Over a dozen years ago, out of the laboratory of Elizabeth Jaffee, M.D., came an unprecedented development that promised to dramatically change the prognosis of pancreatic cancer, one of the most aggressive and deadly cancers known to man.

Jaffee, a leading cancer immunology and pancreatic cancer expert, developed a pancreatic cancer vaccine that supercharges the immune system, turning immune cells typically tolerant of cancer into “fighter cells” that seek and destroy pancreatic cancer cells throughout the body. Fourteen patients with pancreatic cancer who had undergone surgery to remove their tumors but were at risk of recurrence received the experimental vaccine in the early 90s. Three are alive today and remain cancer-free. Considering the high rate of recurrence typical among patients with pancreatic cancer who undergo surgery, these early vaccine results represent a remarkable breakthrough.

Equally notable is the phenomenal growth of the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins pancreatic cancer program over the past decade, largely propelled by Jaffee’s significant and evolving achievements in immunotherapy. The

(continued on page 4)
The Hopkins Difference

Receiving a diagnosis of pancreatic cancer is scary for patients and their families, but at Johns Hopkins, we can provide hope. We offer patients the most convenient and comprehensive expert assessment of their diagnosis possible. Plus, we provide cutting-edge management options—including the possibility of enrolling in clinical trials that employ promising experimental therapies. We call it the Hopkins difference.

Comprehensive assessment by global experts

The Pancreatic Multidisciplinary Cancer Clinic at Johns Hopkins was born out of the desire to create a personalized, convenient, comprehensive and thoughtful analysis of each patient’s diagnosis and treatment plan. Oftentimes, patients who suspect they have pancreatic cancer must endure multiple visits with various physicians over several days before receiving a diagnosis and learning about their treatment options. At our multidisciplinary pancreatic clinic, we are committed to a single-day comprehensive evaluation of each patient by some of the most renowned pancreatic cancer clinicians and specialists in the country. Each patient’s case is presented before 20 to 50 members of the pancreatic cancer team, including oncologists who specialize in surgery, radiation therapy and immunotherapy.

“One of the benefits of our clinic is that it really is a one-stop shop. Within one or two days, patients can get a comprehensive evaluation from some of the top experts in the world,” says Joseph Herman, M.D., co-director of the Pancreatic Multidisciplinary Cancer Clinic.

After specialists create a consensus plan, they meet with the patient and family to present a clear diagnosis and management options.

“We really educate patients on their options and side effects. And instead of us saying, ‘This is what the standard of care is,’ we say, ‘Based on the standard of care, our expertise and your situation, here’s what we think.’ We also provide alternate choices. After patients are thoroughly educated about their options, we ask them what they prefer, what they want,” Herman says.

Cutting-edge radiation options

At Johns Hopkins, our emphasis on translational research means that we make every attempt to bring new breakthrough treatments to our patients as soon as scientific methods demonstrate their safety and potential to improve patient outcomes.

Radiation techniques serve as a prime example. Stereotactic body radiation therapy uses narrow beams of radiation
coming from different angles to target the tumor and spare surrounding normal tissue. It is a newer, experimental form of radiation that shortens the course of radiation therapy from weeks to days, does not require concurrent chemotherapy and has, to date, resulted in less toxicity than traditional radiation. “We’ve treated over 100 patients with this new modality, which can be delivered in five days as opposed to five or six weeks. Our results are very exciting,” Herman says.

Other novel forms of radiation utilized by Johns Hopkins expert radiation oncologists include intraoperative radiation, which delivers radiation directly to the site of the tumor during surgery, and the NanoKnife, which applies electrical pulses to radiate the tumor while sparing surrounding healthy cell tissue.

Just as our radiation oncologists utilize the most innovative techniques available for the management of pancreatic cancer, so do our surgeons. In fact, Johns Hopkins’ surgeons regularly operate on challenging, complicated pancreatic tumors that involve complex vascular resection and reconstruction—with outcomes similar to surgical procedures involving far less invasive tumors.

The Whipple procedure, one of a few surgical options available for select pancreatic cancer patients, was perfected at Johns Hopkins by John Cameron, M.D. He has performed more Whipple procedures than any other surgeon in the world and has applied his expertise to train other Johns Hopkins surgeons on the operation. The Whipple, which takes about six hours, involves the removal of the head of the pancreas, most of the duodenum—a part of the small intestine, a portion of the bile duct, the gallbladder, associated lymph nodes and, in some cases, the entire duodenum and a portion of the stomach.

“Data show these complicated procedures are best done at high-volume institutions. We are the busiest pancreatic cancer center in the country,” says Christopher Wolfgang, M.D., Ph.D., director of the pancreatic surgery section and co-director of the Pancreatic Multidisciplinary Cancer Clinic at Johns Hopkins. “We have the most experience, and probably the biggest concentration of clinicians and scientists focused on this disease.”

It’s the combination of clinicians and scientists working in tandem that makes Johns Hopkins different from most institutions that treat pancreatic cancer. “We can take cutting-edge laboratory research, at the right stage, and translate it into clinical trials. We’re looking at genetics, pancreatic cancer biology and early detection. What will make survival rates better is early detection followed by better treatments,” Wolfgang says.
New Research
(continued from page 1)

vaccine—which remains under investigation as researchers continue to probe its efficacy alone and in combination with other therapies—has garnered worldwide attention and helped attract the best and brightest young clinician-scientists to the pancreatic cancer team at Johns Hopkins.

A gift for growing the vision
Critical to furthering cutting-edge translational pancreatic cancer research and the best patient care possible is the generous gift of $20 million by Albert P. “Skip” Viragh Jr., a mutual fund leader in Maryland and patient with pancreatic cancer treated at Johns Hopkins. Viragh succumbed to pancreatic cancer at the age of 62. But with his unprecedented contribution to the Johns Hopkins Kimmel Cancer Center in 2009 earmarked expressly for pancreatic cancer, Viragh’s legacy continues to make an enormous impact through the work of scientists and clinicians at the Skip Viragh Center for Pancreas Cancer Clinical Research and Patient Care, co-directed by Jaffe and medical oncologist Daniel Laheru, M.D.

“The gift has allowed us to expand from a small, translational group of clinician-scientists to a large group with the ability to recruit the best scientists as faculty. It has also allowed us to start novel clinical research. We’re accelerating the delivery of innovative techniques to patients in ways we couldn’t have without the center, and we’ve tripled the number of patients we see in a week in our Pancreatic Multidisciplinary Cancer Clinic from four to six patients to 14 to 16,” Jaffe says.

Co-directors’ synergy sets a positive tone
While the generous donation has made the center’s development and growth possible, it was inspired by Jaffe and those who have followed her lead, principally Laheru.

A native of Utah, Laheru had every intention of returning to his home state upon completing his clinical fellowship in medical oncology under Jaffe in 2001. But her mentorship changed his sentiments about the future.

“I was completely overwhelmed with Liz’s passion and vision of how immunotherapy can be applied to pancreatic cancer. She was one of the first people to understand the complexities between the two,” Laheru recalls. “She really helped define my professional career for me at Johns Hopkins: to help find new treatments for pancreatic cancer.”

The positioning of their offices, adjacent to one another, offers ample opportunities for collaboration between the two co-directors. It’s also a tangible representation of their working relationship and, by extension, those of other faculty members. “There are no egos allowed in this group. We’re all here to fight this horrendous disease,” says Jaffe.

Cultivating the next generation of pancreatic cancer clinician-scientists
This philosophy extends to the emerging scientists and clinicians who have joined Jaffe and Laheru in their battle against pancreatic cancer. The unprecedented immunotherapy research conducted by Jaffe’s laboratory has drawn talented, motivated young researchers to the center. The Viragh gift has made it possible to hire them, and they follow in the footsteps of Jaffe and Laheru but make their own mark, too.

“We hire top talent and then let them go,” Laheru says. “We’ve encouraged them to make their own observations. This is the fun of having talented young faculty members. They’re not just following conventional wisdom; they’re thinking about how they, too, can make an impact. It’s among our proudest moments to see young scientists make original discoveries.” (See “Young Investigators” on page 6.)

Initially, Laheru wasn’t convinced there was a place for him at Johns Hopkins post-fellowship. “I thought Liz could do it all. But she said to me, ‘You have to understand. I cannot do everything here. I need someone on the clinical side to translate our laboratory ideas and tell us what we should focus on,’” he says.

Now, some 14 years later, Jaffe and Laheru continue to maintain a solid working relationship. Together, their leadership serves as an umbrella for exemplary clinical care and research within the center. “We design clinical trials together. We work together on trials. He comes back from the clinic with observations. It’s not like I’m sitting in the lab and he’s in the clinic,” Jaffe says.
Cherrie’s Inner Strength
An Unimaginable Story of Medicine, Attitude and Perseverance

It’s mid-morning at the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, and a dozen or so patients occupy the Outpatient Clinic’s chemotherapy bays. Some doze, and others sit quietly with loved ones who’ve come to help them pass the time.

Then, in walks Cherrie Lavine. She’s dressed in fitted jeans and shiny black boots. A splash of makeup graces her bright, youthful face. If you didn’t know better, you’d assume she was there to keep a friend or family member company, or that she’d just begun her journey with cancer and the disease hadn’t yet affected her. Either assumption would be incorrect.

Lavine, just 46 years old, has been battling cancer for six years. In 2007, she developed breast cancer and underwent a bilateral mastectomy in Virginia, where she currently resides. In 2011, cancer struck Lavine again. This time, it was pancreatic cancer. Her oncologist in Virginia told her there was nothing he could do for her. “He totally gave up on me,” Lavine says. But she didn’t give up on herself.

“I wiped away the tears, got on the phone and called Johns Hopkins,” she says.

Shortly afterwards, Lavine met with Daniel Laheru, M.D., co-director of the Skip Viragh Center for Pancreas Cancer Clinical Research and Patient Care. She was weak and had lost a significant amount of weight. Nonetheless, Lavine’s condition didn’t seem to faze Laheru.

“I did not see a loss of hope in his face. He has held my hand all the way through,” Lavine says.

She began a two-year period of chemotherapy treatments replete with side effects, including fatigue and hair loss. “With chemotherapy, some days you have down days, but I wanted people to be able to look at me and say, ‘If she can do it, I can, too.’ That’s how I carry myself every day,” Lavine says. “You’ve got to have that inner strength to continue.”

Lavine’s unwavering positive attitude has proven to be critical. Shortly after completing the two-year chemotherapy regimen for her advanced pancreatic cancer that had spread to her liver, Laheru noted the disease to be “remarkably, unusually, stable.” Then, just months later, Lavine learned her odyssey with cancer wasn’t over yet.

A routine follow-up surveillance scan showed another tumor. This time, it was ovarian cancer. Lavine subsequently learned that the standard chemotherapy she had been receiving for her pancreatic cancer was probably responsible for curbing the growth of the ovarian tumor, which Laheru believes had been present for some time. When she stopped receiving treatment for pancreatic cancer, the ovarian tumor began to grow unchecked.

Once again, Lavine was undeterred. When she learned that her ovaries might have to be removed—a possibility that did come to fruition—she didn’t balk. “I said, ‘Listen. If they have to go, they have to go.’”

Following this most recent surgery, to ensure no tumor cells were left behind, Lavine underwent stereotactic body radiotherapy, a form of radiation therapy that uses narrow beams of radiation coming from different angles to very precisely target tumors without harming surrounding normal tissue. “They got everything out, but they didn’t want me to have any microscopic stuff left,” she says.

Now, as Lavine reclines on a chemotherapy bay cot, a bag of liquid slowly dripping into her body—adjuvant chemotherapy post-ovarian cancer surgery—she looks at peace with her circumstances. Her husband, Trevor, sits at her side. Lavine describes him as an excellent cook; he makes sure she eats the most nutritional diet possible. The support of a loving husband helps Lavine maintain a positive outlook in the face of such a difficult medical history—one that she’s continually managed to challenge successfully. But in addition to a loving husband and an undeniable natural inner grace, Lavine has another asset on her side.

“If there was anyone in whose hands I’d put my life, it would be here with the doctors and nurses at Johns Hopkins,” she says. “I know that they do everything in their power to make sure everything goes all right.”

Cherrie Lavine
Young Investigators
Advancing Progress Against Pancreatic Cancer
Pancreatic cancer is an aggressive and complex disease that poses baffling questions about how it originates, grows and spreads. But over a decade ago, when Johns Hopkins immunotherapy expert Elizabeth Jaffee, M.D., first developed a pancreatic cancer vaccine in her laboratory, the formerly dismal outlook for patients with this disease began to brighten.

It was then that Jaffee, co-director of the Skip Viragh Center for Pancreas Cancer Clinical Research and Patient Care, and others began to recognize that immunotherapy could eventually pave the way for earlier detection, more effective treatment and better rates of survival for pancreatic cancer. The key to making this happen would lie in scientists’ continued efforts to better understand the interplay between the immune system, cancer genes and other cellular mechanisms that drive pancreatic cancer.

Following in Jaffee’s footsteps, young investigators Dung Le, M.D., Eric Lutz, Ph.D., and Lei Zheng, M.D., Ph.D., are working to further harness the power of immunotherapy against pancreatic cancer while Ana De Jesus-Acosta, M.D., and Zeshaan Rasheed, M.D., Ph.D., are exploring genetic alterations and cancer-initiating cells. Critical to their groundbreaking work is the leadership of Jaffee and Daniel Laheru, M.D., co-director of the Viragh Center, as well as a generous $20 million gift from former Johns Hopkins pancreatic cancer patient Skip Viragh.

“Dung Le, Eric Lutz, Lei Zheng, Ana De Jesus-Acosta and Zeshaan Rasheed are among the group of bright, young scientists supported through Skip Viragh’s legacy. They are working with Dr. Jaffee and me to optimize the effects of Dr. Jaffee’s pioneering pancreatic vaccine and to develop new therapeutic approaches for pancreatic cancer,” says Laheru.

Dung Le

Dung Le, M.D., was the first Viragh Scholar recipient. She graduated from the Johns Hopkins University School of Medicine in 2001, and although that was barely a decade ago, she is already making a name for herself in the international research community.

As a trained medical oncologist who has the privilege and the challenge of seeing patients and conducting research, Le acknowledges the inroads that scientists have made in pancreatic cancer but is acutely aware of the work that still needs to be done. “Patients with metastatic pancreatic cancer still succumb to their disease. You want to do more,” she says.

She is doing just that. Much of Le’s research focuses on using combination strategies to enhance the efficacy of the GVAX pancreatic cancer vaccine originally developed by Jaffee.

In a recently published phase I clinical trial, principal investigator Le demonstrated the ability to extend the survival—with manageable toxicity—of patients with previously treated metastatic pancreatic cancer when treating them with the vaccine CRS-207. A weakened form of listeria bacteria, CRS-207 is genetically engineered to express mesothelin, a protein on the surface of pancreatic cancer cells that the immune system can be trained to recognize and attack.

“Interestingly, the trial revealed that patients with prolonged survival had previously received the GVAX vaccine,” Le notes.

This did not come as a complete surprise to Le and her colleagues, as earlier studies in mice predicted that combining GVAX and CRS-207 would lead to better outcomes. Subsequently, Le is the lead investigator on a multicenter phase II study combining the two vaccines in patients with metastatic pancreatic cancer. The study is showing positive results.

In yet another promising study in which Le served as the principal investigator, patients previously treated for advanced pancreatic cancer received either ipilimumab (IPI), an antibody
that activates the immune system, or a combination of IPI and the GVAX vaccine. Some patients who received the combination showed evidence of up to 81 weeks of prolonged disease stabilization; seven “combination” patients experienced declines in antigen CA19-9, a foreign substance released by pancreatic tumor cells. While some patients administered only IPI demonstrated evidence of stable disease, the biochemical response occurred only in patients receiving the combination of IPI and GVAX.

“This is the first time we have the agents we need that we can combine. The excitement is palpable. We’re starting to see signs of efficacy. I think over the next few years, we’re going to see a lot of exciting new things,” Le says.

**Lei Zheng**

Le’s colleague Lei Zheng, M.D., Ph.D., shares her excitement regarding the advancements being made in pancreatic cancer research. Zheng is also exploring how to further the significance of the pancreatic cancer vaccine.

Zheng is conducting a clinical trial in which patients who have surgically treatable pancreatic cancer receive the GVAX vaccine before and after their surgery. Upon examining tumors removed by surgery in these patients, Zheng and his colleagues made an unprecedented discovery.

For the first time, they found that the GVAX vaccine induces the formation of lymph node-like structures within the tumors. More significantly, Zheng and associates demonstrated that the signatures in these lymphoid structures can be used to predict patients’ response to the vaccine therapy and to reveal pathways that can be modulated to further enhance the vaccine’s efficacy.

Inspired by these results, Zheng’s laboratory recently demonstrated in an animal model of pancreatic cancer that combining the GVAX vaccine with an antibody treatment that blocks the PD-1 pathway—used by the tumor to suppress an immune response—works to significantly enhance the vaccine’s efficacy.

Zheng recognizes that to make progress against pancreatic cancer, research must look beyond actual tumor cells themselves. “Cancer cells hijack the cells around the tumor. I’m studying how they hijack the environment and turn it into one that’s ripe for cancer growth,” he says.

The next step, naturally, is to reverse the hijacked environment—something Zheng hopes to do eventually. It will involve targeting changes that occur in the “microenvironment” around the tumor, inhibiting these changes and ultimately creating an environment less hospitable to cancer.

To manipulate and weaken the environment where aggressive, often fatal pancreatic cancer thrives is a bold goal. But with Zheng and an increasing number of researchers joining this effort, it becomes much more plausible for the future.

**Eric Lutz**

Eric Lutz, Ph.D., says he always had a general interest in research. However, it was a job as a lab technician at Johns Hopkins after his undergraduate degree that introduced him to tumor immunology and hooked him on the specialization.

“I started to believe in Dr. Jaffee’s vaccine. I decided to pursue postgraduate research at Johns Hopkins and train with her. I have not been able to find something that interests me more,” says Lutz, the most recent Viragh Research Scholar.

His keen interest in tumor immunology has rapidly evolved into a scientific expertise that includes efforts to uncover the basic principles that define immunotherapy-induced immune responses and develop new technologies to study these responses within developing human tumors.

Already, Lutz and associates have demonstrated that they can induce tumor mutation-specific antitumor responses in mice that can cure them of tumors. Sixty percent of mice they vaccinated were cured and never developed tumors. Without the vaccine, all of them would have developed tumors within four weeks, Lutz explains.

Encouraged by the antitumor response in mice models, Lutz is forging ahead with a bold new study aimed at analyzing mutation-specific immune responses in patients treated with a whole-cell pancreatic cancer vaccine.

They know that each human pancreatic cancer cell harbors approximately 63 mutations. Now they’re set to determine how to select which of the potential 60 or so mutations should be targeted with treatment and how to best target them with vaccines. “It could be that five mutations are the true targets” he says. “Currently, it’s difficult to hone in on which are the important targets and which ones are just noise. Although it may be possible to target all mutations expressed by a tumor simultaneously, it would be much better if we could accurately predict which mutations are most capable of staving off cancer by serving as tumor rejection antigens and only focus on them.”

In a closely related study, Lutz is working with Zheng on his trial examining tumors of patients who have been treated with the GVAX vaccine prior to surgery. “It’s the first time patients have been treated with the whole-cell vaccine prior to surgery. This
study is giving us our first look at the tumor post-vaccination,” he says.

**Ana De Jesus-Acosta**

Ana De Jesus-Acosta, M.D., is building upon laboratory research that revealed that pancreatic cancer, like many types of cancer, contains colonies of cancer-promoting cells. These cells, while small in number, appear to be a major force in cell growth by evading anticancer drugs and perpetually giving rise to the larger number of cancer cells that make up the bulk of tumors. De Jesus-Acosta is exploring whether targeting these cells with new therapies could help combat pancreatic cancer.

Specifically, she is interested in testing drugs that target and block a gene pathway called Hedgehog pathway that the research showed was more active in pancreatic cancer-initiating cells. In animal models, Kimmel Cancer Center investigators found that blocking Hedgehog activity increased survival. Laheru and De Jesus-Acosta are now translating this laboratory research into a clinical trial for patients with advanced pancreatic cancer to see whether patients who receive a Hedgehog inhibitor in addition to standard drug therapy live longer.

De Jesus-Acosta has also started another clinical study for patients with earlier stage pancreatic cancer whose tumors have not yet spread outside the pancreas but could not be treated with surgery. “Our goal is to knock back the tumor enough with the Hedgehog inhibitor/chemotherapy combination to get patients to surgery,” she says.

**Zeshaan Rasheed**

Zeshaan Rasheed, M.D., Ph.D., is providing the laboratory science for De Jesus-Acosta’s clinical studies, working to advance the understanding of pancreatic cancer-promoting cell colonies. Using biopsy and blood samples voluntarily donated by patients, he is developing technologies to isolate the cancer-initiating cells and measure the effect the inhibitor has on them. He is working on a first-of-its-kind method to collect these elusive cells in circulating blood.

“Although researchers at other institutions are studying Hedgehog inhibitors in pancreatic cancer, our team was the only group to collect biopsy and blood samples,” says Rasheed. As a result, he is now able to conduct one-of-a-kind studies of Hedgehog pathway regulation in cancer-initiating cells. In the first clinical trials led by De Jesus-Acosta, the inhibitor did not thwart pancreatic cancer cell growth as it did in animal models. “The blood and biopsy samples are allowing me to go back into the laboratory and figure out why and make necessary adjustments to the therapy,” he says.

Comparing the molecular composition of tumors from patients whose cancers did not respond to treatment with those that did, he may be able to create a profile of specific characteristics, such as a defined level of Hedgehog activity, to help identify those patients whose cancers are most likely to benefit. This work is part of expanded efforts to sequence the genome of each patient’s tumor cells and improve treatment outcomes through personalized treatment approaches tailored to the unique molecular fingerprint of an individual’s tumor.

New funding from Peter Kovler will allow Jaffee to add a new young clinician-scientist to her laboratory to further speed the transfer of scientific discoveries to patient care. With the commitment and talent of young investigators, research and clinical “firsts” are becoming increasingly common. “We were a small group of cancer immunology experts, but we’ve expanded to include many people and other research interests,” says Jaffee. “I believe this is how we’re going to make the greatest impact.”
A Decade of Pancreatic Cancer Research

Pancreatic cancer is one of the deadliest cancers and among the most underfunded. Limited research funding has hampered progress against the disease. As a result, the understanding of the biology of pancreatic cancer has lagged far behind other cancers.

Ralph Hruban, M.D., Bert Vogelstein, M.D., Kenneth Kinzler, Ph.D.
Research Milestones from the Goldman Center

In 2005, pancreatic cancer received a much-needed infusion of resources when Jane and Amy Goldman made a $10 million gift and established the Sol Goldman Pancreatic Cancer Research Center at the Johns Hopkins Kimmel Cancer Center. Because of their generous support, the Goldman Center is the world’s leader in pancreatic cancer research. The Goldman Family also provided the lead funding to decipher the genetic code of pancreatic cancer, one of the first comprehensive cancer gene analyses ever conducted. “This support has allowed us to greatly advance our understanding of pancreatic cancer,” says leading pancreatic cancer pathologist Ralph Hruban, M.D., director of the Goldman Center.

From that point forward, the work of the Sol Goldman Pancreatic Cancer Research Center researchers has been among the most frequently referenced—with more than 24,000 citations—reflecting their impact against this deadly cancer.

2005

**High-Impact Philanthropy:** The Sol Goldman Charitable Trust established the Sol Goldman Pancreatic Cancer Research Center at Johns Hopkins. The $10 million gift that endowed the Center was one of the largest ever to a pathology department.

2006

**Personalized Cancer Therapy:** Scientists at the Goldman Center have used patients’ own tumors, grown in mouse models, to identify the drugs that will work best against the cancer. Scientists in the Goldman Center have developed mouse “avatars” to test drug libraries to pinpoint agents that will get the best response. In one experiment the team successfully identified two drugs active against pancreatic cancer from a library of more than 3,000 drugs.

2007

**Predicting Pancreatic Cancer:** Johns Hopkins researchers designed a computer program that can predict which changes in the DNA code in the pancreas may cause pancreatic cells to become cancerous and deadly. The investigators say the findings could lead to more focused studies on better ways to treat the disease. The program uses 70 different predictive features for each DNA change, such as the DNA sequence and structure of the resulting protein, to identify any of the distinguishing characteristics of driver mutations — those DNA changes that contribute to cancer — compared with other genetic changes. The results can help cancer biologists set up experiments to see how important these DNA changes really are in pancreatic cancer and whether or not they are good drug targets for potential treatments.

2008

**Blueprint for Pancreatic Cancer:** The complete genetic blueprint for lethal pancreatic cancer and brain cancer was deciphered by the Sol Goldman Pancreatic Cancer Research Center at the Johns Hopkins Kimmel Cancer Center research team. One of the most comprehensive analyses ever undertaken of pancreatic cancer, the new map evaluated mutations in virtually all known human protein-encoding genes, comprised of more than 20,000 genes, in 24 pancreatic cancers. A core set of regulatory gene processes and pathways, about a dozen for each tumor type, were found to be altered in the majority of tumors studied by the researchers.

2009

**Personalized Genome Sequencing:** Scientists at the Sol Goldman Pancreatic Cancer Research Center at the Johns Hopkins Kimmel Cancer Center used “personalized genome” sequencing on an individual with a hereditary form of pancreatic cancer to locate a mutation in a gene called PALB2 that is responsible for familial forms of the disease. The findings, they say, underscore the value of so-called “personalized genome” sequencing, which decodes a person’s genes and compares the changes to those found in healthy people.
“THE MANY ACCOMPLISHMENTS BY SCIENTISTS OF THE SOL GOLDMAN CENTER HAVE HAD A PROFOUND IMPACT ON PANCREATIC CANCER RESEARCH.”

Ralph Hruban, M.D.

2010

Pancreatic Cancer Timeline Reveals Ample Opportunity for Early Intervention: Kimmel Cancer Center and the Sol Goldman Pancreatic Cancer Research Center investigators developed a mathematical model that allows clinicians, for the first time, to calculate the lifespan of pancreatic 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. Instead, the researchers calculated that it takes 11 to 18 years for a cancer to originate and spread beyond the pancreas. New early diagnostic tests to detect these cancers during this ample window would provide an opportunity to intervene, and potentially cure these with surgery, investigators say.

2011

Landmark DNA Study of Pancreatic Cysts: Scientists, including Bert Vogelstein, M.D., Kenneth Kinzler, Ph.D., and Ralph Hruban, M.D., surveyed the DNA in four common types of pancreatic cysts, and have determined that each type bears a distinct pattern of gene mutations. These fluid-filled cysts are identified in more than a million patients each year. Most cysts are benign, but distinguishing between the harmless and dangerous ones is challenging for doctors. The scientists used the findings to develop a gene-based test to distinguish precancerous pancreatic cysts from harmless cysts. A gene test is being developed as an accurate, quantitative way to identify cysts that are more worrisome and to help patients avoid unnecessary surgeries for harmless cysts.

2012

Detectable Lesions Warn of Hereditary Pancreatic Cancer: About 10 to 15 percent of all pancreatic cancers are hereditary. Research, led by Marcia Irene Canto, M.D., M.H.S., revealed that four in ten adults at high risk for hereditary pancreatic cancer have early curable lesions in their pancreas long before they have any symptoms of the deadly disease. In her study, endoscopic ultrasound successfully detected 40 percent of these potential precursors to cancer. Bert Vogelstein, M.D., and his team in the Ludwig Center for Cancer Genetics, is developing biomarkers that predict the malignant potential of these lesions. Researchers hope those findings, used in conjunction with the results from this new study, will help experts find and treat potentially lethal pancreatic cancers while they are still curable.

2013

The Best of the Best: The American Association of Cancer Research (AACR) gave its prestigious Team Science Award to a multi-institutional team led by Ralph Hruban, M.D., for work deciphering the genetic changes that characterize pancreatic cancer.

2014

International Leaders: A worldwide analysis of leaders in pancreatic cancer science and treatment by Expertscape—which ranks disease experts based on their published research—named Johns Hopkins as the leading institution and Goldman Center Director Ralph Hruban as the top international pancreatic cancer expert. Other Goldman Center scientists recognized as leading international pancreatic cancer experts included Joseph Herman, Michael Goggins, Christine Iacobuzio-Donahue, Dan Laheru, and John Cameron.
With Help from His Friends, Ron Smith Is Still Making a Difference

For over 30 years, Ron Smith made himself a household name as a Baltimore news anchor and, in more recent years, on talk radio. When he was diagnosed with advanced pancreatic cancer in 2011, Smith and his wife June decided that the best way to fight the cancer would be through establishing an endowment to advance the state of pancreatic cancer medicine. Today, the Ron Smith Pancreatic Cancer Research Fund at Johns Hopkins continues to reinforce the Smiths’ commitment to helping others fight the disease.

“Ron touched thousands of lives on the airwaves and in print. The fund at Hopkins is a befitting way to keep his legacy alive and continue his commitment to transforming the way pancreatic cancer is detected, diagnosed and treated,” says June Smith.

With generous gifts from the Charles T. Bauer Foundation and many other supporters of Smith’s, including Team Reason, the Ron Smith Pancreatic Cancer Research Fund is already making a difference. Experts believe that one of the keys to improving patient survival is early detection. The majority of patients, some 80 percent, are diagnosed after their cancer has become advanced. As a result, just 15 to 20 percent of patients are good candidates for potentially curative surgery. Johns Hopkins scientist Judy Wang, M.D., hopes to change this dismal statistic. With funding from the Ron Smith Fund, she is working to develop a reliable blood test that could serve as both an early screening tool and as a way to monitor existing patients for cancer recurrence.

Kimmel Cancer Center research has demonstrated that growing cancers shed DNA into the bloodstream. Wang foresees a simple blood test for early detection, but could also be given to existing pancreatic cancer patients who have undergone surgery to monitor for tumor DNA that would foretell a cancer recurrence. She believes a test that reliably detects pancreatic cancer recurrences before they become advanced could extend survival. Though the research still requires much more work, Wang says the implications are profound. “If it works, if we can use this test to find pancreatic cancer earlier, then surgeons and oncologists have a better chance of curing patients,” she says.

Liz and Eric Lefkofsky Fund Cutting Edge Prevention and Treatment Strategies

The aggressive nature of pancreatic cancer underscores the need for new, effective treatments. After losing his grandfather to the disease, Eric Lefkofsky and his wife Liz wanted to do something to help other families facing a diagnosis of pancreatic cancer.

As a result, the Lefkofsky Family Foundation is funding Lei Zheng, M.D., and promising new research that has uncovered what he believes may be a key player in the growth of human pancreatic cancer. In animal models, Zheng found that a gene called annexin A2 promoted the spread of pancreatic cancer. He believes inhibiting the gene in patients could be a promising therapeutic strategy. Zheng and team are now working to develop agents to target the gene, and if successful, plans for clinical trials in patients with advanced pancreatic cancer will follow.

Additional support from the Lefkofsky family is focused on a vaccine approach to preventing pancreatic cancer. Elizabeth Jaffee, M.D, is developing this first-of-its-kind vaccine, which involves the genetic manipulation of listeria monocytogenes, a common bacterium that naturally induces an immune response. Dr. Jaffee has engineered the listeria to target the Kras gene, an early and important genetic change in pancreatic cancer development. This approach has already shown promise in a mouse model of pancreatic cancer development.
New Research Could Be First Step to Preventing Pancreatic Cancer

A primary way pancreatic cancer originates is through fluid-filled cysts called intraductal papillary mucinous neoplasms (IPMNs). These cysts form in the ducts of the pancreas, and left untreated, some progress to pancreatic cancer. They provide an early opportunity to intervene and potentially prevent pancreatic cancer.

Pancreatic cancer expert Christopher Wolfgang, M.D., Ph.D., has received a $100,000 gift from the Leslie F. Schwartz Pancreatic Cancer Research Foundation to explore this potential. Wolfgang says that understanding the genetic alterations contained within IPMNs will help scientists determine how they originate, how to differentiate harmless cysts from those that will become cancers and how to decipher the specific molecular changes involved in the progression from cyst to pancreatic cancer.

"We are so grateful for the foundation’s support. It is funding research that will help us form a timeline of pancreatic cancer origination and progression," says Wolfgang.

Because IPMNs precede pancreatic cancer, they represent an opportunity to identify precursors to the disease and to intervene to prevent cancers. A new research study will build upon earlier work and provide an in-depth analysis of different IPMNs occurring within the same patient. The fluid-filled cysts will be analyzed in as many as five patients, using tumor samples collected from patients and stored in the Johns Hopkins Pancreatic Tissue Bank.

For each patient, Wolfgang and team will study the pathology information, including the size and stage of the cancer at the time of surgery, treatment history, imaging of the primary tumor and tumors recurring in sites outside of the pancreas. In addition, genetic sequencing of the coding or functionally active region of the genes contained within each tumor sample also will be performed. The researchers will catalog all acquired gene mutations identified through sequencing, focusing on an anticipated 50 to 60 mutations per cancer. This will allow the research team to form a timeline of cancer origination and progression. More importantly, this study has the potential to identify the initial genetic changes that initiate pancreatic cancer and may serve as the basis for the development of early detection.

"Thanks to Leslie’s indomitable spirit and the generosity of our donors, we are pleased to be in a position to provide financial assistance to the pancreatic cancer early detection project undertaken by Dr. Christopher Wolfgang and his distinguished colleagues at Johns Hopkins," says Schwartz foundation President Mark Schwartz. "We hope that this research will bring us closer to the development of universally reliable methods for the early detection of pancreatic cancer."

McGlinn Fund Is Rocking Out a Cure

Recent Montgomery Blair High School senior Max Poole has taken a creative approach to honoring the memory of his grandmother Marguerite Mulligan McGlinn, who died of pancreatic cancer when he was 11 years old. During his senior year—with the help of family, friends, and fellow musicians—Poole founded Rock Action, a concert series that benefits pancreatic cancer research at the Kimmel Cancer Center. It provides young musicians exposure to bands by setting up for concerts.

Money raised by Rock Action benefits the Marguerite Mulligan McGlinn Research Fund in Pancreatic Cancer to support the startup costs associated with clinical research of the disease. Every research study conducted requires a significant amount of behind-the-scenes work, from reviewing laboratory protocols to submitting the studies for review, and it is often not covered by research grants. The Marguerite Mulligan McGlinn Fund is playing a heroic role in bridging these funding gaps and speeding the pace of research.
Help Us Make a Difference

Each contribution to the Skip Viragh Center for Pancreas Cancer Clinical Research and Patient Care at the Johns Hopkins Kimmel Cancer Center makes a difference in the lives for cancer patients here at Johns Hopkins and around the world.

Our physician-scientists are leading the way on many of the scientific breakthroughs in pancreatic cancer, and your donation will support patient care and innovative research that is translated to better, more effective treatments.

You may designate a gift to a specific faculty member.

To make your donation online
Go to www.hopkinscancer.org and click “Make a Gift.”

To mail your donation, send to:
Dina Mallis Klicos
The Johns Hopkins Kimmel Cancer Center
Development Office
750 E. Pratt St., Suite 1700
Baltimore, MD 21202

To contact our Development Office by phone or email:
Phone 410-361-6391
Email: dklicos@jhmi.edu

If you prefer not to receive fundraising communications from the Fund for Johns Hopkins Medicine, please contact us at 1-877-600-7783 or JHHOptOut@jhmi.edu. Please include your name and address so that we may honor your request.