been reduced by approximately $80 million over the last two years, and fewer than 20 percent of NCI grant applications to support cancer research were funded in 2006.

Those studies that are supported by the NCI often target more common cancers such as breast, lung, colorectal, and prostate cancers. It is very difficult for researchers to be awarded federal grants to study rare cancers, as acknowledged by Duke researchers including Spector and Kelley. Kelley believes that he is the only researcher in the country who has a grant to study chordoma.

Nevertheless, researchers have found creative ways to fund their work in rare cancers. Some have included those studies as part of their larger studies. Wei Chen, PhD, assistant professor of medicine at Duke, has been investigating the Hedgehog, WNT, and TGF beta pathways and how these pathways impact cancers such as breast and pancreatic. Chen has received grants to identify and study compounds that may block these pathways in several types of cancer and thus stop the progression of cancer.

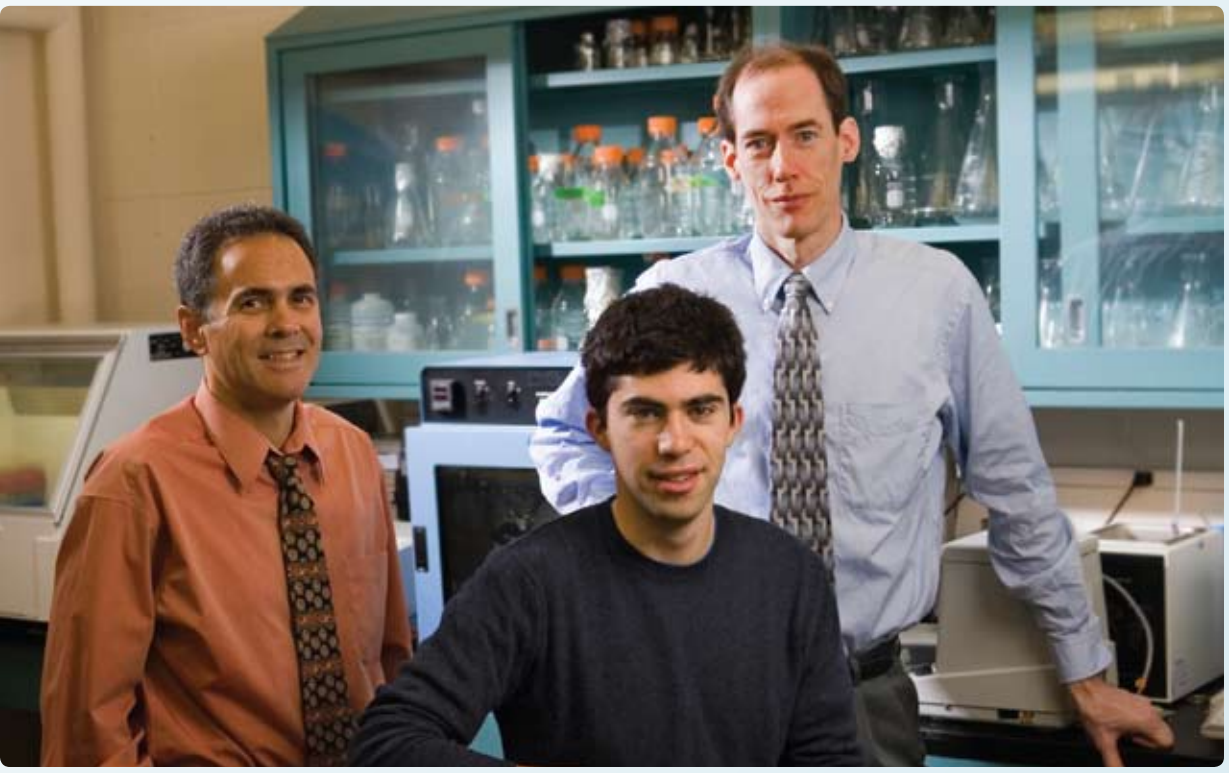
"We've discovered that chordoma may be

impacted by these pathways as well," says Chen.

Pharmaceutical companies are also a major source of funding for many cancer research studies. However, for-profit corporations are motivated to fund the development of drugs that can treat many people in order to maximize profit.

"We had one pharmaceutical company interested in funding our research on cholangiocarcinoma (cancer of the bile ducts that affects 2,000-3,000 people a year)," says Michael Morse, MD, associate professor of medicine at Duke. "However, they ended up not funding our project and decided to focus their drug development efforts on more common cancers."

Still, Morse says, once you have some proof that you may have a good discovery, then the money may come in. "The key is you need that initial seed support. If you find evidence and have substantial findings, then you have a better chance of receiving pharmaceutical funding."



Neil Spector, MD; Josh Sommer; and Michael Kelley, MD

In 1982 Congress passed the Orphan Drug Act to entice pharmaceutical companies to create drugs that will impact rare diseases—and not just cancer. The act provides research funds, tax credits, and special legal protections to those involved in such research. More than 300 drugs have deemed "orphan" by the FDA in the 25 years including Gleevec, which is marketed for seven different types of rare cancers. However, even the financial and legal benefits that have emerged from the act are often not enough to persuade companies to invest in the development of these drugs.

Accrual of patients to clinical trials is another obstacle in the study of these rare cancers. Investigators often find it difficult to identify enough patients to participate in their studies since there are not many patients with these particular conditions. Rizzieri often works with the researchers at neighboring University of North Carolina and Wake Forest University to accrue patients for his studies. "It's essential to partner with other hospitals when studying rare diseases," he says.

The Duke Comprehensive Cancer Center has also formed partnerships around the world, in China and Singapore. "A cancer in the United States may only have a few hundred or a few thousand cases a year, but in China because of the large population, a cancer may have tens of thousands of cases," says Chen. "It will be faster and easier to accrue patients for clinical trials when working with our partners in China."

Some researchers studying rare diseases often join collaborative groups. Duke is a participant in the Sarcoma Alliance for Research Through Collaboration (SARC) which provides the infrastructure for collaboration between medical institutions from around the world for the development of new standards for sarcoma treatment, education, and prevention. Sarcoma is a term that describes about 50 different types of soft-tissue cancer and seven types of bone cancer. Only 10,000 or so patients are diagnosed each year with all sarcomas, including chordoma.

Rich Riedel, MD, assistant professor of medicine at Duke, is leading several new sarcoma studies. One of the studies is using gene expression profiling to better understand the biology of individual sarcoma subtypes. With this knowledge, he hopes to use current chemotherapies more effectively and identify key biologic pathways that may be targeted with novel therapies.

But Progress Is Being Made

For patients diagnosed with rare types of cancer, it is often difficult to find physicians who have heard of or even treated that particular disease. Kenneth Rhinehardt, who lives in Marion, North Carolina, was diagnosed with a soft-tissue sarcoma near his hip.

Doctors initially thought it was osteoarthritis. Eventually they discovered the sarcoma. The first oncologist he visited wanted to remove his hip and leg.

Family and friends recommended that Rhinehardt go to Duke for a second opinion. In October 2006 Rhinehardt met with Brian Brigman, MD, an orthopaedic surgical oncologist and sarcoma specialist. Brigman told him he could remove the tumor and save the leg. A year after surgery, Rhinehardt's cancer is gone and he feels good.

R. Edward Coleman, MD, professor of radiology, and Morse are studying two rare neuroendocrine tumors: pheochromocytoma and paraganglioma. They are conducting clinical trials for a radioactive targeted therapy agent known as iobenguane I 131. A phase I trial was completed in 2007 at Duke to determine the correct dose to administer to patients. Initial results of the trial showed that the patients' tumors had shrunk.

A phase II trial of iobenguane I 131 recently opened. The initial positive results from the phase I trial have attracted patients from across the country to Duke to participate.

"Since we've already seen positive results, we are very anxious to conduct more trials of this treatment," says Coleman.

Spector has also had success in early trials of lapatinib for patients with inflammatory breast cancer (IBC), which is diagnosed in about one percent of all breast cancers in the United States, but is much more deadly. Since IBC is so biologically different than other breasts cancers, patients with this disease are often excluded from clinical trials for new breast cancer therapies. But initial trials of the lapatinib among IBC patients are promising.

"The environment at Duke is very unusual," says Spector. "There is a collaborative and entrepreneurial spirit here, and researchers are passionate about curing cancer -- all types of cancer. At most institutions, a student like Josh couldn't walk into the offices of researchers, engage them in a fairly untapped area of research, and then see them working together and making progress in a matter of months."

Sommer has already found several pathways that are likely to be involved in regulating the growth and survival of chordoma cells. Spector's laboratory has also found similar pathways and has further identified some cancer drugs already approved for treating other tumors, that exert anti-tumor activity against chordoma cells lines in the laboratory. These drugs would need to be tested in clinical trials to see if they are effective in humans.

After working in Kelley's lab for over a year, Josh is now pre-med and plans to become a physician-scientist like his mentors Kelley and Spector. Though Josh has found hope in his work at Duke, he knows that some day his chordoma might return.

"I am working as fast as I can to find a cure for my disease," Sommer says. "The type of collaboration I see at Duke is really inspiring, and we need more of it. We also need more funding to have any real shot at finding a cure soon. We're discovering that chordoma shares much in common with many other uncommon cancers, so I hope this work will lead to faster treatment development for all of us who have been affected by orphan cancers." ✻

CANCER CENTER Notes

DUKE RESEARCHERS INVESTIGATE USE OF TRADITIONAL CHINESE MEDICINE IN CANCER CARE

Amy Abernethy, MD, director of Duke's Cancer Care Research Program, and seven members of the program visited China in the fall of 2007. The delegation toured several cancer hospitals to learn more about Traditional Chinese Medicine (TCM), how it is used in China, and how it meshes with Western medical approaches such as chemotherapy which are increasingly used among the Chinese population of 1.3 billion people.

"China is separated from the United States not only by an ocean of water, but also by a sea of tradition," explains Abernethy. "Their medical practices date back at least two, and possibly several more, millennia."

A core purpose of TCM is to improve the vital energy, or "chi," of the patient, thereby improving his or her overall function and state of wellbeing. "This goal is consistent with the purpose of what we call 'supportive care,' in the United States," says Abernethy.

Some TCMs are also thought to be able to treat the cancer.

Historically, patients receive most TCM as herbal teas which combine multiple ingredients. Today, medicine based on certain herbal preparations are delivered intravenously in the hospital, and the use of oral capsules in China is increasing. TCM has few toxicities (unpleasant or dangerous side effects). Nonetheless, cost is a major factor in determining who receives cancer care of any sort in China, and medications created based on TCM principals can even match chemotherapy in its high out-of-pocket expense.

Until recently, despite centuries of tradition and use, only anecdotal claims have supported TCM's efficacy. In the United States, oncologists want to see rigorous research evidence before offering TCM to their patients. Intensive efforts are now under way in China and particularly Hong Kong to test TCM agents using Western research methods. Duke is involved in a trial of one such TCM based medicine called Kanglaite.

The active ingredient in Kanglaite is a lipid (fat) extract derived from the seed of an Asian grass. This extract is used in China to treat patients with lung and liver cancers as well as cancer-associated anorexia-cachexia syndrome (CACS). CACS is characterized by loss of appetite, weight, muscle mass, and adipose tissue. When delivered through infusion in Chinese studies, Kanglaite has been shown to decrease tumor size, enhance the effects of chemotherapy and radiation therapy, reduce the need for additional drugs, and alleviate symptoms associated with CACS such as nausea and fatigue. Beginning in late December 2007, Duke enrolled 99 patients with inoperable non-small cell lung cancer in an observational study to gain a better understanding of the cancer patient's experience of CACS. Subsequently, Abernethy and colleagues will conduct a clinical trial of Kanglaite to improve CACS symptoms. Results will be forthcoming in 2009. Other studies of Kanglaite to treat lung and pancreatic cancer are planned. *

Duke Medicine Receives CEO Cancer Gold Standard Honor

Duke Medicine has earned the CEO Cancer Gold Standard, which recognizes an organization's commitment to the health of its employees and their families. Duke is one of only 15 organizations nationwide and one of only two cancer centers in the country to receive this honor.

In 2001, former President George H.W. Bush called for business leaders to be "bold and venturesome" in their efforts to prevent cancer in the workplace and in their leadership in the overall fight against cancer. To earn the Gold Standard accreditation, an organization must establish programs to reduce cancer risk by discouraging tobacco use and encouraging physical activity, healthy diet and nutrition; detect cancer at its earliest stages; and provide access to quality care, including the availability of clinical trials.

CEO ROUNDTABLE ON CANCER

Duke Medicine became tobacco-free in July 2007, prohibiting the use of all forms of tobacco inside and outside of the medical center. In an effort to assist employees, Duke continues to offer free smoking-cessation programs as well as free programs designed to improve nutrition and exercise habits.

The Gold Standard accreditation is awarded by the CEO Roundtable on Cancer, a non-profit corporation comprised of executives from major American organizations. *

Duke Opens Multidisciplinary Clinic for Sarcoma Patients

A new sarcoma clinic has opened at Duke, allowing patients to receive a multidisciplinary team approach to their care.

The clinic allows patients to make one visit to Duke to see Brian Brigman, MD, PhD, an orthopaedic surgeon; Rich Riedel, MD, a medical oncologist; and radiation oncologists Nicole Larrier, MD, or David Kirsch, MD, PhD. The physicians meet with a patient during his or her initial appointment, and then work together to create the most effective treatment plan for the patient.

Nurse Sherry Dufore; Drs. Kirsch, Brigman, Riedel, Larrier; PA Susan Blackwell

"Since most sarcoma patients require a combination of treatments to treat their disease most effectively, this multidisciplinary approach is an efficient way for patients to talk to multiple doctors during one visit," says Brigman.

Sarcoma is a term that describes approximately 50 different types of soft-tissue cancer and seven types of bone cancer. Each year, 10,000 patients are diagnosed with all types of sarcomas, compared to 178,000 women diagnosed with breast cancer and 218,000 men diagnosed with prostate cancer. Sarcoma is also one of the more common cancers in children; about 20 percent of the sarcoma patients treated at Duke are children.

According to Brigman, many community physicians are not familiar with sarcoma. Many hospitals do not treat sarcoma patients, and of those that do, even fewer offer a multidisciplinary approach to care.

Although Duke physicians have been treating sarcoma patients for many years, Riedel is the first medical oncologist at Duke devoted exclusively to sarcoma. He joined the Duke faculty in July 2007 as the recipient of the Maria Garcia-Estrada Career Development Award in Sarcoma. Garcia-Estrada was a former Duke golfer who was diagnosed with sarcoma in 2005, two years after graduating, and died seven months later. Jim Heinz, her mentor at Marquette Partners, helped to raise $500,000 to recruit a faculty member to Duke to study sarcoma. "This generous funding will allow for the further development of our sarcoma research efforts as we work to improve therapeutic options for our patients," says Riedel. *

Philanthropists' Gifts Support Investigation of Link Between Cancer and Environment

Alice and Fred Stanback of Salisbury, North Carolina., donated $2 million in December 2007 to the Duke Comprehensive Cancer Center and Duke's Nicholas School of the Environment and Earth Sciences, continuing their support of a collaborative research initiative between the two institutions. Duke is one of only two universities in the country that can lay claim to a National Cancer Institute-designated cancer center, as well as one of the nation's premier schools of the environment.

"The Stanbacks are wonderful, supportive friends and advisors to both the Cancer Center and the Nicholas School," says H. Kim Lyerly, MD, director of the Cancer Center. "It is our goal and that of the Nicholas School to use this gift to support researchers from both institutions who will dedicate their lives to investigating the link between cancer and the environment."

William L. Chameides, dean of the Nicholas School, says, "Every year, humans add myriad new chemicals to the environment. In many case, we have little information on the health and environmental effects of these chemicals. The Stanback family's generous support will enable us to continue and expand our interdisciplinary efforts to understand the threats these chemicals may pose and find sustainable alternatives."

Mr. Stanback and his son Brad serve on the Board of Visitors of the Nicholas School, and Mrs. Stanback serves on the Cancer Center's Board of Overseers. The Stanbacks' previous gifts to both the Cancer Center and the Nicholas School have been used to create the partnership between the two institutions and provided seed money for nine novel collaborative projects to investigate links between environmental toxins and cancer.

It also provided funding to host major scientific conferences on cancer and the environment, such as the Fourth Aquatic Animal Models of Human Disease Conference, which brought scientific experts and policymakers from around the world to Duke in January 2008.

The new Stanback gift will make it possible for Duke to step up its research activities to map out the pathways by which specific toxic chemicals cycle through the environment, enter the human body, and propagate the mutagenic transformations that lead to cancer.

"During my childhood, I heard about the loss of the forest and conservation," explains Mr. Stanback. "When I got older, I read more and began to understand the huge effect that the environment has on our bodies and our lives.

"My hope is that working together the Cancer Center and Nicholas School can have a larger impact on these issues than they could working independently," continues Mr. Stanback. "These two institutions hold an enormous amount of knowledge and expertise. When you combine that expertise with the respect and authority that the Duke name demands, then you create a powerful team."

One of the recipients of the Stanback's initial gift was Randy Jirtle, PhD. Jirtle (featured in the cover story of this issue) was nominated for *Time* magazine's 2007 "Person of the Year" award, for his pioneering work in epigenetics and genomic imprinting.

"Imprinted genes are unusually vulnerable to pressures in our environment -- even what we eat, drink, and breathe," explains Jirtle. "I am truly grateful to the Stanbacks for their interest in environmental affects and for their support of my research and that of others who continue to explore this fascinating and important link." ✻

H. Kim Lyerly, MD, (right) director of the Duke Comprehensive Cancer Center, and Darell Bigner, MD, PhD, director of the Preston Robert Tisch Brain Tumor Center at Duke, presenting the Shingleton Award to Jean Case.

Case Family Honored with Shingleton Award

The Duke Comprehensive Cancer Center honored the Case family for its work on behalf of brain tumor patients with a presentation of the Shingleton Award, the center's most prestigious service award. Named in honor of the late William W. Shingleton, MD, founding director of the Duke Comprehensive Cancer Center, this annual award is presented to individuals who have demonstrated an ongoing interest in fighting the battle against cancer through their long-standing commitment of time, energy, and resources.

In May 2001, Dan Case, along with his wife Stacey and his brother and sister-in-law Steve and Jean Case, co-founded Accelerate Brain Cancer Cure (ABC^2), a non-profit organization committed to finding a cure for brain cancer. The creation of ABC^2 came just months after Dan's diagnosis with brain cancer. Dan died in June 2002. Since then, ABC^2 has funded more than $5 million in brain cancer research, including 11 projects at Duke, more than any other institution.

In the fall of 2007, Jean Case accepted the award on behalf of the family during the Shingleton Award Dinner. Jean is chief executive officer of the Case Foundation, which she and Steve founded in 1997. The foundation has funded the efforts of many organizations around the world including ABC^2. Steve Case was co-founder of AOL and former chairman of AOL Time Warner, and is current chairman and CEO of Revolution and chairman of the Case Foundation. ✻

GIFT FUNDS SCHOLARSHIP IN HONOR OF DUKE ALUM

Robert Fitzgerald received his PhD from the department of pharmacology and cell biology at Duke more than 60 years ago, but he never forgot the university and the role it played in shaping his prolific research career. Fitzgerald passed away in January 2007 at age 88, leaving a sizeable gift to the department of pharmacology and cancer biology.

For more than 45 years, Fitzgerald was a highly regarded dental researcher for the U.S. government. While at the National Institutes of Health from 1948 to 1969, his studies investigating the bacterial causes of tooth decay were regarded as some of the most influential research on this subject of its time. Fitzgerald spent the next 25 years as chief of the dental research unit at the Miami VA Medical Center, receiving several prestigious awards from the International Dental Foundation, International Association for Dental Research, and the Secretary of Veteran Affairs.

Robert Fitzgerald, PhD

Fitzgerald's endowment gift to Duke will be used to establish Robert Fitzgerald Scholar Awards, which will be presented to top graduate students in the pharmacology and cancer biology department.

"All graduate students receive a stipend, but the monetary component of these Fitzgerald Scholar Awards will supplement the usual stipend and greatly benefit the student recipients," says Department Chair Tony Means, PhD, who also serves as deputy director of the Cancer Center. "This money will be available for many, many years to assist the entry of our most promising students into a career in biomedical science. We are very grateful to Dr. Fitzgerald."

"He was very proud of his degree from Duke," says Fitzgerald's niece Sister Regina Bechtle, a member of the Sisters of Charity of New York. "I found his Duke graduation program while searching through his belongings. He called himself 'just a poor kid from the Bronx.' His donation to Duke was his way to show how grateful he was to the places that made him who he was." ✻

ASK THE EXPERT

H. Kim Lyerly, MD

Pamela Douglas, MD, MACC

Amy Abernethy, MD

Lee Jones, PhD

CARDIOLOGY, EXERCISE, AND CANCER

"A 60-year-old woman came into the clinic recently. She was a five-year survivor of breast cancer and was doing well. But she had begun to experience a shortness of breath and fatigue. It turned out that her heart was weak, a problem that may have been caused at least in part by the chemotherapy she had received as part of her cancer treatment."
—Pam Douglas, MD, Duke cardiologist

What is the connection between the heart and cancer?

Pamela Douglas, MD, MACC
Ursula Geller Professor of Research in Cardiovascular Diseases

Chemotherapy can be very effective in curing cancer. It is extending the lives of many patients fighting this disease. However, while patients are living longer, some of them are developing heart disease. Heart disease can be a side effect of chemotherapy, especially anthracyclines, a type of chemotherapy that may cause heart weakening in up to one-quarter those patients receiving it. Even the side effects of the newer targeted therapies such as Avastin and Herceptin include an increased risk of high blood pressure and heart disease.

At Duke, we are conducting studies so that we can better understand the risks of heart disease in cancer patients. We are studying the cardiac side effects of new cancer drugs closely during the clinical trial phase. We also want to look for improved diagnostic tests so that we can identify problems of the heart earlier in cancer survivors.

Patients who are receiving chemotherapies should not stop taking these powerful and life-saving medicines. However, even more than everyone else, they should eat a healthy diet, exercise, quit if they are smoking, and get regular screenings of blood pressure and cholesterol levels.

Is there a relationship between cancer and exercise?

Lee Jones, PhD
Exercise physiologist and assistant research professor

Unfortunately, there has not been much research to determine how exercise may improve heart health in cancer patients. However, at Duke we are leading studies to investigate the effects of exercise on patients with different types of cancer. We are actually doing the first clinical trials among breast cancer patients to determine if exercise helps to protect their hearts and improve the efficacy of their chemotherapy at the same time.

I am also researching how exercise training and a patient's functional capacity (i.e., aerobic and muscular strength) impacts other aspects of cancer management including the effectiveness of their treatment, the extent of treatment symptoms, cognitive function, chance of recurrence, and quality of life. I truly believe that all cancer patients can benefit from regular exercise regardless of their disease stage and level of functionality.

Does exercise improve a patient's mental health as well?

Amy Abernethy, MD
Director, Duke Cancer Care Research Program

I am conducting research that explores how cancer survivors can live a healthy life both physically and mentally. Depression impacts about 20 to 25 percent of cancer patients, and heart disease is correlated with depression. We are working to improve the psychological and quality of life issues for cancer patients, which may also partially lower their risk of heart disease. We also believe that exercise may play a role in improving the quality of life in cancer patients.

Why is the Duke Comprehensive Cancer Center interested in studies involving exercise and heart health?

H. Kim Lyerly, MD
Director, Duke Comprehensive Cancer Center

A major advantage that the Duke Comprehensive Cancer Center has over many other cancer centers is that we have researchers from a wide variety of departments collaborating with each other. While cardiology and oncology appear at first glance to be unrelated, it has become increasingly more evident that the two are intertwined. Studies have found that drugs that help cancer patients fight their disease can also increase the risk of heart problems later. We need to understand why this happens. More importantly, we need to understand how we can protect our cancer patients from developing heart problems.

Duke is fortunate to have outstanding faculty members who are experts in oncology and in cardiology. We have consistently ranked among the top 10 in both specialties by *U.S.News & World Report*. The connection between cancer and the heart is an important area of study, and at Duke we are well-equipped to continue to make important discoveries in these areas that will improve the lives of our patients. ❋

If you would prefer to receive this newsletter by email, please visit **cancer.duke.edu/notes/** to register.

To contact Duke Comprehensive Cancer Center's Office of Development call 919-667-2600.

To make an appointment call 1-888-ASK-DUKE.

For more information visit cancer.duke.edu