ENGINEERING CURES
Physicians and Engineers Working Together to Fight Cancer
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Engineering Cures

Engineers are bringing new technologies to fight against cancer. Working with researchers at the Kimmel Cancer Center, they are helping make new personalized cancer therapies a reality for patients like Jerry Morton.

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The latest research from the Kimmel Cancer Center including new discoveries in cancer genetics and “microbeads” that fight liver cancer.

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Gifts and donations that are funding our cancer research and advancing clinical care.

On the Cover: This robot, developed by engineer Dan Stoianovici, is used to treat prostate cancer.

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JOHNS HOPKINS is uniquely positioned to make revolutionary advances against diseases, like cancer. Advances that could not even be imagined 10 to 15 years ago are now happening. I am proud to tell you that our researchers have been at the center of these amazing accomplishments.

For certain, we are doing things a bit differently now. We are transforming cancer medicine away from a model in which we see patients for the first time when they begin experiencing symptoms to one that detects, manages, and many times eradicates cancers before patients even know they have them. This new system, driven in large part by our pioneering discoveries in cancer genetics and epigenetics, is one that preserves health by preventing cancers, very accurately predicting who will get them, and personalizing treatments to each individual patient, making sure he or she gets the treatments that will work against the unique cellular characteristics of the cancer.

As you will read in this issue of Promise & Progress, we have a new partner in this work. Researchers in the Whiting School of Engineering, long recognized for using the principles of engineering to fight human diseases, are now working side by side with cancer researchers and clinicians to improve the tools we use to make progress in the laboratory and at the bedside. Robotics and other surgical devices, computational and computer sciences, nanobiotechnology, molecular imaging, and other vital engineering-based expertise and advances are helping us achieve our mission to best prevent, detect, treat, and monitor cancer.

As a result of these and other collaborations, we are already using scientific discoveries to guide our clinical care. These discoveries are helping to ensure we get the right treatments to the right people at the right time.

The Kimmel Cancer Center is an incredible discovery engine, and our brilliant team of investigators and clinicians has led the way in developing tests that detect cellular alterations that identify cancers, predict which therapies they will respond to, and monitor them for recurrence. Our success is being fueled by generous support such as that received from the Commonwealth Foundation for Cancer Research and David H. Koch. The Commonwealth Foundation gift is allowing us to create the Center for Personalized Cancer Medicine (see page 36), and the Koch Cancer Research Building is home to our next generation sequencing laboratory, which is essential to our breakthrough research in cancer biology that makes personalized therapies possible.

The next step is to adapt these technologies so that they can be used routinely to make clinical decisions about how to best treat cancers, not just at the Kimmel Cancer Center, but at cancer centers and hospitals around the world. We are ushering in a new era of cancer medicine.

William G. Nelson, M.D., Ph.D.
Marion I. Knott Professor and Director
The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins
GENETIC DISCOVERIES IN HEAD AND NECK AND BRAIN CANCERS

SCIENCE

Genetic sequencing offers powerful clues to understanding the function of various genes and their roles in cancer, and Kimmel Cancer Center investigators have produced some of the most seminal findings in cancer genetics.

Cancers are not “one size fits all” as the discoveries of Nickolas Papadopoulos, Ph.D., Kenneth Kinzler, Ph.D., and Bert Vogelstein, M.D., and their research team have revealed. As a result, therapies cannot be one size fits all either. Their work in mapping the diverse genetic landscape of dozens of cancers is leading to prevention, early detection, and treatment strategies personalized to target the unique cellular characteristics of each individual patient’s cancer. In the coming years, this approach is expected to revolutionize cancer therapy, improving outcomes by giving clinicians the information they need to deliver the right therapies to the right patients and to monitor, in real time, whether or not new target-specific drugs are blocking the cellular malfunctions now known to be caused by genetic alterations.

These researchers have recently sequenced the cancer genomes of two more malignancies—head and neck cancer and a brain cancer known as oligodendroglioma.

HEAD AND NECK CANCER GENOME

Little was known about the genetic causes of head and neck cancers, and this new research revealed mutations in two genes, NOTCH 1 and FBXW7, never before associated with the cancer. In a surprising twist, the researchers found that NOTCH 1, identified as a cancer cell growth-promoting oncogene in blood and bone marrow cancers, is a malfunctioning tumor suppressor gene in head and neck cancers. “The mutational analysis of NOTCH clearly indicated the power of genetic changes determining the function of these genes,” says Papadopoulos. This key finding demonstrates that genes are not preset to be either oncogene or suppressor gene, as previously thought, but instead their roles can vary among tumor types depending upon mutations. The same gene can act as a cancer growth promoter in some cases and as a growth suppressor in others, say the experts.

Their mutational analysis also confirmed previous findings by Kimmel Cancer investigators who in 2000 linked the Human papillomavirus (HPV) to head and neck cancers and classified it as a unique subset of head and neck cancer with its own biology and associated with an improved prognosis. The researchers uncovered the reason for the improved outcomes, finding four times fewer mutations in HPV-related cancers than non-HPV-related cancers and no mutations to the common cancer-related p53 gene. Another environmental risk factor, cigarette smoking, was associated with markedly increased numbers of mutations. Tumors from head and neck cancer patients with a history of smoking had twice as many mutations as tumors from non-smokers.

Researchers will now work to decipher the function of the genes discovered and potential ways to target them therapeutically.
OLIGODENDROGLIOMA

BRAIN CANCER

Researchers have long known that up to 70 percent of oligodendrogliomas are characterized by a fusion of two chromosomes that results in the loss of many genes. What had eluded scientists, until now, were the specific mutated genes that allowed the cancer to develop.

After sequencing this cancer, one that typically strikes younger people in their thirties and forties, the Kimmel Cancer Center team solved the mystery by uncovering mutations to two genes, CIC and FUBP 1. Two-thirds of the tumor samples studied contained mutations in these genes. “Whenever we find genes mutated in a majority of tumors, it is likely that the pathway regulated by that gene is critical for cancer development and the biology of the tumor,” says Kinzler.

The research team also found mutations in the PIK3CA gene, which has been well studied in cancer and is already the focus of several clinical trials of targeted therapies. As a result of these findings, scientists suspect that oligodendroglioma patients with PIK3CA mutations could potentially benefit from these experimental therapies and may be included in these clinical trials.

“Knowing the genetic roadmap of a cancer is the key to attacking it,” says Kinzler. Having identified these key gene mutations, investigators can now focus on determining at what point in the cancer process they occur, whether they guide prognosis, and if they might be good targets for treatment.

The oligodendroglioma research was funded by the Virginia and D.K. Ludwig Fund for Cancer Research, the Pediatric Brain Tumor Foundation, the Duke Comprehensive Cancer Center Core, the Burroughs Wellcome Fund, The James S. McDonnell Foundation, state funding from Sao Paulo (FAPESP), the National Cancer Institute, and the National Institutes of Health.

Editor’s Note: Under agreements between the Johns Hopkins University, Genzyme, Exact Sciences, Inostics, Qiagen, Invitrogen, and Personal Genome Diagnostics, Papadopoulos, Vogelstein, and Kinzler are entitled to a share of royalties received by the University on sales of products related to genes and technologies described in this article. These researchers are co-founders of Inostics and Personal Genome Diagnostics, are members of their Scientific Advisory Board, and own Inostics and Personal Genome Diagnostics stock, which is subject to restrictions under Johns Hopkins University policy.

IN BRAIN CANCERS, TWO OR MORE TARGETS ARE BETTER THAN ONE

Clinical Cancer Research, December 15, 2010

Brain cancers represent one of the most difficult types of cancer to manage. Tumors that respond initially to treatment eventually become resistant. Now, research by Charles Eberhart, M.D., Ph.D., reveals new clues about how cancer gene pathways conspire to circumvent therapy.

Similar to a computer network that increases its computing capabilities by linking several computers together, groups of genes work together through pathways to enhance cell function. Cancer cells manipulate these pathways to drive tumor growth and spread.

Research by Eberhart and team reveals that inhibiting a single cancer cell development pathway with drug therapy can disrupt and may actually increase activity in other pathways and raise the risk of tumors becoming resistant to therapy.

The research team studied an agent that targets and blocks a known cancer gene pathway called Notch in glioblastoma brain cancer cell lines. They found that when they inhibited Notch, activity increased in two other common cancer pathways known as Hedgehog and Wnt. Eberhart speculates that tumors compensate for therapy directed at one pathway by turning on a different one. Combining the Notch inhibitor with a second drug to also block Hedgehog dramatically decreased cell growth, by as much as 90 percent, in the cell line studies. The combined approach had an antitumor effect, increasing natural cell death and hindering cells’ ability to form clusters or colonies. They achieved similar results in laboratory studies using human glioblastoma samples removed during surgery.

Glioblastoma is one of the most aggressive types of brain cancer. Even when tumors initially respond to treatment, they almost always eventually become resistant. As a result, most patients die within two years of diagnosis. This research may help experts better understand the cellular mechanisms that make the cancer so deadly.

Clinical trials evaluating Notch and Hedgehog inhibitors in several types of cancer are now under way at the Kimmel Cancer Center and other cancer centers across the U.S.

The research was funded by the National Institutes of Health, the Brain Tumor Funders Collaborative, the American Cancer Society, and a National Cancer Institute Brain Tumor SPORE grant.

PANCREAS CANCER TIMELINE REVEALS AMPLE TIME FOR EARLY INTERVENTION


Kimmel Cancer Center and Sol Goldman Pancreatic Cancer Research Center investigators have developed a mathematical model that allows clinicians, for the first time, to quantify the development of pancreas cancer and how best to treat it. Their work disproved common scientific thought that this type of cancer progresses to a deadly stage very early in its development.

To the contrary, the research team calculated that it takes an average of 11 years before a cancer cell arises from a precancerous pancreas lesion. Still
another seven years may pass as that cancer grows to form a tumor, giving at least one cell the potential to break away and spread the cancer outside of the pancreas in a process known as metastasis. This spread represents a lethal turning point in the progression of the cancer, and once it occurs, the research team reports that these patients die, on average, two and half years later.

While the research reveals a large window of time before a pancreas cancer turns deadly, currently, “pretty much everybody is diagnosed after that window has closed,” says pancreas cancer expert Christine Iacobuzio-Donahue, M.D., Ph.D.

New, early diagnostic tests to detect these cancers during this 11 to 18 year window would provide an opportunity to intervene and potentially cure these cancers with surgery investigators say.

Their goal is to create a screening method, similar to those used to screen for breast and colon cancers, to detect very early pancreas cancers, long before they cause symptoms.

Iacobuzio-Donahue suggests that just as colonoscopies are used to look inside the colon for precancerous lesions called polyps, physicians could use a similar technique called endoscopy, which uses an endoscope inserted through the mouth, to examine the pancreas for precancerous lesions.

To make their calculations, the team studied tissue collected at autopsy from seven patients who died of metastatic pancreas cancer. A team led by Bert Vogelstein, M.D., the world’s foremost expert in deciphering the genetic blueprints of cancer, identified and classified the genetic alterations in each patient’s pancreas tumor and the sites to which it spread. In all of the patients, the investigators found similar mutations in both the originating tumor and the body sites where it spread, genetically linking the metastatic lesions to the original pancreas tumor from which it arose. They classified mutations that occurred prior to metastasis and those that happened after the cancer began to spread and applied their findings to mathematical models to create a timeline of progression from precancerous lesion to deadly, metastatic disease.

The research was funded by the National Institutes of Health, the Bill and Melinda Gates Foundation, the Uehara Memorial Foundation, The AACR-Barletta Foundation, the John Templeton Foundation, the Sol Goldman Pancreatic Cancer Research Center, the Michael Rolfe Pancreatic Cancer Foundation, the George Rubis Endowment for Pancreatic Cancer Research, the Joseph C. Monastra Foundation for Pancreatic Cancer Research, the Alfredo Scatena Memorial Fund, Sigma Beta Sorority, the Skip Viragh Foundation, the Virginia and D.K. Ludwig Fund for Cancer Research, the Joint Program in Mathematical Biology, and J. Epstein.

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**CELL CYCLE CLOCK LINKED TO CHILDHOOD CANCERS**

Immunity, February 24, 2011

Researchers linked a molecular cell cycle “clock” which regulates the timing of how DNA is broken up and copied to form new immune genes to chromosomal abnormalities found in children with leukemia and lymphoma, cancers that originate in immune system cells.

This regulatory function manages how DNA segments are split off and then reshuffled inside dividing immune cells in a process known as recombination. It is an exceedingly complex biological process that occurs repeatedly as cells divide. In the time it takes to read this sentence, about 10 million recombination events will occur inside the human body. Although most of the time they occur seamlessly, the sheer numbers mean that potential mismatches of genetic bits could lead to genetic rearrangements that may wreak havoc in the immune system and sometimes lead to cancer.

“We are exposed to the possibility of cancer every time we make a new immune cell,” says Stephen Desiderio, M.D., Ph.D., director of the Institute for Basic Biomedical Sciences, the Institute for Cell Engineering Immunology Program, and a Kimmel Cancer Center investigator. “One of the many safeguards in place to ensure that this doesn’t happen appears to be a cellular clock that times these potentially dangerous events and regulates them.

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Desiderio and team’s work focused on a molecular knife—a gene called Rag2—that chops up DNA inside of immune system cells. Rag2 is normally available during a precise window of time during the cell cycle and then cleared away to ensure proper DNA assembly. Desiderio and team showed that if Rag2 is mutated and does not become disabled before DNA replication, it could chop the wrong genetic material at the wrong places and wrong times. The result is strange bits joined together in odd ways causing abnormal chromosomes, like those seen in children with leukemia and lymphoma, to occur.

“Knowing the underlying mutations that make it more likely for a child to get these chromosomal abnormalities could mean, at the very least, we might be able to identify children at risk and watch them more closely,” says Desiderio.

“Perhaps in the future, the knowledge could lead to new therapies.”

The research was funded by the National Cancer Institute and a gift to the Institute for Cell Engineering Immunology...
CELLS MANIPULATED TO REPAIR DISEASED LIVER

In work that could one day help people with liver cancer, researchers returned a variety of adult human cells, including liver, bone marrow, and skin cells, to an embryonic state. In animal models, these cells took root in the liver and regenerated damaged tissue.

This early science may provide a foundation for producing functional liver cells for patients who have liver diseases and need transplants, says Yoon-Young Jang, M.D., Ph.D., the Kimmel Cancer Center scientist who led the study. The liver is one of the few organs that naturally regenerates damaged tissue, but Jang says that certain diseases, including cancer, eventually destroy this natural ability.

Currently, the only option for many patients is to receive a new liver or liver cell transplant. Transplantation relies on the availability of donor liver tissue, and mature liver cells, she says, are difficult to isolate or grow in the laboratory. “Our findings could be applied clinically as an alternative to liver transplant, overcoming the problem of long waiting lists for organs and concerns about immune system rejection of donated tissue,” says Jang. The cells Jang used in her research can be made from a tiny amount of many kinds of tissue and can be grown indefinitely in the laboratory.

The research uses induced-pluripotent stem cells (iPSCs), cells that are made from adult cells and genetically reprogrammed to revert to an embryonic stem cell-like state, with the ability to transform into different cell types. Jang and team generated iPSCs from a variety of adult human cells, including liver cells, bone marrow stem cells, and skin cells. While all of the cells were molecularly similar to each other, they retained a distinctive signature inherited from the cell from which they originated. Still, Jang and team were able to induce the cells, regardless of their origin, to differentiate into liver cells.

Jang says additional studies are needed before clinical trials can begin. By nature of their role to form new cells, the iPSCs intrinsically have the potential to cause tumors, and though no tumors developed in the animal studies, Jang and team are conducting ongoing research to ensure they are stable.

The research was funded by the National Institutes of Health and the Maryland Stem Cell Research Fund.

DUAL APPROACH BETTER FOR LIVER CANCER

A combined treatment for liver cancer that uses one oral drug and another delivered directly to tumors via tiny drug-filled microbeads could potentially improve outcomes for patients with these fast-growing and often deadly tumors.

Both the oral drug, sorafenib, and the one used in the microbeads, doxorubicin, have been approved individually for liver cancer treatment. Investigators are hopeful that combining them through this novel delivery method could make treatment more effective against liver cancer, which is seeing increased incidence in the United States.

“Both therapies have increased survival rates in advanced liver cancer, and combining them may push those survival rates further,” says interventional radiologist and study leader Jean-Francois Geschwind, M.D. He and his team treated 35 patients, using the oral drug to block the formation of blood vessels that nourish tumors and the microbeads to provide prolonged delivery of an anticancer drug directly to the tumor.

Geschwind used a method known as chemoembolization, using a tiny catheter, the size of a single hair, inserted into the tumor to deliver approximately 200,000 cancer-drug filled microbeads. For three or more weeks, the drug seeps out of the microbeads to attack cancer cells. Geschwind, surgeon Timothy Pawlick, M.D., medical oncologist David Cosgrove, M.D., and...
collaborators believe this dual approach could prolong the antitumor effects of chemoembolization.

Liver cancer tends to grow rapidly without causing noticeable symptoms. As a result, Geschwind says it is inoperable by the time most patients are diagnosed, offering a dismal survival outlook of less than a year. In these patients, he says, chemoembolization can often increase survival by as much as 10 to 15 months.

Clinical studies of chemoembolization, with and without the oral drug, are ongoing. “We’re on the path to improving the standard of care for liver cancer,” says Geschwind.

This study was funded by Bayer HealthCare and Onyx Pharmaceuticals, which manufactures sorafenib, and Biocompatibles, makers of the microbeads. Geschwind and Pawlick are consultants to Bayer HealthCare Pharmaceuticals, and Geschwind is a consultant to Biocompatibles. The terms of these arrangements are being managed by The Johns Hopkins University in accordance with its conflict-of-interest policies.

GENETIC CAUSES OF A TYPE OF PANCREAS CANCER UNCOVERED

Science Express, January 20, 2011

Kimmel Cancer Center researchers in the Ludwig Center have once again pieced together the genetic puzzle of a cancer, this time deciphering the genetic causes of a type of pancreas cancer known as neuroendocrine or islet cell tumors.

This is the latest work from the team who has led the world in uncovering the genetic causes of dozens of cancers, including colon, breast, brain, pancreas, and head and neck cancers.

In this cancer, researchers uncovered a unique genetic code specific to each patient that predicts how aggressive the disease is and how well it will respond to specific treatments. “This tells us that it may be more useful to classify cancers by gene type rather than organ or cell type,” says Nickolas Papadopoulos, Ph.D., director of translational genetics.

Pancreatic neuroendocrine tumors make up about five percent of all pancreas cancers. Some of these tumors produce hormones that leave telltale biological signs of their existence, including changes in blood sugar levels, weight gain, and rashes. Hormone-free tumors do not produce these signs making them difficult to detect and difficult to distinguish from other types of pancreas cancers.

To better understand how these stealth tumors develop and grow, the investigators studied 68 non-hormonal pancreatic neuroendocrine tumors. Their work revealed several common gene mutations, including two genes that had not been previously linked to cancer. In addition, they found that patients whose tumors contained mutations in three genes, called MEN-1, DAXX, and ATRX, survived at least 10 years after diagnosis while more than 60 percent of people whose tumors did not have the mutations, died within five years of diagnosis. The team also found mutations to a family of genes called mTOR in about 14 percent of tumors that they believe would be good targets for personalized therapy. Patients whose tumors contain alterations to mTOR would be candidates for treatment with agents that inhibit these genes, says Papadopoulos.

The research was funded by the Caring for Carcinoid Foundation, the Lustgarten Foundation for Pancreatic Cancer Research, the Sol Goldman Pancreatic Cancer Research Center, the Joseph Rabinovitz Fund for Pancreatic Cancer Research, the Virginia and D. K. Ludwig Fund for Cancer Research, the Raymond and Beverly Sackler Research Foundation, the AACR Stand Up to Cancer’s Dream Team Translational Cancer Research Grant, and the National Institutes of Health.

Editor’s Note: Papadopoulos and other members of the research team are co-founders and members of the scientific advisory board of Inostics, a company developing technologies for the molecular diagnosis of cancer.

ANTIFUNGAL DRUG WORKS AGAINST PROSTATE CANCER

The American Society of Clinical Oncology Annual Meeting, June 2011

A drug used to treat nail fungus appears to keep prostate cancer in check. In a study of the oral antifungal, called itraconazole, researchers found that it helped some men with advanced prostate cancer, keeping their cancer stable, delaying progression and the need for chemotherapy.

Forty-six men with prostate cancers which had spread to other organs and who were not responding to hormone therapy (the standard course of treatment for metastatic prostate cancer) were treated with either low or high doses of itraconazole. While low doses had minimal effect, the high dose treatment led to stable or declining levels of PSA (prostate specific antigen), a prostate cancer marker, in 11 of 24 men who received it.

Kimmel Cancer Center researcher Emmanuel Antonarakis, M.D., led the team that came upon the drug and its anticancer potential when reviewing a database of more than 3,000 FDA-approved drugs. In laboratory tests by Jun Liu, Ph.D., the drug was able to shrink human prostate tumors implanted in mice. It appears to work by blocking tumor vessel blood growth and disrupting a main cancer-initiating gene pathway called Hedgehog.

Antonarakis and team are planning larger studies of the high-dose itraconazole therapy.

This research was funded by the Department of Defense Prostate Cancer Research Program, the Commonwealth Foundation for Cancer Research, the David H. Koch Charitable Foundation, a 2009 American Society of Clinical Oncology Young Investigator Award granted to Antonarakis, and the National Cancer Institute.
EFFECTIVENESS OF HALF-IDENTICAL TRANSPLANTS CONFIRMED

The results of two clinical trials found that bone marrow or blood stem cell transplants using half-matched bone marrow or umbilical cord blood are comparable to fully matched marrow. The finding means that nearly all patients in need of a transplant can find donors, says bone marrow transplant researcher Ephraim Fuchs, M.D., who helped develop half-match, or half-identical, (haploidentical) transplants.

Bone marrow transplantation is a potentially curative therapy for cancers of the blood and immune cells, such as leukemia and lymphoma. Although patients and physicians may seek donors through national registries, frequently no match is found, and the search can take weeks to months, time that delays treatment and allows the cancer progress. “People are dying waiting for matched donors from a registry,” says Fuchs.

He began research of halploidentical, or half-identical, transplants as an option for these patients. Half-identical matches are parents, children, and most siblings, so virtually every patient has a suitable donor. To make it work, however, he and his team had to circumvent a life threatening complication, known as graft versus host disease (GVHD), that occurs when the donor immune system sees its new host as a foreign invader and launches an attack against the patient’s tissue and organs. Fuchs and team pioneered a post-transplant therapy, using the drug cyclophosphamide, that reprograms the immune system and prevents severe GVHD.

With the ability to safely perform half-identical transplants and evidence that they are as clinically effective as full matches, the treatment will likely be expanded to autoimmune diseases, including aplastic anemia, lupus, sickle cell anemia, and lupus.

Funding for the clinical trials was provided by the National Heart, Lung and Blood Institute and the National Cancer Institute.

GETTING BREAST CANCER DRUGS RIGHT TO THE SOURCE

Science Translational Medicine

To best treat the precursors of breast cancer, Kimmel Cancer Center investigators recommend going directly to its source. Breast cancers most often arise in the cells that line the breast ducts, and Breast Cancer Program directors Saraswati Sukumar, Ph.D., and Vered Stearns, M.D., have developed a method to deliver anticancer drugs directly to these ducts. In this intraductal therapy, anticancer drugs are administered via a tiny catheter inserted through the nipple into the breast ducts.

Sukumar developed and proved the therapy to be effective in animal models over the last decade and now Stearns has demonstrated in a small study of 17 patients that it can be done safely in humans. “This has been classic translational medicine collaboration between a bench researcher and a clinician scientist,” says Sukumar, Barbara B. Rubenstein Professor of Oncology.

The intraductal delivery resulted in a higher concentration of anticancer drugs in the breast than in the bloodstream, while typical intravenous chemotherapy provided relatively high concentrations of drugs in the blood but very little, if any, in the breast, says Stearns, the Breast Cancer Research Chair in Oncology. “Our results support the theory that by treating the breast tissue directly we can reach a much more potent drug concentration where it is needed and with far fewer adverse effects on tissue outside the breast,” she says.

In her animal models, Sukumar tested intraductal delivery of four standard anticancer drugs. One, called 5FU, proved to
be the most effective, both in preventing and treating cancers. More important, it appears to initiate an immune response, at least in animal models, that suppresses tumor formation in non-treated ducts. Sukumar says this is a key finding as some breast ducts in women are not connected to the nipple and, therefore, are not reachable by intraductal chemotherapy.

Sukumar and Stearns are now planning studies of intraductal 5FU therapy as a way to prevent breast cancer in women who have an inherited predisposition to the disease or who have precancerous breast lesions. Sukumar says, “In principle, one could do such a procedure every ten years or so to keep one’s breasts tumor-free, as an alternative to having the breasts removed.”

This research was funded by the National Cancer Institute, Windy Hill Medical Center, the Mary Kay Ash Foundation and the Susan Love Research Foundation.

GENE TEST IDS BAD PANCREATIC CYSTS
Science Translational Medicine
Kimmel Cancer Center scientists have developed a gene-based test to distinguish precancerous pancreatic cysts from harmless cysts. The investigators estimate that these fluid-filled cysts are identified in more than a million patients each year, and their test may eventually help some of these patients avoid unnecessary surgeries for harmless cysts,” says Vogelstein.

Genetic analysis of the kind reported in the new study offers a new way to sort the potential of these cysts to become cancerous. Further studies on a larger number of patients must be done before the gene-based test can be widely offered. Vogelstein says, however, that the technology for developing a gene-based test in this case is relatively straightforward because “the mutation occurs at one spot in both of the genes.”

Major funding for the study was provided by the Lustgarten Foundation, a private, nonprofit foundation dedicated to funding pancreatic cancer research. Other funding was provided by the Virginia and D.K. Ludwig Fund for Cancer Research, the Sol Goldman Center for Pancreatic Cancer Research, the Joseph L. Rabinowitz Fund, the Michael Rolfe Foundation, the Indiana Genomics Initiative of Indiana University, which is supported in part by Lilly Endowment Inc., the J.C. Monastra Foundation, Swim Across America and the National Institutes of Health.

WATCH AND WAIT APPROACH FOR PROSTATE CANCER
Journal of Clinical Oncology
A Johns Hopkins study of 769 men from across the United States with low-grade prostate cancer finds no harm in delaying treatment for men 65 or older as long as the cancer’s progression and tumor growth are closely monitored through “active surveillance” and there is no dramatic worsening of the disease over time.

“This study offers the most conclusive evidence to date that active surveillance may be the preferred option for the vast majority of older men diagnosed with a very low-grade or small-volume form of prostate cancer,” says study leader and urologist H. Ballentine Carter, M.D. “These are men with a favorable risk disease profile to begin with.”

The study, which ran from 1995 to 2010, is believed to be the largest and longest study of men initially diagnosed with the earliest stage of prostate cancer. These men have cancers characterized as slow-growing and very nonaggressive and have a very small chance of dying from the disease. “The vast majority of these men are ideal candidates for active surveillance because they are older and are able to avoid the risks and complications associated with surgery and radiation treatments, including incontinence, impotence, and other bowel and urinary problems.

Some 217,000 men in the United States are diagnosed each year with prostate cancer, the majority of them are older than 65 and have a low risk of dying from the disease if treatment is deferred, Carter says. Yet, more than 90 percent of these men with low-risk disease, including some 80 percent of those over 75, are likely to choose some form of treatment instead of surveillance. “Our findings really underscore the need to address excessive treatment of this milder stage of the disease in older men, especially seniors,” says Carter.

Current guidelines endorsed by the National Comprehensive Cancer Network already list active surveillance as a preferred course of action for many older men, especially seniors, and could be broadened as a result of the study. Carter and team are working with the Prostate Cancer Foundation to develop a web-based educational program on active surveillance for men newly diagnosed with the disease.

The study was funded by the Prostate Cancer Foundation and the Patrick C. Walsh Prostate Cancer Research Fund.
SAFER RADIATION THERAPY

The Joint Annual Meeting of the American Association of Physicists in Medicine (AAPM) and Canadian Organization of Medical Physicists

Radiation therapy is an effective and safe staple of cancer treatment. However, the multistep complexity of radiation therapy, and the numerous precision measurements its use entails, can sometimes lead to mistakes, with patients getting too little radiation where it’s needed, or too much where it isn’t.

Radiation oncology and molecular radiation sciences expert Eric Ford, Ph.D., and pediatric radiation oncologist Stephanie Terezakis, M.D., led the first-ever safety analysis of radiation oncology. Working with researchers at Washington University in St. Louis, Ford and team gathered data on about 4,000 “near miss” events that occurred during 2008 to 2010 at both Johns Hopkins and Washington University. They focused their attention on 290 events that, had they not been caught in time, could have resulted in serious harm to patients. They determined that a combination of approximately six common quality assurance (QA) measures, including use of hardware built into many radiotherapy-delivery machines and a relatively simple checklist, would have prevented more than 90 percent of the potential incidents. The checklist includes reviews of patient charts before treatment by both physicians and radiation-physicists who calculate the right dose of radiation and a mandatory “timeout” by the radiation therapist before radiation is turned on to double-check that the written treatment plan and doses match what’s on the radiation delivery machines. “While clinicians in this field may be familiar with these quality assurance procedures, they may not have appreciated how effective they are in combination,” says Ford.

By contrast, a common QA measure known as pretreatment IMRT (intensity modulated radiation therapy), was found not to be useful. In this measure, staff performs a “test run” of the radiotherapy device at its programmed strength with no patient present. “This is important to know, because pre-treatment IMRT often consumes a lot of staff time,” he says.

In a follow up study surveying radiation therapy specialists, Ford and team identified fear of getting colleagues in trouble, liability issues, and embarrassment as the most common explanations given for not reporting errors. He and Terezakis are members of the AAPM Working Group on the Prevention of Errors, which is developing a way to have treatment errors and near-misses reported and sent to a central group for evaluation and dissemination to clinics, says Ford. “It could work in ways similar to how air and train accidents are reported to the National Transportation Safety Board,” he noted.

The study was funded with a pilot research grant from Elekta Inc.

TO DETECT COLON CANCER, LOOK IN THE MOUTH

Familial Cancer, June 2011

Oddly enough, looking inside the mouth may be the best way to detect a hereditary form of colon cancer. According to researchers, people who have a hereditary colon cancer syndrome known as familial adenomatous polyposis (FAP) also have abnormally dense blood vessel growth in the lining of their mouths.

“A higher blood vessel density in the mouth may reflect an abnormal state of cells lining the digestive tract, including the oral cavity, that predisposes people to colorectal cancer and precancerous polyps,” says Francis M. Giardiello, M.D., director of the Johns Hopkins Hereditary Colorectal Cancer Program.

FAP, an inherited genetic disease that causes hundreds of precancerous polyps to form in the colon, some of which eventually develop into colon cancer, is currently diagnosed with costly DNA tests and colonoscopies, and sometimes still goes undetected until colon cancer develops.

As a result of this work, Giardiello and team developed a simple and quick screening test. Working with collaborators at the Catholic University of America, researchers developed an automated camera-like device that measures the vascular density in the lining of the mouth.

The investigators tested their device, scanning the lower lip of 33 patients enrolled in the Johns Hopkins Colorectal Cancer Registry as well as 50 people with no personal or family history of colorectal cancer. Measurements were significantly higher among FAP patients when compared to healthy controls.

Measurements were also high when the test was performed on five of Giardiello’s patients who have multiple polyps but no known underlying genetic cause. “These results suggest that the high vascular density may be an alternative marker for colon cancer risk, even when we can’t find the gene mutation causing it.”

The research was funded by the John G. Rangos Sr. Charitable Foundation and the Clayton Fund.
Engineering Cures

JOHNS HOPKINS PHYSICIANS, SCIENTISTS, AND ENGINEERS WORKING TOGETHER TO FIGHT CANCER

by Valerie Matthews Mehl
PHOTO BY KEITH WELLER
Dan Stoianovici and team have developed a revolving needle that works like a drill, rotating as it enters an organ, creating less force against the tissue, and therefore, providing more precise placement. See his story on page 25.
ADD ENGINEERS TO THE LIST OF SPECIALISTS ENGAGED IN THE FIGHT AGAINST CANCER.

It is not unexpected. Johns Hopkins is revered for its brain trust and the willingness and desire of its leadership to apply knowledge to improve the health and wellbeing of humans. Johns Hopkins, after all, was the site of the first department of biomedical engineering—the very first organized effort that applied the tools of engineering to human medicine. It is a brilliantly simple concept. Gather together the smartest people, give them the freedom to pursue novel approaches, and good ideas will almost always result. This is perhaps the cornerstone of Johns Hopkins’ pioneering success in so many fields. With world-class programs in engineering and medicine and some of the most talented scientists in both fields, why not bring them together.

“MORE INTERACTION stimulates creative ideas,” says Kimmel Cancer Center Director William Nelson. “It leads to connecting two things together that have never been connected before. With more of this happening it is almost certain that something innovative will come about.”

The Cancer Center at Johns Hopkins was built on the premise of collaboration. The urgency of the problem demanded no less. Laboratories were located directly off the patient wings to ensure the quick transfer of discoveries from scientists to clinicians. Nowhere at Johns Hopkins was the physician-scientist, those who work both at the bench and the bedside, more visible than in the Cancer Center. Kimmel Cancer Center investigators and clinicians were doing “translational” medicine—transferring basic science discoveries to cancer medicine—long before there was a word for it.

Therefore, it is not surprising that a new and different type of collaboration has emerged. This way of working, one could say, is in our metaphorical “genes.” Pioneering discoveries in genetics and epigenetics by Johns Hopkins Kimmel Cancer Center investigators have revealed the very origins of cancer and uncovered new targets for treatment and drugs that hit these targets. Engineers bring technologies that allow researchers to pick the best target, deliver drugs effectively to the target, and monitor whether or not it gets the job done. Cancer researchers made personalized cancer medicine possible. Engineers made it doable.

“We have to ask ourselves, ‘Why is Johns Hopkins so successful?’” says Dean of the Whiting School of Engineering Nicholas Jones. “The collaborations between investigators in the trenches all the way up through the Deans and Directors of departments surely must have something to do with it.”

Collaborations between oncologists and engineers are certainly not new to the Kimmel Cancer Center. Diseases like cancer demand forward-thinking study, and our investigators have always looked to innovation to develop new methods to control and cure cancer. Engineers and physicists, including John Wong, Justin
Hanes, and Martin Pomper work in the cancer center with the sole purpose of using their skills to aid oncologists in diagnosing and treating cancer. Surgeons like Michael Choti have solicited the expertise of engineers for more than a decade to bring added precision through image guidance and robotics to cancer surgery.

Every instrument used and the process by which they operate were developed by engineers.

Under the leadership of Jones, the Whiting School of Engineering has infused considerable resources into the department to accommodate the growth in clinically relevant programs, such as nanotechnology, computer science, and robotics. In recent years, he has added a new engineering building and a computational and robotics facility. New programs, including the Engineering in Oncology Center, Institute for Nanobiotechnology, the Center for Cancer Nanotechnology Excellence, The Center for Nanomedicine, and Physical Science Oncology Center fund and foster research projects between Kimmel Cancer Center scientists and engineers.

The strength of these collaborations and their potential to improve healthcare has not gone unnoticed. If investments are a measure of our success, then the Kimmel Cancer Center and Whiting School have earned high marks. Both have recently received separate $30 million gifts. These funds will help support personalized approaches to treating cancer, stemming from Johns Hopkins research that distinguishes unique genetic and epigenetic differences among individual patients’ cancers, explaining, at least in part, why traditionally developed drugs help some people and not others.

The Kimmel Cancer Center received its gift, a grant from the Commonwealth Foundation for Cancer Research, to create a Center for Personalized Cancer Medicine. It supports collaborations and research that accelerate the pace of developing targeted therapies based on the distinctive cellular fingerprint of each individual patient’s cancer. The Whiting School of Engineering grant comes from Johns Hopkins alumnus John C. Malone and will be used to foster interdisciplinary research efforts where researchers will collaborate with colleagues from other Hopkins divisions to learn to tailor therapies for individual patients and devise systems-based approaches to medical problems, with an initial emphasis on cancer.

“This is a watershed moment,” says Nelson, M.D., Ph.D. “There are many opportunities for engineers and physicians to make cancer medicine better. Across a whole spectrum of components—molecular genetics, epigenetics, imaging, diagnostics, and treatment—we are doing pioneering work in engineering and in medicine. Hopkins is probably better positioned than anyone to make revolutionary advances in human diseases, like cancer, that could only be imagined a decade ago. It’s just a question of how we bring it all together.”

THERE ARE MANY OPPORTUNITIES FOR ENGINEERS AND PHYSICIANS TO MAKE CANCER MEDICINE BETTER. ACROSS A WHOLE SPECTRUM OF COMPONENTS—MOLECULAR GENETICS, EPIGENETICS, IMAGING, DIAGNOSTICS, AND TREATMENT—WE ARE DOING PIONEERING WORK IN ENGINEERING AND IN MEDICINE.

GENETICS, EPIGENETICS, AND PHYSICS

Cancer is a genetic disease. That was proven by researcher Bert Vogelstein and team who first illustrated it in colon cancer, laying out an accumulation of genetic errors over time that cause cancer to arise and grow. Since that pioneering work in the 1980s, the same team has mapped the genetic blueprint of nearly 100 cancers. Other errors, called epigenetic events, that alter the DNA without mutating it were also proven by Kimmel Cancer Center researchers to contribute to the origination and progression of cancer. Now with collaborations through the Engineering department’s Physical Science Oncology Center, Johns Hopkins teams are deciphering a third contributor called physical oncology. It is focused on solving the mystery of how cancer cells break away from the original tumor and form new tumors in other parts of the body. This little understood process is called cancer metastasis, and it is at the heart of what makes the disease so deadly. Cancers that spread are cancers that kill.

“Every tumor has mutations. But now, we are also looking at its structural differences,” says Kimmel Cancer Center investigator and pancreas cancer expert Anirban Maitra. “What are the physical consequences of the genetic and epigenetic events on the cell? How does it change the cell structurally so that it can become metastatic?” asks Maitra. Epigenetics expert Stephen Baylin agrees. “We know that cancer cells have the ability to reprogram to respond to and see cues in their environment,” says Baylin. “Understanding what these cues are would be very helpful.”

Maitra says genetic events happen first in cancers, but it’s what happens afterwards that scientists must begin to take a look at to get the full picture. We need only look to lower life forms like worms and plants to know there is more. “Worms have as many protein encoding genes as humans, yet humans are more evolved. There are layers of regulation and cellular characteristics beyond coding genes that we don’t yet fully understand and some of them likely sustain cancer” he says.

Maitra has teamed up with Denis Wirtz, a chemical and biomolecular engineer and director of the Physical Sciences Oncology Center to help unravel some of these (continued on page 14)
mysteries. “If we all take pieces of the puzzle, we can figure this out,” says Maitra. “Johns Hopkins is ahead of the game here because we do not work in isolation. Multidisciplinary collaborations aimed at moving research discoveries to patient care are the Hopkins model. Human tissue and clinical research are revered and encouraged here. We recognize that engineers are doing vibrant research that is directly relevant to our work, so it only makes sense that we engage in collaborations.”

Wirtz developed a technology that, in minutes, can take thousands of distinct structural measurements on tens of thousands of individual cells. It’s not easy for a cancer cell to metastasize. “It’s like a steeple chase. The cancer cell has many obstacles to overcome,” says Wirtz. It must break away from the original tumor and the organ from which it arose, squeeze into narrow capillaries, make it through the sheer force of the bloodstream, and set up residence in a new and foreign environment.

Maitra and Wirtz are working to uncover the physical changes to a cell that help drive it away from its home and, against all odds, allow it to survive and thrive in a new and foreign place. Most cancers can be cured if they are detected and treated before they have begun to spread. If researchers can figure out how metastasis occurs, they could develop ways to prevent the deadliest event in cancer progression.

Wirtz likens a cancer cell that metastasizes to a decathlon athlete. A decathlon competition, whose winner is considered the world’s greatest athlete, features competitors who have physical attributes that make them stronger, faster, and simply more adept than other athletes. “Millions of cells are shed by tumors every day, but only one or two of them will have what it takes to become metastatic. These are the decathlon cells. We need to figure out what the physical properties are that give these cells an edge,” says Wirtz.

Maitra and Wirtz are now using his cellular measurement tool in the laboratory on human cancer cells to identify specific cellular characteristics that may determine how aggressive a cancer will be and how it will respond to treatment. Monitoring and measuring how cells change will allow scientists to predict which ones are likely to become the lethal, metastatic type.

“This kind of technology allows us to further personalize cancer medicine,” says Maitra. Within the next few years Wirtz and Maitra hope to move the technology into clinical use to help select drugs that will work best against a cancer based on the genetic, epigenetic, and physical characteristics of tumor cells. “The engineers have the coolest tools around, and they are looking to us for the right biological uses,” says Maitra. “Now, we can use this new tool to correlate gene abnormalities with particular cellular characteristics and drug sensitivity so that we can get the most effective treatments to each patient.”

The work of Stephen Baylin (center) and his colleagues, clinician-scientists James Herman (right) and Malcolm Brock (left), resulted in some of the first uses of epigenetic abnormalities as cancer biomarkers for diagnosis and to predict how a cancer would respond to treatment.
BLOOD CELLS BECOME BEATING HEART CELLS

With one look through the microscope, these cells are immediately and unquestionably identifiable. Though silent in this microscopic form, the rhythmic and continuing up and down motion causes the mind to think it hears the iconic thump thump—thump thump—thump thump of a beating heart. What appears beneath the lens of the microscope are single heart cells, no bigger than the tip of a needle, but as they beat, they are like tiny micro-cosms of the life-sustaining organ.

STILL, MORE AMAZING than the cells themselves is the story of their origin. Days earlier they were human blood cells, like those that course through our veins and arteries, until researchers Elias Zambidis and Paul Burridge altered their destiny and transformed them into living, functioning heart cells. Now, instead of cells that are pumped out by the heart, they are part of the heart.

In a collaboration between the Kimmel Cancer Center, Institute for Cell Engineering, and Department of Biomedical Engineering, Zambidis, Burridge, and team successfully turned blood stem cells into functional, beating heart cells.

Their methodical two-year study resulted in a simple, straight-forward recipe for changing blood stem cells into heart cells, and called upon the expertise of basic scientists, stem cell engineers, and biomedical engineers. What they accomplished was previously considered impossible by international leaders in the field of regenerative medicine, and provided more evidence of the ingenuity, collaboration, and the relentless pursuit of answers that allow Johns Hopkins scientists to do what others cannot.

“Many scientists previously thought that a nonviral method like the one we used to induce blood cells to turn into highly functioning cardiac cells was not within reach, but we found a way to do it very efficiently,” says Zambidis.

For Zambidis, whose research interests are in pediatric oncology and cancers of the blood, the special “plasticity” of the blood stem cell that allows them to be transformed to a heart cell, holds important clues about how leukemia and other blood diseases develop and how they can be controlled. Burridge, who plans to specialize in cardiology, will focus his continued research on refining the technique in hope that, one day, a patient’s blood cells can be directly turned into heart cells to therapeutically repair hearts damaged by heart attack and other diseases.

To take cells from one source, in this case, blood, and transform them into a heart or other cell type, scientists typically use viruses to deliver genes that will cause the cells to revert back to stem cells with open-slate potential to give rise to virtually any type of cell. Viruses, however, can mutate genes and initiate cancers in newly transformed cells. As a result, Zambidis, a cancer researcher, chose to use plasmids, rings of DNA that replicate briefly inside cells and eventually degrade, to deliver the genes.

To cause the actual transformation from one cell type to another, newly-reverted stem cells are placed in a controlled environment and bathed in a broth of growth factors and nutrients. The recipe for this “broth” varies from lab to lab and cell line to cell line, but Zambidis, Burridge and team created a universal recipe that, in their studies, worked consistently on nearly a dozen cell lines, and worked as well in transforming adult stem cells as it did in embryonic stem cells. To augment the cell transformation, the researchers created an oxygen-deprived environment that mimicked the natural human environment of these primitive cells.

Once transformed, the team set out to validate that the cells didn’t just look like heart cells but functioned like them as well. For this, they solicited the expertise of bioengineers, who developed and applied a miniversion of an electrocardiograph to the cells and proved that the cells were behaving like a normal human heart.

The discovery was only possible because Burridge was willing to do what scientists before him were not—his homework. For two years, he undertook the admittedly tedious job of combing through dozens of journal articles citing the varied techniques used to create cardiac cells. Next he made charts to analyze the wide range of techniques. Finally, after testing more than 100 combinations, Burridge was able to narrow the choices down to four to nine essential ingredients for each stage of cardiac development. “We took the recipe for this process from a complex minestrone to a simple miso soup,” says Zambidis.

He cautions that the cells are not ready for human testing, but says the team continues to develop their methods, most recently turning blood cells into retinal, neural, and vascular cells. He is eager for other scientists to test the method in their own laboratories.
studied increased two to 25-fold. Based on these findings, clinician-scientists Ros Juergens, Charles Rudin, and Brock initiated a clinical study of epigenetic therapy for patients with advanced and heavily treated lung cancer, and a small percentage of patients experienced very robust and long-lasting responses.

With funding from Stand Up to Cancer (SU2C), Rudin, Brock and team are hoping to develop these findings into a personalized treatment approach for lung cancer, and Wang’s work in developing a nanobased assay to test for alterations in these and other genes is central to that.

SU2C support allowed the researchers to do an unusual thing—to go back and find out what happened to the patients they thought they didn’t help. They reviewed the records of patients who were participating in a clinical trial of epigenetic therapy because their lung cancers had not responded to standard therapy. Specifically, Rudin, Brock and team were interested in some 40 patients who were taken off of the epigenetic treatment trial because their tumors continued to grow. What they found surprised them all. Although many patients seemed to progress while on therapy, many, including those who had received just two or three treatments, had unprecedented and long-lasting responses. The team poured over every scan and every clinical report, and even re-biopsied some tumors, and could come up with only two explanations. Either the epigenetic therapy sensitized their cancers to subsequent treatment with standard drugs, or their improvement was a direct response to the targeted therapy.

Targeted therapies do not work like the old cytotoxic chemotherapies, which do not discriminate between cancer cells and normal cells. Instead they specifically seek out and reprogram the malfunctioning mechanism within cancer cells that is causing the tumors. As a result, Baylin says, targeted therapies shrink tumors more slowly over time as they make their repairs and genes are returned to normal function.

Jerry Morton, a 61-year-old retired firefighter, was building a sandbox for his grandson two years ago when he learned he had small cell lung cancer. The cancer had already spread throughout his lungs and to his liver. “I didn’t expect to live long enough to complete it,” says Morton. “Today, that sandbox is finished.” Morton’s tumors melted away on the epigenetic treatment. When he recently developed a new, small tumor of the same type Rudin, Brock, and team again tried epigenetic therapy, and Morton, once again, appears to be benefiting. “The team has evidence that the status of epigenetic alterations in these four genes, assayed in the blood by sensitive technologies that Dr. Wang is working to perfect, can predict the good responses in patients like Mr. Morton,” says Baylin. “It is a perfect illustration of the value of collaborative research and translational, personalized cancer medicine.”

With such promising results, Baylin and team are now planning another trial for newly diagnosed patients. If findings continue to show that the epigenetic-targeted therapy works, Wang figures prominently in the wide clinical application. What Brock, Herman, and Baylin do in their basic science laboratory to screen for the epigenetic alterations would be difficult to routinely do in a clinical lab, so they asked for help from engineers. Wang, who works in the Institute for Nanobiotechnology, is using nanotechnology, engineering at a molecular level, to develop a broad-based test that could be used routinely in any clinical laboratory to predict which patients would benefit from the targeted therapy. “This facet is critically important in taking these therapies beyond our own walls. Without the nano-tech approach, testing for the alterations might be too cumbersome for a clinical lab,” says Baylin. If ongoing trials confirm the earlier findings, Wang’s test can help ensure that the Johns Hopkins-based discovery becomes available to lung cancer patients everywhere.

**ENGINEERING MOLECULES**

Nanotechnology, in essence, refers to the field of engineering that focuses on ultra-tiny functional devices and structures that are so minute they cannot be seen by the human eye. Think of it as engineering at the molecular level. Like their scientist counterparts in molecular genetics, engineers who specialize in nanotechnology work in the realm of invisibility and had to develop new technologies just to perform their craft.

Where nanotechnology intersects with medicine is the focus of the Johns Hopkins Institute for Nanobiotechnology. It began in 2006, bringing together scientists and students from engineering, physics, chemistry, biology, medicine, and public health to apply the technology to the treat-
ment of diseases. It was the brainchild of Peter Searson and Denis Wirtz, both engineers, whose work was centered on the physical sciences. They began to wonder what Johns Hopkins engineers and physicists could contribute if they collaborated with medical scientists and directed their research towards health care and medicine. Research teams comprise both engineers and medical research scientists, a point Searson says cannot be overstated. “The engineers attend lab meetings and visit the clinic and work directly with clinicians so that we understand the problems clinicians are facing,” says Searson. The model has been quite successful, earning the Institute two large NIH center grants; one for the Physical Science Oncology Center and another for the Center for Cancer Nanotechnology Excellence (CCNE).

“Physicians and engineers approach problem solving in different ways,” says cancer immunology expert Hy Levitsky, who trained in bioengineering before going into medicine and is now working with engineers to improve cancer vaccines. “As an oncologist, I can point to a problem, but I don’t have the expertise to know the spectrum of possible solutions. Engineers can look at the problem from a very different perspective. When we bring the two perspectives together, we arrive at unique approaches we may not have otherwise found.”

A TROJAN HORSE FOR THE CANCER WAR

Justin Hanes, a chemical and biomedical engineer specializing in nanotechnology for cancer treatment, explains that a nanoparticle is to a soccer ball what a soccer ball is to the planet earth. Suffice it to say that we’re talking very small.

As small as they are, part of their value in cancer medicine is that they are bigger than other things. Nanoparticles are much larger than small molecules—agents commonly used to treat cancer. Hanes says hundreds of thousands of small molecules can fit into one nanoparticle. As a result, they can be loaded up like a Trojan horse and sent out to deliver their cargo to tumors.

AS AN ONCOLOGIST, I CAN POINT TO A PROBLEM, BUT I DON’T HAVE THE EXPERTISE TO KNOW THE SPECTRUM OF POSSIBLE SOLUTIONS. ENGINEERS CAN LOOK AT THE PROBLEM FROM A VERY DIFFERENT PERSPECTIVE. WHEN WE BRING THE TWO PERSPECTIVES TOGETHER, WE ARRIVE AT UNIQUE APPROACHES WE MAY NOT HAVE OTHERWISE FOUND.

Hanes is a member of the CCNE which has the specific aim of using nanotechnology to improve the treatment of cancer. He is excited about the prospects of nanotechnology to improve the delivery of anticancer drugs and combat toxicities. “Right now, we use systemic cancer therapies, which are incredibly useful, but typically a very small percentage of the chemotherapy ends up in the tumor. The rest of it poisons normal cells throughout the body,” explains Hanes. He uses nanotechnology in an attempt to reverse that ratio so that anticancer drugs go directly to tumors with very little injury to normal cells. “Think of a tumor as a weed in a prized rose garden. What we do now is spray the entire rose garden with weed killer,” says Hanes. “But, we can only spray so much poison or we risk killing the roses.” The project he is working on with lung cancer experts Charles Rudin and Craig Peacock is a nano-based treatment that seeks out and targets cancer cells. “Like a pre-addressed envelope, we are developing methods to direct them to where we want them to go,” says Hanes.

Hanes directs the Center for Nanomedicine where he and his colleagues are currently working on anticancer-drug-filled nanoparticles that can be inhaled into the lung. His team created the first nanoparticle system that can penetrate the mucus lining the lung airways. In the past, inhaled forms...
LIVER CANCER SURGEON Michael Choti is moving gaming systems from the family room to the operating room. In collaboration with experts from engineering, Choti and team are applying the image-guided technology used in interactive gaming systems like the Nintendo Wii® and Microsoft Kinect® systems to medicine.

These newer iterations of video games use cameras, motion sensors, tracking systems and accelerometers to allow players to interact directly with the game. Choti, Emad Boctor, a radiology and computer science engineer, and Philipp Stolka, a post-doctoral engineering fellow, are working to apply the same technology to create image guidance and tracking devices for use in cancer surgery and treatments. “Current robotic and image-guided tracking systems tend to be cumbersome and extremely expensive,” says Choti. “Our approach makes use of sophisticated and mobile, but relatively cheap technology, which should broaden its appeal.”

A Wii remote contains accelerometers and infra-red cameras that calculate relative position and orientation and beam the information continuously to the game controller via a “Bluetooth” radio link. A computer receives and processes the Bluetooth signals. In one adaptation, Choti and team used the Wii remote to transform standard ultrasound imaging into a more readable 3-D imaging. Although 3-D ultrasound probes exist, Choti says they are unwieldy and expensive. However, with the position and orientation information from the Wii remote and local optical sensors, a computer could straightforwardly turn the 2-D ultrasound image into a more readable and useful 3-D ultrasound image. “Our setup, in principle would, allow clinicians to convert a 2-D ultrasound probe into a 3-D probe that’s portable and easy to use in a variety of applications,” says Choti.

In another application, Choti and his engineering team showed that Kinect, the optical hardware from Microsoft, Inc., and image-recognition algorithms used to identify and track the location and orientation of objects in its visual field, could be adapted to locate and track the motions of a biopsy needle.

One of the next steps in the development of these systems will be to combine the tracking of an imaging device such as an ultrasound probe with the tracking and 3-D guidance of a surgical instrument such as a needle, says Choti. “That combination would give us a relatively inexpensive and portable system for image-guided surgical procedures,” he says. Microsoft executives have expressed interest in working with Choti and team to develop the technology specifically for medical applications.

“This shows the value of looking at other fields, whether it is engineering, geology, or computerized gaming,” says Choti. “Collaborations—and Hopkins is good at collaboration—can lead to unexpected uses of technology that are of value to patients.”
SHOW THAT THE TUMOR HAS GROWN.

WAITING THREE MONTHS FOR A SCAN TO
ON TO SOMETHING NEW, RATHER THAN
RIGHT DRUG.

CELLS LIGHT UP, WE KNOW WE HAVE THE
WE CAN GIVE ONE DOSE OF A DRUG. IF
WE KNOW THE TUMOR HAS GROWN.

Pomper says molecular radiology has
the ability to image inside the cell and
reveal to clinicians when a cancer cell is
poised to metastasize, permitting a therapeu-
tic strike before the cancer makes this
critical and often deadly transformation.

More recently, Pomper has been
developing agents that make cancer cells
fluoresce so that they can be tracked and
monitored—tracked so that scientists
know where new targeted agents are
going, and monitored so they know if the
agents are having any benefit. “This helps
us to see quickly if drugs are hitting their
targets and doing what we expected them
to,” says Pomper. “We can then personal-
ize treatments to individual patients. We
can give one dose of a drug. If cells light
up, we know we have the right drug. If
not, we know to move on to something
new, rather than waiting three months for
a scan to show that the tumor has grown.”

Currently, this type of molecular imaging
is done primarily in research studies and
in conjunction with pathology and scans
to validate its capabilities. Once proven,
however, Pomper says, it has the potential
to complement, if not replace, CTs and
biopsy as the primary method for detecting
and monitoring cancers.

QUANTUM DOTS

Light-emitting nanoparticles known as
quantum dots are another molecular
imaging technique Pomper is exploring
with Institute for Nanobiotechnology
director Peter Searson. These cancer-
specific quantum dots are what investiga-
tors call theranostics (therapeutic and
diagnostic) for their ability to aid both in
the detection and treatment of cancer.
Pomper says they can be engineered
using a special coating that makes them
seek out and bind only to cancer cells, and
they can also be loaded with drugs to
carry to tumors. In collaboration with
Searson and Anirban Maitra, Pomper is
attaching targeting molecules to quantum
dots that are attracted to proteins over-
expressed in pancreas cancer and working
on methods to make the quantum dots
circulate throughout the bloodstream to
target tumor cells. “These would be like
radioactive warheads that can travel
throughout the body and not cause any
damage until they come into contact with
a cancer cell,” he says.

IMAGING IN CANCER VACCINES

In another example of targeting and
monitoring treatments, cancer immunology
expert Hy Levitsky is working with
engineer Jeff Bulte to improve cancer
vaccines. Bulte, a radiologist and
biomedical, chemical, and biomolecular
engineer, has devised
a way for Levitsky to monitor and track
the activity of immune-boosting cells in
response to cancer vaccines.

Several key biological events must occur
after injection with a cancer vaccine to get
the immune system to kill cancer cells.
Levitsky says the antigens contained in
the vaccine must move from the injection
site into the lymph nodes, where immunity
is initiated. Cells, called antigen-presenting
cells, have the pivotal job of capturing
the antigens and delivering them to the
lymph nodes. This critical step of antigen
transport is often the place where vaccine
therapy breaks down. “If we don’t get
this step to happen efficiently, there is no
hope that the vaccine will work,” says
Levitsky. As a result, clinicians almost
always use adjuvants—additional treat-
ments given in conjunction with cancer
vaccines to help antigen-presenting cells
make the journey to the lymph nodes.

(continued on page 22)
MORE INTERACTION stimulates creative ideas,” says Kimmel Cancer Center Director William Nelson. “It leads to connecting two things together that have never been connected before. With more of this happening it is almost certain that something innovative will come about.

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Bulte and Levitsky recruited M.D., Ph.D. student Chris Long to work jointly between the two laboratories to devise a method to quantify this process of antigen delivery. Long developed a technology that uses MRI (magnetic resonance imaging) and iron nanoparticles to track these vaccine-transporting cells. The magnetic iron particles become visible when exposed to a strong magnetic field, such as that used in MRI. Long was the first scientist to show that antigen-presenting cells can capture iron-particle labeled antigens and be tracked inside the body. Before this work, cells could only be labeled through contrast agents administered outside of the body. The method allows Levitsky to know exactly how many antigen-presenting cells capture vaccine antigen and make it to the lymph nodes and also to test how well vaccine adjuvants are improving this transport. “Within three to five days of vaccination, we can see if the vaccine is working as it should,” says Levitsky. “Adjuvants are almost always given with vaccine therapy, so this technology aids us in a critical area of cancer research.” More important, Levitsky says it could be moved to humans quickly. “All pieces of this project—the adjuvants, MRI, and contrast—have already been used safely in humans, just not in this way,” he says.

Imagine going down the vessel tree, delivering a chemotherapy-filled liquid that gets drugs to the tumor and then polymerizes [undergoes a chemical reaction] to block off further blood supply to the tumor as you watch it all unfold.

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Cancer imaging expert Hy Levitsky

CANCER IMAGING DEVICES
Scientists in the Department of Biomedical Engineering make image-guided devices for diagnosis and treatment of diseases, including cancer.

Devices that produce remarkably clear and detailed images of cells are aiding oncologists, radiation oncologists, and surgeons in the detection and treatment of cancer. Xingde Li adapted a device he developed to look at the walls of blood vessels and arteries for use in cancer. Li’s optical imaging device can be placed in a patient’s esophagus where it produces super-high resolution images of the esophageal wall. The images are so clear clinicians are able to decipher normal cells from a benign inflammatory condition called Barrett’s esophagus that can predispose those affected to developing esophageal cancer.

A similar device is in development to assist neurosurgeon Alfredo Quinones-Hinojosa in delicate brain cancer surgery. When removing a tumor from the brain, the command center for all that is human, surgeons work diligently to protect brain tissue not invaded by the tumor. Surgeons walk a clinical tightrope—they must remove as many tumor cells and as few normal cells as possible. Leave tumor cells behind and the tumor may return, but harm normal brain cells, and the patient could lose important mental and physical functions. Typically, surgeons will start at the border of the tumor, painstakingly shaving off very small sections, piece by piece. Figuring out when they are finished can be a difficult
problem, so Li is working on a microscopic device that surgeons can place against cells to quickly distinguish tumor cells from normal cells.

Department chairman Elliot McVeigh and team also are working to make lung cancer detection safer and more accurate. The quality of CT scans has improved so greatly that it can detect tiny tumors in the lung no larger than a few grains of rice. This type of early detection, occurring before a cancer produces any symptomatic evidence of its existence, could allow for earlier intervention. To intervene, particularly with targeted therapies personalized to the specific DNA alterations in a tumor, clinicians must be able to get an accurate biopsy of the tumor. Usually this is done through bronchoscopy, but it is not an exact method. “I’ve watched many bronchoscopies, and sometimes it can take 10 to 20 attempts to get the right tumor sample,” says McVeigh. “This can be very traumatic for the lung and the patient. We want to help the physician get the important cells while causing the least amount of tissue damage.” His team has developed a targeted system that can be used in combination with CT images, the bronchoscope, and fluoroscopy to provide real-time moving images inside the lung. It transforms the tumor into an easily visible target that makes even tiny tumors easier to see and biopsy.

Image-guided methods for localized delivery of chemotherapy are another focus for McVeigh. Imagine a patient in an MR (magnetic resonance) scanner, and her physician is using the images it displays to clearly see and direct a needle or catheter directly to her tumor, injecting high doses of anticancer drugs into and around the tumor. In some cases, the physicians could potentially place a needle into a blood vessel feeding the tumor and inject an agent that would harden and starve a tumor to death. The precise hardening agents to be used are still being studied. “Imagine going down the vessel tree, delivering a chemotherapy-filled liquid that gets drugs to the tumor and then polymerizes [undergoes a chemical reaction] to block off further blood supply to the tumor as you watch it all unfold under image guidance,” says McVeigh.

In essence, this method gets the cancer drug directly to the tumor and then blocks the exit, keeping the anticancer drugs in and the tumor-nourishing blood supply out.

“Our clinicians are wonderful about embracing engineers,” says McVeigh. “One of the best things about Johns Hopkins is that so many are hugely famous for their work, but you wouldn’t know it. You sit at a table and talk to them about a project, and you go back and read about them and learn they are ridiculously famous. People here are great to work with. They are not protective about their ideas. They share them. It’s in the culture of Johns Hopkins. It’s who we hire.” McVeigh says he finds that scientists and clinicians at Johns Hopkins are focused on the overall mission rather than their own, individual accomplishments. “I can show up at any lab meeting anywhere in this institution and be welcomed. This is the perfect research environment.”

MAKING SENSE OF IT ALL

In terms of engineering, perhaps one of the greatest contributions to cancer research is in the computer engineering and computational science that has allowed researchers to make sense of the volumes of data generated by genetic and epigenetic discovery. “Engineering is not only responsible for instruments we use in sequencing the genomes of cancer but also in helping us interpret the raw data we get from it,” says leading cancer genetics expert Bert Vogelstein. “It is much like hieroglyphics went it comes out. It is computer scientists and engineers that turn it into meaningful data.”

Their laboratories are not like those we typically associate with medical research. Take for example the laboratory of Rachel Karchin, a computer scientist in the department of biomedical engineering. Instead of benches, there are desks with computers. Just beyond the computer lab is a large, dark glass-enclosed room filled nearly floor to ceiling with computers. Green lights that glow and blink as if communicating in some futuristic code are the only outward sign of the complex calculations occurring within.

(continued on page 24)
Karchin is working with Kimmel Cancer Center investigators Bert Vogelstein, Kenneth Kinzler, Victor Velculescu, and Nickolas Papadopoulos to help them sift through the vast genetic blueprints of cancer to identify mutations that warrant further study. “Our role it to try to distinguish which of these mutations are worth investing lab resources, money, and time in following up,” says Karchin.

ENGINEERS ARE THE TECHNOLOGY EXPERTS, AND PHYSICIANS AND SCIENTIST ARE THE DISEASE EXPERTS. BOTH ARE NEEDED TO CONQUER DIFFICULT PROBLEMS LIKE CANCER.

The mutational landscape of tumors is quite diverse, characterized by alterations in a variety of genes which differ from patient to patient. Karchin is helping them separate the wheat from the chaff, deciphering the mutations that are actually driving the cancer from those that are just along for the ride. A cancer cell acquires thousands of different alterations, but only a few of these changes will lead to cancer. “We make it tractable,” says Karchin. “We offer a way to prioritize large amounts of data. Karchin is well schooled in this type of work. She received her doctorate in computer science, with a focus on computational biology, from University of California, Santa Cruz, where the human genome was assembled in 2000. She came to Johns Hopkins University in 2006 to join its Institute for Computational Medicine. The opportunity to work with researchers of the magnitude of Vogelstein drew her here, she says. “Johns Hopkins makes it possible to forge collaborations with people across many disciplines, and these collaborations are speeding the pace of discovery,” says Karchin.

Karchin and team have helped Kimmel Cancer Center researchers predict which changes in the genetic code may cause pancreas cells to turn cancerous. Cancer researchers sequencing the DNA from pancreas tumors and comparing it to normal tissue, found nearly 1,000 alterations unique to the pancreas tumors where just one letter in the ATCG chemical alphabet was changed. They turned this sequence data over to Karchin’s team for assessment.

The researchers developed a computer program that listed all of the individual genetic changes suspected of causing cancer and those highly unlikely to cause cancer. It employed 70 different predictive features for each change to distinguish characteristics of the so-called driver mutations—those alterations that contribute directly to the cancer development—from other genetic changes. They used the program to assess the 1,000 pancreas cancer associated alterations, scoring them with numbers between zero and one, with zero indicating a likely driver and one indicating an unlikely driver. “Our results can help cancer researchers set experiments to see how important these changes are in pancreas cancer and whether or not they are good targets for potential drug treatments,” says Karchin. “Researchers may want to make a mouse model of a mutation that could be important in cancer so that they can test an inhibitor drug. We help them figure out which mutation to pick.”

DECODING THE DATA

Like Karchin, Steven Salzberg is focused on helping investigators interpret the billions of data points generated by human genome sequencing. Researchers sequencing the genomes of a variety of human diseases have called upon his expertise. He and his team have developed computer software that has been used around the world to whittle the data down to the few mutations that could potentially be targeted clinically. As Johns Hopkins uses its genetic discoveries to personalize medicine to the unique cellular characteristics of each individual’s disease, scientists like Salzberg play an essential role.

Salzberg, a biologist and computer scientist, came to Johns Hopkins to focus more intensely on human genomics. Until now, his work has primarily focused on bacterial, viral, animal, and plant genomes. In 2001, he was called in to help sequence the anthrax sent through the mail in the 2001 terrorist attacks, and is now part of the Johns Hopkins research teams helping cancer centers make sense of complex cancer genomes. Salzberg and colleagues identified mutations that helped the FBI trace the anthrax to a single vial at Ft. Detrick in Frederick, Md. Cancer investigators are hopeful he can again help zero in on a killer: this time the target is genes that cause cancer.

Salzberg’s team has developed one of the first off-the-shelf programs that systematically and accurately find fusion genes. These are, as the name implies, two pieces of different chromosomes that become fused together in error. It turns out that fusions rarely happen in anything but cancer so they have become a major focus in cancer research. This jumbled up DNA is not a therapeutic target, but because it is so specific to cancer, it can serve as a biomarker for early detection of tumor cells before they are visible and as a way to monitor whether a treatment is working. If cancer cells are disappearing then so should the fusion genes.

Until recently, cancer researchers did not appreciate the importance of these types of alterations or how common they were in cancer, says bioinformatics expert Sarah Wheelan. Genetics and epigenetics expert Victor Velculescu came upon similar types of alterations or how common they were in cancer, says bioinformatics expert Sarah Wheelan. Genetics and epigenetics expert Victor Velculescu came upon similar types of alterations or how common they were in cancer, says bioinformatics expert Sarah Wheelan. Genetics and epigenetics expert Victor Velculescu came upon similar types of alterations or how common they were in cancer, says bioinformatics expert Sarah Wheelan.
that alterations such as this can only be found by aligning the cancer genome back to the normal genome and looking for differences. “Steve’s programs do this and may find things we have been missing,” she says.

Salzberg and colleague Mihaela Pertea also have written a program to find mutations in the breast cancer-associated BRCA1 and BRCA2 genes. With only raw data from a gene sequencer, their program quickly tests a sample for any one of about 70 known mutations to these genes. “We’re trying to make this easier for people to do,” says Salzberg. “The software is very efficient, and it can be run on a standard desktop so that anyone with modest computing experience can do it.”

Personalized cancer medicine is only possible if clinicians can rapidly access and interpret the individual information on each patient’s cancer, and this work is proof-of-concept that it can be done. While the initial work was done for breast cancer mutations, Salzberg says his program, which contains a library of mutations that can be added to, was written so that it could be used to find any known mutation in essentially any cancer. “We are still a few years away, but it demonstrates that we can do this in the physician’s office,” says Salzberg. The cost—about $5000 to sequence a genome—may be the only major limiting factor, but he and other scientists say these costs are declining.

Helping Salzberg and Wheelan toward these personalized medicine goals is Alexander Szalay, an astrophysicist and acclaimed computer science visionary. Szalay, the director of the Johns Hopkins Institute for Data-Intensive Engineering and Science, designed new computer architecture that the Space Telescope Institute uses to measure the three-dimensional positioning in space of over 200 million galaxies. His technology is now being used to pour through huge amounts of data related to cancer DNA to draw clinically relevant conclusions. In fact, while Salzberg’s office is located on the Johns Hopkins medical campus, he has his computer servers in Szalay’s Physics department computing facility on the Homewood campus a few miles across town.

Szalay is developing algorithms and databases that store genetic information and can connect it to patient-specific cancer problems. It has the capability to store data on 14,000 individual patient genomes per year and tie them securely to patient records. His algorithms allow researchers to do in real time what would take a basic science laboratory a year to accomplish. Szalay’s technology allows them to quickly query information on large groups of cancer patients and find out what they have in common. For example, they could find similarities among patients who were treated for a particular cancer and relapsed. “These pieces are essential to being able to assess genetic information on tumors better and faster, and they are necessary to providing personalized therapies,” says Wheelan.

Salzberg is hoping to collaborate with Gary Rosner, the Kimmel Cancer Center’s...
director of quantitative sciences, to better understand how cancers spread. By comparing tumor samples from several sites of metastasis to samples of normal tissue, Salzberg hopes to quantify the accumulating genetic mutations and determine the order in which the tumors occurred, providing a schematic for how a particular cancer progressed. “Perhaps we can help cancer researchers get a better handle on the course of metastasis,” says Salzberg.

Salzberg perhaps most succinctly explains the value of the engineering and cancer researcher collaboration. Engineers are the technology experts, he says, and physicians and scientists are the disease experts. Both are needed to conquer difficult problems like cancer. “Cancer is complicated,” he says, “but together we might figure it out.”

**COMPUTER-ASSISTED INTERVENTIONS**

After working for 19 years as a research manager at IBM, engineer Russell Taylor became interested in the role of computers and robots in surgery and medicine. He recognized that the same combination of innovation, computers, and technology that revolutionized the electronics industry had the potential to do the same for health care. Taylor decided that if he wanted to pursue medical applications, he ought to be in the same place as his customers. He came to Johns Hopkins in 1995 and focused his efforts on building an engineering research laboratory that used computers, robots, and information-based technologies to help plan, carry out, and assess new treatments for a variety of diseases, including cancer. The concept earned him $33 million in seed funding from the National Science Foundation to begin the Center for Computer-Integrated Surgical Systems and Technology, which opened in 1997.

Taylor’s philosophy combines practical business sense with forward-thinking science. “Start with everything you know about the patient, including images, lab results, and clinical data, and add in what you know in general about people and diseases based on statistics and anatomy,” says Taylor. “Combine all of this to make a computer representation, and use it to plan an intervention. Then use computer-based technology to help a surgeon carry out this plan and to assess the results.”

His years in electronic manufacturing gave him the industry contacts and knowledge to develop and outfit a unique laboratory—one that could not only create innovative approaches for challenging medical problems, but carry them through from inception to production.

**COMPUTERS, ROBOTS, SENSORS, IMAGING DEVICES AND GUIDANCE SYSTEMS INTERFACE WITH CLINICIANS SO THEY MANEUVER INSIDE THE BODY WITHOUT OPENING PATIENTS UP.**

Wong wanted to develop a system that would store data from clinical trials in a way that the information did not just help measure the usefulness of potential new therapies being studied, but could also be queried at any time in the future to improve the care of all patients. They looked to the data archive of Alexander Szalay as the model. The system Szalay and team created not only stored data but also able to perform interactive, on-the-fly analyses. Wong, fellow Radiation Oncology physicist Todd McNutt, and Taylor envisioned a similar system that could be applied to radiation therapy.

“When we participate in a multicenter clinical trial, we send the data off, and it stays there,” says Wong. “We move on to the next trial and the next patient, and start from scratch.” They envisioned a system that stored data on all previous patients and used advanced computer technology to cull information and apply it to the planning and treatment of each individual patient. Instead of relying only on their specific patient or trial experiences, radiation oncologists could now use data from all those patients to improve the treatment of new patients.

Most adults make better decisions than children, largely because they have years of life experience to call upon—memories of things they’ve done; what worked, and what did not. In many ways, the system that Taylor, Wong, and McNutt have devised is simply a grander, technology-based form of what our brain helps us do everyday. Now, however, physicians not only benefit from their own experiences with patients but also with the experiences and results of countless physicians and patients, avoiding what does not work and zeroing in on what does.
SHE WAS WALKING down the steps at home when her leg suddenly gave way. Her mother, Clara, knew something was wrong when her doctor didn’t even ask for an x-ray. Instead the family was sent straight to Johns Hopkins Hospital, where they learned Carla had bone cancer known as osteosarcoma. To cure the cancer growing inside the femur bone in her leg, doctors would have to amputate her leg.

For anyone this would be difficult to accept, but for a vibrant young high school student like Carla, who loved to dance, it was unimaginable. Still Carla was brave. “The leg has to go,” she said.

Carla’s mother Clara was serving in the military and decided to take Carla to the Walter Reed National Military Medical Hospital. With the country at war, the military had become an expert in prosthetics. It turns out that one of the military’s collaborators in improving prosthetics was engineers at the Johns Hopkins Applied Physics Laboratory (APL).

In 2009, the APL was awarded a $30.4 million contract under the Defense Advanced Projects Agency Revolutionizing Prosthetics Program, an ambitious effort to provide the most advanced medical and rehabilitative technologies for military personnel injured in the line of duty. Among their projects is a next-generation mechanical arm that mimics the properties and sensory perception of the real thing.

Clara told the staff at Walter Reed, “I need my daughter to have what the soldiers have.”

Carla still had difficult challenges to face. The loss of Carla’s limb made her a visible representation of illness. When she returned to school she faced teasing by a few mean-spirited students. However, over time things began to change. With the help of her new, state-of-the-art prosthetic and the doctors at Walter Reed, Carla began to walk easily and fluidly, without pain.

The real turnaround, however, came the following summer when Carla decided to attend Amputee Coalition of America’s (ACA) youth camp. Carla remembers smiling when she arrived at the camp. “I realized I wasn’t the only one going through this. There were kids missing one leg, two legs, and arms. They were amazing people,” Carla says. “I wanted to be amazing, too.”

Carla rediscovered herself. “I found I could do anything I wanted. I could be the person I was before I got sick.” Carla, a beautiful young woman with bright eyes and a warm personality, is quick to smile, even when recounting the difficult details of her battle with cancer. “I learned I was normal,” she says. “I didn’t care what people thought about my leg anymore. I was wearing skirts and shorts. I felt like a million bucks.”

Since then, Carla has faced and beaten a recurrence of her cancer. She is a patient ambassador for the Kimmel Cancer Center, a volunteer at Walter Reed, and a counselor at the ACA camp. She graduated from the Community College in Baltimore County and has registered for the spring semester in Towson University in Maryland to pursue a career in veterinary medicine.

“When I look forward in life,” Carla says, “I see myself as a person who can take chances, who can become a leader, who can understand what people are going through, because I’ve been through a difficult situation. People with prosthetics should know they don’t have to feel limited in any way. They can run, dance, ride a bike, and wear heels,” says Carla. “I wanted to deal with cancer, to be a cancer survivor, and move on with my life. I’ll never forget what happened, but I won’t let it affect the person I become. Sometimes,” she says, “I forget I have a prosthetic.”
“Rare cases, a doctor may see every two years,” says Wong. “But now he or she can go back and look at certain attributes of prior similar patients and make a better informed treatment plan.” Keeping data allows care to more quickly reflect advances in science. “Let’s say there is a discovery in the future that completely changes how a cancer is staged. If that’s the case, then all of my previous study of that stage won’t apply anymore,” says Wong. “But, if you keep the data, when a new discovery happens, you simply go back to the original data and recalibrate it and make it useful again.”

They have piloted their concept, called Oncospace, in head and neck cancers which McNutt says are very geometrically complex and among the most difficult cancers for radiation physicists and oncologists to plan, often requiring 10 to 20 plan revisions. There is a lot of anatomy in the area of these tumors. Critical structures, such as the voice box and salivary glands, must be spared radiation to prevent harmful and unpleasant side effects to patients. In their new data-mining approach, the team analyzes the geometry of the patient and tumor. Then they go to a database of all patients who should have been as

and so their work is not supported by public funding. While the National Cancer Institute has encouraged their efforts, it will not fund it, so forward progress is often dependent on the ability to find private support.

In the operating room, Taylor also is using technology to improve treatment. Basically, Taylor says, they put a computer between the patient and the surgeon and use technology to enhance his or her capabilities, mainly by giving the surgeon more information. To do this, they engineer a variety of technologies. They use computers, robots, sensors, imaging devices, and guidance systems to interface with clinicians so that they can maneuver inside the body without opening patients up and still clearly see and precisely manipulate their anatomical targets.

With an impressive resume, which includes work on technology used in the da Vinci robotic surgical system for minimally-invasive surgery, Taylor is piloting new advanced technologies that can be used in laparoscopic surgery for liver cancer, kidney cancer, prostate cancer treatment, and other malignancies. Among his inventions are high-dexterity robotic devices that can, for example, get into a bone where a cancer has spread and clean out tumor cells. The snake-like device is deployed through a tiny hollow pipe that moves around the cavity. Other appliances, including water jets and brushes, can be used in conjunction to help remove cells. The void in the bone is then filled with a special cement to maintain bone strength and stave off treatment-related fractures. These nimble, image-guided robotic devices also are being explored for head and neck surgery where surgeons must maneuver with little visibility below the vocal cords and other areas.

Cancer surgeon Michael Choti was one of Taylor’s first collaborators. A recent project involving Choti, radiologist Emad Boctor, and others from the center uses ultrasound elastography to help Choti improve treatment for patients with advanced liver cancer. For many patients, Choti can avoid cutting these tumors out by using special devices to burn or ablate lesions in the liver. The problem for Choti and other surgeons is that there is no real quantitative measurement to let them know that the tumor, and an adequate margin around it, is completely destroyed. They must rely on visual observations and generalized time recommendations. Surgeons want—to heat just what they need to—no more, no less, so Choti and the other team members are piloting the elastography tool that acts as a gauge for the firmness of tissue being heated. “Cooked” tissue will be stiff, so the new technology allows surgeons to direct the right amount of heat to cancerous lesions.
and monitor the surrounding normal tissue to prevent damage.

Taylor and team also are working with Choti and other Johns Hopkins surgeons on improving technologies to advance minimally invasive surgery. These approaches require precise and clear image guidance because surgeons have to be able to see their target without actually opening the patient up. “Targeting and monitoring has been suboptimal and a major roadblock to advances,” says Choti. “Our goal is to do these procedures the best way they can be done, and our collaborations with engineers have been invaluable in making this happen,” says Choti. “It brings innovation to the bedside and helps to keep it cost effective.”

BIG SHINY OBJECT SYNDROME
 Radiation oncology is unique among other cancer-related specialties in that it is completely dependent upon technologically-advanced equipment, such as linear accelerators, to deliver the precisely targeted X-ray beams that cut through and destroy tumor cells. Patients hear advertisements about one machine or another, and they think if a hospital doesn’t have a particular one, they’re not practicing good medicine. In many instances, Wong says, the information is marketing driven, not fact-driven, and it is confusing patients. All too frequently claims of clinical benefit are made with no scientific evidence to back it up.

In this new age of medicine-driven marketing, it is Wong’s job to help Radiation Oncology and Molecular Radiation Sciences director Ted DeWeese determine which advanced technologies are needed to improve patient care and which are simply a product of aggressive advertising by industry and for profit health care practices. “Here with Dr. DeWeese, we do it right,” says Wong. “We don’t believe in purchasing big, expensive pieces of equipment simply because it’s the newest thing out there. The truth is many of the machines actually do the same thing. The only people really benefitting are the people making and selling them. We’ll explore these technologies because we want to be sure Hopkins tells people how to do it right,” says Wong.

Radiation treatment, Wong says, is in essence a form of minimally invasive surgery. Instead of scalpels, radiation oncologists use precisely targeted beams of radiation to cut through tissue and tumors. The main reason there is no scientific evidence to support many of the industry claims is that, for radiation oncology, there was no way to do the research. “There was no laboratory counterpart for what we do in the clinic,” says Wong. So, he called in Taylor to build a downsized version of a human machine for mice. It’s radiosurgery for mice. With unprecedented precision, Wong uses the machine to perform human-quality radiosurgery on mice so that he can have a realistic model to study what doctors do in treatment. “In radiation oncology, we didn’t have the means to study mechanisms in animals, and this machine helps us do that,” says Wong. The miniature machine allowed Wong’s medical collaborators to uncover the causes of—and how to avoid—radiation treatment-induced bone fractures. In radiation oncology there is nearly equal interest in how to destroy tumors as there is in how to prevent damage to normal tissue, so being able to study human therapies in animal models is paramount to developing more effective and safer ways to treat patients.

While fancy machines are often the focus of attention, Wong says, the biggest problem in radiation oncology often is not the treatment technology but rather the ability to characterize the tumor. “If I don’t know where the disease is, it doesn’t matter how great the equipment is, I can’t treat it,” says Wong. “People at Hopkins ask, ‘What is the problem? What is the solution?’” This, he says, is where the collaboration between engineers and Cancer Center experts comes into play. Cancer imaging experts like Martin Pomper are helping make cancers more visible, by engineering light-emitting pharmaceuticals that are specific to cancer cells to make them glow. “Now, I can see the cancer, and not just the more obvious tumor but other cells that may be hiding,” says Wong. Taylor is building robotic devices that integrate image guidance and combine technologies, such as ultrasound and CT, to provide clearer and more detailed pictures of tumors and anatomy.

“These types of advances are unique to Johns Hopkins,” says Wong, “and they are a direct result of the Kimmel Cancer Center and Engineering collaborations.”
IN THE NEWS
THE LATEST CANCER NEWS from the JOHNS HOPKINS KIMMEL CANCER CENTER

NOTEWORTHY

Pancreatic Cancer
A PATIENT AND HIS DOCTOR BALANCE HOPE AND TRUTH
In this book, pancreas cancer patient Michael J. Lippe and his Kimmel Cancer Center oncologist Dr. Dung T. Le alternate chapters. Lippe writes about the early signs that something was wrong; Le continues with a description of pancreatic cancer, its symptoms, and its treatments. Lippe further discusses his prognosis, the prospect of death, and how he began to cope, while Le explains the importance, for both doctor and patient, of balancing hope and truth. Lippe talks frankly about the toll the disease takes on his marriage and family, and Le offers a general picture of what most patients can expect with their illness. The book concludes with Lippe and Le’s reflections on their partnership in treating cancer, lessons they learned, and thoughts about the positive things that sometimes emerge from illness.

Pancreatic Cancer offers clear explanations of the disease, what people with the disease will feel physically and mentally, and the current treatments and future directions of research. The authors hope that their honest yet hopeful perspective will help all people with cancer and those who care about them.

NCI CHOOSES JOHNS HOPKINS TO CATALOG CANCER PROTEINS
The National Cancer Institute (NCI) selected Johns Hopkins as one of eight institutions to develop a catalog of proteins created by cancer cells. The information, which will be made available to other researchers, could be used to develop new ways to detect cancer and treat the disease.

The network, called the Clinical Proteomic Tumor Analysis Consortium, will leverage information already revealed about cancer genes through the Human Genome Project and The Cancer Genome Atlas network to predict proteins produced by tumors. Principal investigator, Daniel Chan, Ph.D., professor of pathology, oncology, radiology, and urology and director of Hopkins’ Biomarker Discovery Center, says that protein signatures can be used to spot cancer or its recurrence in patients and as potential targets for new therapies. The information can be combined with genetic information from patients to create a complete picture of cancer.

Chan says the Johns Hopkins team will focus on ovarian cancer and expects to receive $2 million annually for five years from the NCI.

NOW ON VIDEO
THE FINE PRINT OF CANCER SERIES TAKES YOU THROUGH THE PARTS OF THIS DISEASE THAT HAVE NOTHING TO DO WITH TREATMENT, BUT EVERYTHING TO DO WITH SURVIVAL.

CHEMO SCHOOL
CHEMO SCHOOL IS AN INTRODUCTION TO CHEMOTHERAPY AT THE JOHNS HOPKINS KIMMEL CANCER CENTER.

CHEMO SCHOOL IS DESIGNED TO TAKE THE FEAR OUT OF CHEMOTHERAPY FOR BOTH THE PATIENT AND THEIR CAREGIVERS.

FROM THEIR FIRST STEPS INTO THE CHEMOTHERAPY ROOM TO RECEIVING IVs, INFUSIONS OR PILLS, CHEMO SCHOOL WILL EDUCATE AND INFORM THE PATIENT WHO IS PRESCRIBED CHEMOTHERAPY.

PANCREATIC CANCER
IN THE PANC MD VIDEO SERIES JOHNS HOPKINS PANCREATIC CANCER EXPERTS DISCUSS MULTIDISCIPLINARY CARE.

READ
FORMER NPR BLOG – OUR CANCER – JOINS HOPKINS
JOIN LAURIE SINGER SIEVERS ON OUR CANCER, A BLOG FOR CAREGIVERS AND PATIENTS. SUBSCRIBE TO GET POST ALERTS AND JOIN IN THE DISCUSSION.

IF YOU HAVEN’T DONE SO ALREADY, SUBSCRIBE TO CANCER MATTERS, OUR CANCER CENTER BLOG.
INTERESTED IN WRITING ABOUT A CERTAIN TOPIC OR HAVE A STORY YOU’D LIKE TO SHARE ON OUR BLOG? PLEASE E-MAIL US AT WASTA@JHMI.EDU.

LISTEN
CANCER NEWS REVIEW – PODCAST
KEEP YOUR CANCER IQ CURRENT WITH KIMMEL CANCER CENTER DIRECTOR DR. BILL NELSON AS HE DISCUSSES THE TOP CANCER STORIES EACH MONTH.
PRETTY IN PINK
In honor of Breast Cancer Awareness month the iconic Johns Hopkins Dome was lit up in pink, a tradition which Hopkins began in 2009.

LEARN MORE ABOUT BREAST CANCER ON THE WEB
C-ANSWERS
Kimmel Cancer Center experts discuss breast cancer as part of our new video series C-Answers. Watch to get answers to commonly asked questions and get the latest information about advances in research, treatment, and clinical trials.

TOP DOCS MOONLIGHT AS GROCERY BAGGERS
Breast Cancer Program Directors Drs. Sara Sukumar and Vered Stearns served as guest grocery baggers at Safeway’s Boston Street, Md. location in support of the store’s annual breast cancer fund raising campaign. Since 2003, Safeway has donated more than $1 million to the Kimmel Cancer Center Breast Cancer Program.

PINK PICNIC
BJs Wholesale Club in Owings Mills, Md. hosted a “Pink Picnic” luncheon to celebrate breast cancer survival and honor those who offer hope and support to breast cancer patients and survivors. The event included talks by Kimmel Cancer Center Breast Cancer Program Director Dr. Vered Stearns.
NEW APPOINTMENTS AND ARRIVALS

Roisin M. Connolly, M.B., BCh, B.A.O., M.R.C.P.I., has joined the Breast Cancer program as an assistant professor of oncology. She graduated with first class honors from the Medical School in Trinity College, Dublin, Ireland where she received the Sir James Craig Memorial Prize for first place in Medicine. She also was awarded the prestigious Reuben Harvey Prize by the Royal College of Physicians in Ireland for first place nationally in Medicine, Surgery and Obstetrics. At the Kimmel Cancer Center, she will focus on drug development and clinical trial design, and will establish a continuity outpatient clinic where she will see patients with breast cancer.

Russell Hales, M.D., has joined the Department of Radiation Oncology and Molecular Radiation Sciences as an instructor. He is focusing on clinical and research efforts in thoracic malignancies, including developing a thoracic multidisciplinary clinic and participating in the development of the Lung Cancer Center of Excellence at Johns Hopkins Bayview. His research interests include novel radiation sensitizers in non-small cell lung cancer and characterization of organ motion in thoracic tumors.

Danijela Jelovac, M.D., was appointed an assistant professor of oncology. Danijela is a clinical investigator specializing in women’s cancers, most specifically, breast and female reproductive cancers. She has joined the Kimmel Cancer Center as an assistant professor of oncology and will treat patients primarily at our Bayview campus. She completed a postdoctoral research fellowship with aromatase inhibitor expert Angela Brodie, Ph.D, at the University of Maryland and recently finished her fellowship at the Kimmel Cancer Center, working with Dr. Deborah Armstrong and other members of our Breast Cancer Program.

Ronan J. Kelly, M.D., has joined the Upper Aerodigestive Program as an assistant professor of oncology. He was recruited from the National Cancer Institute (NCI) where he was a thoracic oncology clinical investigator, writing and directing a number of innovative investigator-initiated clinical trials. In addition to his work at NCI, Kelly served for two years as the Medical Director at Roche Pharmaceuticals in Ireland. At the Kimmel Cancer Center, he will continue his research in lung cancer and cancers of the thymus gland and tissue and begin researching esophageal cancer.

Jenny Kim, M.D., instructor in oncology, is a new member of the Genitourinary Cancer Program and will focus on developing a clinical research program, including personalized medicine strategies, for kidney and bladder cancers. Her research accomplishments include work with Dr. Brian Rini, an international expert on kidney cancer drug development.

Evan J. Lipson, M.D., will be working in cancer immunology as a new instructor in oncology. His long-term goal is to develop translational clinical strategies to treat melanoma, focusing on immunotherapies, including melanoma vaccines and immune-modulating monoclonal antibodies, and molecularly targeted agents. He was selected to be the Chief Fellow in 2010 and has spent the past two years training in clinical research in melanoma with Drs. William Sharfman and Suzanne Topalian.

Eric Raabe, M.D., Ph.D., an instructor in oncology in the Division of Pediatric Oncology, will work as a physician-scientist focusing on pediatric brain tumor research and treatment. After spending a year working in Africa as part of the Baylor International Pediatric AIDS Initiative, he came to Johns Hopkins as a pediatric oncology fellow. Working in the laboratory of Dr. Charles Eberhart in Neuropathology, Raabe successfully established a human neural stem cell system to create genetically accurate models of pediatric brain tumors. He will continue his research and will also work closely with Dr. Kenneth Cohen, Clinical Director of Pediatric Oncology and brain tumor expert.
Rachel Rau, M.D., is a new member of the Pediatric Oncology Program. A physician-scientist, she will focus on translational childhood leukemia research. She completed her residency and fellowship at Johns Hopkins and was selected as chief resident of the Hopkins pediatric residency program and chief fellow of the Hopkins/NIH pediatric oncology fellowship program. Rau has been conducting research in the laboratory of pediatric oncology leukemia expert Dr. Patrick Brown and will continue to study the unique biology of leukemias with the aim of identifying new therapeutic targets.

Zeshaan Rasheed, M.D., Ph.D., has joined the Gastro-intestinal Cancer Program as an assistant professor of oncology. He recently completed his medical oncology fellowship at the Kimmel Cancer Center and was recruited to develop a translational laboratory program focused on pancreatic cancer stem cells and their role in pancreatic cancer development and progression. His fellowship work in the laboratory of William Matsui last year earned him recognition as the first and only recipient of the new AACR “Pathway to Leadership” award in pancreatic cancer in 2010. In addition, he was named a Viragh Clinical Research Scholar and will continue to participate in the Pancreatic Multidisciplinary Clinic, the outpatient clinic and inpatient service.

Kristin Redmond, M.D., M.P.H., instructor in oncology, has joined the Department of Radiation Oncology and Molecular Radiation Sciences. She is a member of the Stereotactic Spine Program and focuses on diseases of the spine and central nervous system.

Dipali Sharma, Ph.D., associate professor of oncology, is a new member of our Breast Cancer Program. She is a leading translational scientist in the field of obesity and cancer research and will lead the Center’s research efforts to further understand the connection between obesity and cancer and develop prevention strategies. Her work focuses on the molecular and hormonal mechanisms underlying the obesity-cancer connection, and she has established important links between adipocytokines (cell-to-cell signaling proteins secreted by body fat) and cancer progression.

Thomas Smith, an international leader in the field of palliative care, has been named the director of Palliative Care for Johns Hopkins Medicine and the inaugural Harry J. Duffey Family Professor of Palliative Care in the Department of Oncology. He will lead palliative care efforts throughout Johns Hopkins, including the Kimmel Cancer Center. His research focuses on neuropathic pain, care at the end of life, and bending the cost curve in patients with life-limiting conditions.

Chenguang Wang, Ph.D., has been appointed an assistant professor of oncology in the Division of Biostatistics and Bioinformatics. As a statistician, he has a strong background in oncologic clinical research, particularly in clinical trials and observational studies. His current research focuses on the analysis of longitudinal data subject to “missingness,” or where there are missing values in data. Before joining Johns Hopkins and completing his doctorate, he was a statistician with the Children’s Oncology Group’s (COG) Statistics and Data Center at the University of Florida and the Center for Devices and Radiological Health at the U.S. Food and Drug Administration.
**HONORS AND AWARDS**

Kimmel Cancer Center Deputy Director and leading epigenetics expert **Stephen Baylin, M.D.**, received the American Cancer Society’s highest recognition, the Medal of Honor Award for his basic research and pioneering body of work in cancer epigenetics.

Pediatric oncologist **Patrick Brown, M.D.**, received a four-year, $720,000 grant from the American Cancer Society for his research exploring epigenetic therapies for childhood leukemia.

Kimmel Cancer Center nurse **Laurie Bryant, R.N.**, was named a 2011 finalist for the Daily Record’s Health Care Heroes Award. She was recognized as a mentor to undergraduate students interested in medicine, medical students, interns and residents, teaching them clinically and modeling the important role of nurses in defining problems and recommending care. She has also started one of the most successful unit-based volunteer programs at Johns Hopkins.

The Society of Neuro-Oncology honored **Peter Burger, M.D.**, with its Lifetime Achievement Award recognizing his more than 35 years of contributions to the field of neuro-oncology.

**Michael Carducci, M.D.**, received the Michaele Christian Oncology Development Award in honor of his contribution to the development of novel agents for cancer therapy.

**Andrew Ewald, Ph.D.**, received the American Association of Anatomists Morphological Sciences Award and will present an award lecture at the group’s annual meeting. The award recognizes Ewald’s advances in the understanding of the cellular and molecular basis of the growth, remodeling, and cancerous transformation of epithelial tissues, cells that cover the surface of virtually every organ and structure in the body.

**Kimmel Cancer Center Translational Research Director and pancreas cancer expert Elizabeth Jaffee, M.D., Ph.D.**, appeared on the Dr. Oz show to discuss advances in pancreas cancer research and her vaccine studies.

The Department of Defense Congressional Directed Medical Research Programs presented **Robert Kurman, M.D.**, with a $9.5 million Ovarian Cancer Research Program Consortium Award. The Consortium is a major multi-institutional collaborative research effort aimed at identifying and characterizing early cellular changes associated with ovarian cancer.

**Lana De Souza Lawrence, M.D.**, received the ASCO Conquer Cancer Foundation Breast Cancer Symposium Merit Award. The award, which includes a $25,000 grant, recognizes researchers’ contributions to progress against breast cancer, was given to De Souza Lawrence for her research on triple-negative breast cancer.

**Robert Miller, M.D.**, and **Julie Brahmer, M.D.**, were recipients of the 2011 American Society of Clinical Oncology (ASCO) Statesman Award. The award recognizes ASCO members for extraordinary volunteer service, dedication and commitment.

**Barry Nelkin, Ph.D.**, was awarded a $1.2 million grant from the American Cancer Society for his research on the development, genetic characterization, and application of new scientific models for medullary thyroid cancer.

Kimmel Cancer Center director **William Nelson, M.D., Ph.D.**, was one of only two investigators to receive the A. David Mazzone-Prostate Cancer Foundation Challenge Award aimed at accelerating scientific discovery and new treatments for prostate cancer. Nelson was recognized for his innovative research on the reversal of gene silencing. The award includes a five-year, $5 million research grant.

**Martin Pomper, M.D., Ph.D.**, was named the William R. Brody Professor of Radiology. Pomper is the inaugural recipient of this professorship, designated for a radiologist physician scientist who excels in translational innovation in imaging.

Pediatric Oncology clinician-scientist **Eric Raabe, M.D., Ph.D.**, received a three-year, $330,000 grant from the St. Baldrick’s Foundation to support his research of Pediatric brain tumors.
Richard Roden, Ph.D., received the V Foundation Translational Research Grant which includes a three-year, $600,000 grant. The grant is aimed at transforming basic scientific discoveries into clinical applications, such as new diagnostics and treatments.

Charles M. Rudin, M.D., Ph.D., received the 2011 Caring for Carcinoid Foundation-AACR Grants for Carcinoid Tumor and Pancreatic Neuroendocrine Tumor Research. The two-year, $250,000 grant will support Rudin’s research of novel therapeutic approaches for carcinoid tumors and pancreatic neuroendocrine tumors.

Lillie Shockney, R.N., B.S., M.A.S., received the Amoena Corp. award for “Outstanding Contribution to the Breast Center Industry. Amoena Corp. is a women’s wellness company focused on helping women following breast surgery. Shockney also was inducted into the Nu Beta Chapter of the Sigma Theta Tau International Honor Society of Nursing. She was named editor-in-chief of the Journal of Oncology Navigation and Survivorship, a new journal for nurses implementing strategies in patient navigation and survivorship care.

Kimmel Cancer Center Senior Director of Development Ellen Stifler was named a member of the Senior Management Team for the Fund for Johns Hopkins Medicine.

Sara Sukumar, Ph.D., won a BioMaryland LIFE Prize, which includes a $50,000 award, for her discovery of methylated gene biomarkers that may better predict how patients whose breast cancers are estrogen receptor (ER) negative will respond to various treatments and potentially if they are at risk for future recurrences.

The National Institutes of Health Center for Scientific Review appointed Connie Trimble, M.D., to a four-year term on its Cancer Immunopathology and Immunotherapy Study Section. Trimble was selected based on her achievements in cancer immunology and will review and make recommendations on grant applications submitted to the NIH and survey the state of immunology research.

Victor Velculescu, M.D., Ph.D., received a Paul Marks Prize for Cancer Research. The award recognizes young investigators who have become leaders in cancer research through significant contributions to the understanding of cancer.

The V Foundation awarded Vasan Yegnasubramanian, M.D., Ph.D., its Martin D. Abeloff, M.D., Scholar Award. The award, which includes a two-year $200,000 grant, supports his research to identify DNA-based biomarkers that can help risk-stratify men with prostate cancer and aid in the clinical decision-making.

The Brupbacher Foundation in Zurich presented Bert Vogelstein, M.D., with its Charles Rodolphe Brupbacher Prize for Cancer Research. The prize is given biennially to a scientist “internationally acknowledged for meritorious achievements in the field of fundamental research.” Vogelstein was selected for his pioneering research of colon cancer development. Vogelstein also has been named one of the Johns Hopkins University’s 17 inaugural Gilman Scholars. The newly created designation, named for the University’s visionary first President Daniel Coit Gilman, recognizes individuals who are exemplars of the highest ideals of the university, demonstrated through a record of distinguished research, artistic and creative activity, teaching and service.

The V Foundation awarded Vasan Yegnasubramanian, M.D., Ph.D., its Martin D. Abeloff, M.D., Scholar Award. The award, which includes a two-year $200,000 grant, supports his research to identify DNA-based biomarkers that can help risk-stratify men with prostate cancer and aid in the clinical decision-making.
FINGERPRINTING CANCER
COMMONWEALTH FOUNDATION

GIFT CREATES NEW CENTER FOR PERSONALIZED CANCER MEDICINE

A $30 million gift to Johns Hopkins from the Commonwealth Foundation for Cancer Research will push the pace of developing targeted therapies based on an individual cancer patient’s genetic “fingerprint” by establishing a Center for Personalized Cancer Medicine.

The gift will be used to support innovative research and new technologies that pinpoint the unique cellular characteristics of each patient’s cancer. Targeting these alterations will improve treatment outcomes, thwart cancers before they develop and slash the costs of new drug discovery.

Johns Hopkins scientists have led the field in deciphering the genetic landscape of cancer and uncovering key genetic mutations and pathways. This work has had immediate application to patient care. For instance, a test called PARE or personalized analysis of rearranged ends, not only detects cancer but also can tell if a therapy is working by measuring, in real time, the amount of cancer DNA in the bloodstream. The personalized test can tell if a person is cured with surgery or if there are cancer cells left behind and will require additional treatment.

“This is a watershed moment,” says Kimmel Cancer Center Director William G. Nelson. “With this gift from the Commonwealth Foundation, we’re poised to change cancer medicine.”

Funds for the new Center will initially support three pilot projects over four years focused on genetic research from changes to the genes themselves to changes to the DNA inside genes, known as epigenetics, are aimed at better diagnosis, treatment and even prevention. Investigators will examine which genomic and epigenomic determinants impact responses to treatment in patients; study individualized early detection of human cancers by developing clinical tests that use genetic and epigenetic changes as markers for early diagnosis; and individualized immunotherapies using the specific genetic makeup of each patient’s tumor.

The Center will include cancer experts from many disciplines at Johns Hopkins such as oncology, engineering, public health and surgery. Nelson indicated that a hallmark of Johns Hopkins is collaboration across specialties. A recent gift to Johns Hopkins University to support an individualized health initiative at Malone Hall will enhance efforts in the Center for Personalized Cancer Medicine.

“The convergence of brilliant scientific minds with this significant gift has brought us to a point where we can alter the course of cancer in ways we could only imaging just a decade ago,” says Nelson.
ONE NIGHT, ONE SHOW, ONE CAUSE

The Baltimore Sound Stage was the site of the annual benefit concert hosted by PRS Guitars and featured an amazing evening of entertainment, including alternative rock band Vertical Horizon, Davy Knowles of Back Door Slam, Dave Weiner of the Steve Vai Band, blues guitarist Donna Grantis, the Paul Reed Smith Band, and our own Kimmel Cancer Center director William Nelson. Dr. Nelson traded his lab coat for a guitar and appeared on stage as a guest artist. Six PRS guitars, autographed by the Baltimore Ravens and other celebrities, were given as door prizes to a few lucky attendees. Several more guitars, embellished with original designs by local artists, were auctioned at the event.

One Cause is the flagship benefit concert of PRS Guitars. Since 2000, PRS Guitars has raised more than $2 million for the Kimmel Cancer Center’s Living with Cancer Resource Program, which provides free supportive care programming and education to patients and families.

BREAST CANCER SUPPORT

Susan G. Komen for the Cure Maryland Executive Director Robin Prothro presented Antonio Wolff, M.D., with a $75,000 check to support breast cancer clinical trials.

BOBBIE BURNETT’S ANGELS “MAKING A DIFFERENCE”

Bobbie Burnett and the Caring Collection were recently featured in an NBC Nightly News segment called “Making a Difference”. Bobbie and her dedicated group of volunteers, who have been making and selling stained glass angels since 1982, were recognized for their work in bringing hope and comfort to cancer patients and families around the world, and for donating proceeds of nearly $1 million to the Kimmel Cancer Center and other Maryland institutions. Learn more about the Caring Collection at www.caringcollection.org.

THE FRIENDS OF SKIP VIRAGH HELPING FIGHT PANCREAS CANCER

Carl Verboncoeur considers some of the best times of his life the years he worked side by side with Skip Viragh at Rydex Investments. He still clearly recalls the Rydex founder A. P. “Skip” Viragh, Jr’s hard fought battle with pancreas cancer, a disease that ultimately claimed Viragh’s life. Verboncoeur, who once served as Rydex CEO, says he wanted to do something to honor his boss and friend and to give back to Johns Hopkins whose researchers and clinicians work so hard to fight the disease. He and his wife Lynn started the Friends of Skip Viragh Memorial Fund and are supporting the studies of leading cancer pancreas experts Elizabeth Jaffee and Daniel Laheru. “Johns Hopkins is on the forefront of pancreas cancer research and care,” says Laheru, “and generosity like this gives us the means to explore novel therapies that may improve the lives of patients fighting this disease.”

SIDNEY KIMMEL’S COMPANY MAKES MULTIMILLION GIFT TO KIMMEL CANCER CENTER

The Jones Group honored Sidney Kimmel, its Founder and Chairman, with a $6 million donation to the Kimmel Cancer Center to mark the 40th anniversary of his founding the company.

In recognition of Mr. Kimmel’s accomplishments and contributions to the company, including his many years of outstanding leadership, the Board of Directors announced that the company will donate $8 million to support his many charitable initiatives, including a $6 million donation to the Kimmel Cancer Center.
PHILANTHROPY

JUST suppose
A CAMPAIGN TO CURE CHILDHOOD CANCER

HELPING US TURN RESEARCH INTO RESULTS—AND RESULTS INTO REALITY

Cancer strikes more than 12,000 children and teens each year. While pediatric cancers are rare, they claim the lives of more children than any other disease. But, there is good news. At Johns Hopkins, we understand the urgency that pediatric cancers demand. The Pediatric Oncology Program of the Johns Hopkins Kimmel Cancer Center is focused entirely on the research and treatment of childhood cancers. As one of the leading Cancer Centers in the United States, we are at the forefront of developing new treatments and designing clinical trials. With world-class expertise, a culture of cross-disciplinary collaboration and a proven track record of successfully bringing therapies from the laboratory to patients, our researchers are leading the field in developing treatments and cures for childhood cancer.

“We’re the ones leading the way—finding the genes, studying what they do in terms of the biology of a particular pediatric cancer, and developing molecularly targeted therapy against it,” says Donald Small, M.D, Ph.D, Kyle Haydock Professor and Director of Pediatric Oncology.

For the first time in the history of cancer medicine, the technology exists to quickly decipher the cellular causes of every cancer. Kimmel Cancer Center researchers have pioneered the science that has led us here and were the first to crack the genetic code of a pediatric cancer. Through collaborations with Johns Hopkins engineers, we are developing the technologies and methods needed to manage the immense amounts of data this research generates and apply it to cancer medicine. What we learn, will allow us to target the very biological mechanisms that cause a cancer to grow and spread. With these discoveries, we can begin to alter the course of pediatric cancers in ways we could only image a decade ago. There is much to be hopeful about.

Our goal is to create a $30 million research fund to ensure that these promising initiatives have the steady support they need to result in monumental leaps in knowledge, and ultimately cures for all children with cancer.

We could:
• find cures for those cancers we currently cannot cure.
• improve therapies, develop targeted therapies that kill the cancer without harming the child.
• use biology and laboratory discoveries to improve clinical trials.
• study the short- and long-term consequences of cancer and cancer therapy on the child to improve the quality of life during and after treatment.

Just suppose you could help a child with cancer. You can. Learn more at www.HopkinsMedicine.org/KidsCancer

GO TO www.HopkinsMedicine.org/KidsCancer TO LEARN MORE ABOUT JOHNS HOPKINS PEDIATRIC ONCOLOGY.
SWIM ACROSS AMERICA BALTIMORE
The Baltimore swim held September 18 had more than 600 swimmers and raised more than $525,000 to support the Swim Across America (SAA) Laboratory at the Kimmel Cancer Center. The event was held at the Meadowbrook Aquatic and Fitness Center in Baltimore and included Olympians Tara Kirk, Wendy Weil Weinberg, Brenda Borgh Bartlett, Craig Beardsley, Janel Jorgensen, and Theresa Andrews. Despite the open water swim relocating to the pool because of storm runoff, the event was a huge success. Money raised will support cutting edge cancer research in the SAA Laboratory, directed by Luis Diaz, M.D., including a study examining the use of circulating tumor DNA to detect and monitor more than a dozen types of cancer.

Take a virtual tour of the Swim Across American Laboratory at www.hopkinskimmelcancercenter.org

PANCREAS CANCER RESEARCHER NAMED EVERETT AND MARJORIE KOVLER PROFESSOR
Scott E. Kern, M.D., was named as the inaugural Everett and Marjorie Kovler Professor of Pancreas Cancer Research. Kern, professor of oncology, is co-director of the Kimmel Cancer Center Gastrointestinal Cancer Program. With more than 20,000 journal citations, his pioneering studies of pancreas cancer are widely recognized. His research is the basis of a number of U.S. patents and novel and ongoing therapeutic trials for pancreas cancer at the Kimmel Cancer Center and other cancer centers.

The Kovler Professorship was established by the Blum-Kovler Foundation and foundation Chairman Peter Kovler. It is believed to be the first professorship endowed specifically for pancreas cancer research. “Pancreas cancer does not receive the attention, financially or scientifically, that it should,” said Peter Kovler, whose mother Marjorie Kovler, died of pancreas cancer in 1970 at just 49. The Professorship is named for and memorializes her and his father Everett Kovler. He chose Johns Hopkins, he said, because of Scott Kern and the dedication and excellence of his scientific team. “If Hopkins perceives pancreas cancer as important, then others might follow, and pancreas cancer research might become a scientific priority,” says Kovler.

“Scott is a research-oriented pathologist, bringing together molecular biology and pathology to fight pancreas cancer,” says William G. Nelson, M.D., Ph.D., Director of the Kimmel Cancer Center. “We hope this generous support from the Kovler family will mark the beginning of the end of pancreas cancer.”

AVON WALK
The 2011 Avon Walk, held in Washington, D.C., had 2,200 participants and raised more than $5 million to support breast cancer research. The Kimmel Cancer Center was one of nine organizations awarded a grant. Our Avon Breast Center, designated an Avon Comprehensive Breast Cancer Care Center of Excellence, received $750,000 to support breast cancer research and access to care programs.

ONLINE OPTIONS
WWW.HOPKINSKIMMELCANCERCENTER.ORG
HOW CAN YOU HELP? SEE HOW FINANCIAL CONTRIBUTIONS CAN BE EASILY, AND SECURELY, APPLIED. GO ONLINE FOR MORE INFORMATION.
PHILANTHROPY

RED CARD CANCER & DC UNITED BRING SOCCER CLINIC TO BALTIMORE

Over 150 children from Baltimore City Public Schools attended a Red Card Cancer soccer clinic hosted by Baltimore City Council President Jack Young and D.C. United, raising awareness about the benefits of a healthy lifestyle and exercise.

Kimmel Cancer Center Director William Nelson with D.C. United players, Santino Quaranta, Clyde Simms, Perry Kitchen, Brandon Barklage, Joseph Ngwenya took the field to run drills with the children assembled from public schools all over Baltimore City. In addition to the professional players from D.C. United, collegiate players from Loyola University and the University of Notre Dame of Maryland also assisted at the clinic.

“We’re proud that Red Card Cancer is teaming up with DC United during its Community Soccer Clinic right here in our home town of Baltimore to raise awareness about cancer so that together we can kick cancer out of the lives of everyone,” said Nelson.

Learn more at www.redcardcancer.org

PEDIATRIC CANCER UPDATE

Each year, Giant associates and customers join together to fight pediatric cancer through its Triple Winner Program. The program has raised more than $4.75 million for pediatric cancer research at the Kimmel Cancer Center.

Triple Winner is a scratch card game, and every $1 dollar donation helps fight kid’s cancer and provides participants the chance to win a free product, gift card, or cash prize up to $10,000.

ST. BALDRICK’S FOUNDATION

Pediatric Oncology clinician-scientist Eric Raabe, M.D., Ph.D., was named a St. Baldrick’s Pediatric Neuro-oncology Fellow receiving a three-year grant totaling $330,000 to support his work on pediatric brain tumors.

The award was given by the St. Baldrick’s Foundation, a volunteer-driven charity committed to funding the most promising research to find cures for childhood cancers and give survivors long and healthy lives.

HYUNDAI HOPE ON WHEELS DONATES

Baltimore Area Hyundai Dealers and Hyundai Hope on Wheels selected David Loeb, M.D., Ph.D., to receive the Hope Grant, a $100,000 award to support his sarcoma research. Heather Symons, M.D., was named a Hyundai Scholar and received a $60,000 award to support her research of novel immunotherapies for patients with high-risk hematologic and solid tumor malignancies.

Hyundai Hope on Wheels is the united effort of Hyundai Motor America and its more than 800 dealers across the U.S. to raise awareness about childhood cancer and to celebrate the lives of children battling the disease.
Your own vision for the future can bring a brighter tomorrow to cancer patients and their families. Your gifts to the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins will help ensure that these individuals will benefit from progress in cancer research, treatment, and education.

The Kimmel Cancer Center provides both the most advanced, compassionate treatment and the world-class research – translated to the bedside – that will ultimately defeat cancer.

Outright gifts of cash or appreciated securities are always welcome, and may bring significant tax advantages to you.

Planned gifts – such as charitable trusts – provide income to you for life, as well as considerable tax benefits, while helping to ensure the continuing leadership of the Kimmel Cancer Center at Johns Hopkins.

A bequest to the Kimmel Cancer Center in your will ensures that your vision will be carried out, and may also reduce the estate tax liability of your heirs.

For more information, please contact: Christine A. Lambert, Esq. Johns Hopkins Office of Gift Planning 800-548-1268 or 410-516-7954 e-mail: giftplanning@jhu.edu or visit: www.plannedgifts.org/jhu/

A MAN HAS MADE AT LEAST A START ON DISCOVERING THE MEANING OF HUMAN LIFE WHEN HE PLANTS SHADE TREES UNDER, WHICH HE KNOWS FULL WELL HE WILL NEVER SIT.

— David Elton Trueblood
For additional copies of this publication or further information about the Kimmel Cancer Center, please call (410) 955-1287 or email mehlva@jhmi.edu