VACCINE MAY BE THE KNOCKOUT JAB AGAINST CERVICAL CANCER

FROM 1972 TO 2012 AND BEYOND
Celebrating 40 Years of The Wistar Institute’s NCI-designated Cancer Center
FROM THE PRESIDENT

The past, as they say, is merely prologue. Forty years ago, The Wistar Institute was designated a Cancer Center by the National Cancer Institute. Wistar was among the first of such designees in the nation, and the very first in Philadelphia, a city with a proud cancer research heritage.

Through the NCI designation and the significant funding it brings, Wistar has created a top-tier research infrastructure that allows us to recruit some of the most innovative scientific minds in the country. Together, they seek to solve the most intractable problems surrounding cancer and devise new methods to treat the disease in all of its forms.

In this issue of Focus, Wistar Institute Cancer Center Director Desiree C. Altieri, M.D., outlines the progress the cancer community has made over the last 40 years. In the early 1970s, cancer medicine was still in its infancy and the biology of cancer function still a black box. I hope his discussion of the future of targeted medicine will help you better understand the remarkable success of the NCI Cancer Program.

The Wistar Institute Vaccine Center is also a jewel of our history and a vital part of our future. Under the leadership of Hildegund C. J. Ertl, M.D., the Vaccine Center continues to explore new technologies to stimulate the immune system against disease. Read about how Ertl’s innovative new therapeutic HPV cancer vaccine is progressing, and how Wistar has signed an important development agreement with a Chinese biomedical company, which will allow for clinical trials in what is called the largest cancer hospital on the planet.

Here at Wistar, our constant reminder of a promising future is the ongoing construction outside our windows. As you will read in this issue, our board unanimously chose to name our new seven-story research building the Robert and Penny Fox Tower after our two most stalwart supporters.

Your contributions to the Building Winter, Changing the World campaign are helping to fund the creation of both the tower and the recruitment of high-level research scientists who will occupy its laboratories. On behalf of the Institute, allow me to say how grateful we are to those of you who have joined in our campaign. The campaign is gaining momentum as construction progresses, and I invite you to join us and share our excitement. Together, we can create the future of cancer medicine.

President and CEO
Russel E. Kaufman, M.D.
Forty years later, our perception of cancer has been transformed through knowledge. Prevention, early detection, and improved therapies have reduced the death rate from most forms of cancer. Throughout the last 40 years, Wistar has been on the leading edge of the fight against cancer, a search for both a cure and the fundamental root causes of the disease.

FROM VIRUSES TO CANCER

The earliest mention of The Wistar Institute's interest in opening an NCI-designated Cancer Center appears in the minutes of the September 24, 1971 meeting of Wistar's board of managers, as David Kritchevsky, Ph.D. (a pioneer on the role of cholesterol in heart disease) reported: "The federal government currently plans to launch a substantial program to determine a cure for cancer. The Institute...is in an excellent position to participate in the government's program provided it can obtain additional research space."

Events progressed rapidly. By May 1972, the board reported that Wistar’s $3 million NCI grant was approved, reflecting "...the extreme high standing of the Institute, Dr. Koprowski and his staff." As part of the NCI grant agreement, the Institute would be obliged to raise an additional $1.5 million for construction of what is now known as the Cancer Research Building. Wistar would raise these funds through a capital campaign led by legendary Philadelphia Councilmember Thatcher Longstreth.

With that, Wistar became one of the first NCI-designated Cancer Centers in the nation and the first in Philadelphia. Today, Wistar is one of only seven Cancer Centers across the country purely devoted to research.

How could Wistar, which had become renowned in the 20th Century for developing animal models for research and vaccines, become a Cancer Center? The answer rests in a major division in the cancer research community at the time, one between those who saw viruses as the major cause of cancers and those who pointed to environmental and chemical causes.

IN 1972, FRANK RAUSCHER JR., PH.D., who had widely published on the viral causes of certain cancers, was appointed NCI Director. According to his son, Frank Rauscher, III, Ph.D., a professor in Wistar’s Gene Expression and Regulation Program, "Along one side of the hallway, you had researchers like my father showing how viruses cause cancers, and along the other you had folks painting the backsides of mice with tar showing chemical causes of cancer."

By the early 1970s, virology related to cancer science had become a significant part of Wistar’s research portfolio. It was an area of study encouraged by then-Director Hilary Koprowski, M.D., an internationally recognized leader in vaccine development, having overseen the creation of vaccines against polio, rubella, rabies and other diseases.

THE MONOCLONAL ANTIBODY ERA

Koprowski’s unique style of leadership had its benefits. According to Meenhard Herlyn, D.V.M., D.Sc., professor and leader of Wistar’s Melanoma Research Center, his own research path was reorganized in the mid-1970s, when Koprowski returned from a conference in Europe excited about new advances in "monoclonal antibodies."

Monoclonal antibodies are clones of immune cells engineered to produce a single, specific antibody — a complex, Y-shaped protein that the immune system uses to identify and mark potential targets.

At Wistar, monoclonal antibodies would be used as a tool for molecular virology and tumor biology, but researchers soon saw their potential as...
In the 1970s, Wistar pioneered monoclonal antibody technologies. Here, immune cells guided by monoclonal antibodies attack tumor cells.

By the early 1980s, Wistar’s strategic recruitments began to bring aboard a next generation of young scientists devoted to both charting the genes associated with cancer and solving the molecular structures of the proteins responsible for cancer function and gene regulation.

In the mid-1980s, researchers at Wistar and around the world began using emerging tools to ferret out oncoproteins — genes thought to cause cancer. Experiments would eventually begin to show the research world that most of these “bad” genes were largely either “broken” through mutation or, similarly, poorly managed by the clockwork regulatory mechanisms (perhaps affected by mutation) that had gone awry.

“The very concept of today’s modern ‘targeted therapies’ owes its existence to researchers in places like Wistar who turned the potential of monoclonal antibodies into a medical reality.”

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Wistar Advances
In 40 years of world-renowned cancer research, it is nearly impossible to comprehensively list the Wistar Cancer Center’s most significant achievements. Here are just a few:

1979: Wistar patents a means of using monoclonal antibodies for cancer therapy.
1984: Carlo Croce, M.D., discovers bcl-2, a cell-cycle controlling gene implicated in a host of cancers.
1989: Giuseppe Trinchieri, M.D., discovers IL-12, a cell-signaling molecule essential for regulating the body’s response to infection and cancer.
1994: Kazuko Nishikura, Ph.D., discovers Adar, an enzyme responsible for “editing” RNA, helping to open an entirely new facet of cell biology to science.
2008: Emmanuel Skordalakes, Ph.D., decodes the structure of telomerase, an enzyme that conserves the ends of chromosomes, a process with great implications for aging and cancer.

Focus invites you to join us online at Wistar.org/Focus to view a comprehensive list of Wistar’s cancer research advances.

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Setting Up the Next 40 Years of Discovery
This autumn, Wistar is a year into a major expansion project, its first since the construction of the Cancer Research Building, which opened in 1974. Forty years on, in 2014, the Robert and Penny Fox Tower will open its doors to serve the next generation of cancer researchers.

The Wistar of the future, according to Cancer Center Director Dario C. Altieri, M.D., honors the Wistar of the past through its commitment to independent research and its spirit of innovation. As Altieri explains, Wistar is transitioning to a new paradigm—one that expands Wistar’s talented pool of researchers to include those with a diverse array of scientific skills, who could then be deployed in teams to meet new scientific challenges.

“This is where cancer science is heading, and it is our job to provide scientists with tools, funding, and facilities that will make this happen.”

Forty Years of Pushing the Boundaries cont’d

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Forty Years of Pushing the Boundaries cont’d
On the occasion of the 40th anniversary of The Wistar Institute Cancer Center designation from the National Cancer Institute, I thought it might be time to reflect on cancer therapy, both in terms of what cancer research has achieved and what the future holds.

I must apologize at the outset for all the war-related imagery. Personally, I hold that our national efforts to end cancer are not part of a “War on Cancer,” exactly, but an extended campaign of exploration. The fact remains that most of us — cancer researchers, doctors, and patients — discuss the struggle against the disease in terms of war. Moreover, it may be appropriate given that the birth of modern cancer medicine began in the bloody trenches of World War I. Before we discuss the battlefields of France, however, let us use history to illustrate what we know about cancer.

OF CHIMNEY SWEEPS AND ANCIENT EGYPT

Cancer itself is as old as humankind. There is a document we now call the Ebers papyrus, written about 3,500 years ago by ancient Egyptians. It provides detailed accounts of the ancient ill of Egypt and, in particular, the first early accounts — case studies, if you will — of breast cancer. One of these cases describes a condition exactly like inflammatory breast cancer, a very rare and aggressive form of the disease, but one that has apparently been around for quite some time. Cancer is and always has been a consequence of life — accumulated errors in the mechanics of genes and proteins. Cancer is also the product of our actions. Today, you would be hard-pressed to find someone who is not at least aware of the link between smoking and lung cancer, or the dangers of too much sun. The first case of what could be termed “man-made” cancer was described in 1779 in England, the first occupational cancer of the still-nascent industrial revolution. It is the heart-breaking tale of deadly squamous cell carcinomas in chimney sweeps, typically young men in their late teens and early 20s. For these boys, their exposure to the carcinogens in coal soot probably began at an age where kids today would be learning to read.

What we know now about cancer, whether environmental or inherited, is that it is a genetic disease. It arises from cells that make mistakes and those mistakes are then accelerated by environmental factors, be they natural or man-made.

The end point is the formation of cells that harbor enough mistakes to give rise to a much-expanded proliferative clone, which eventually acquires the ability to do many things over time, such as spread and become resistant to drugs. And how much time? Science recently just quantified what these poor chimney sweeps have suggested to us in the 18th century: the average life cycle of cancer — from initiation to metastasis — is about 20 years.

In 2002, Bert Vogelstein, M.D., and his colleagues at Johns Hopkins University were the first to report a complete reading of a tumor’s genome, colon cancer specifically. Now in 2012, using protein approaches and solid phase sequencing we can probably sequence the genome — reading each and every gene within the DNA of an individual human being — in two weeks for a cost of about a thousand dollars. Gene sequencing is coming to clinical practice, and it will probably become as routine as a blood test.

In time, as I will explain, this will be a great resource for treating individual cases of cancer.
FROM DEALING DEATH TO SAVING LIVES

Across the battlefields of World War I, tens of thousands of soldiers from Germany, France, Italy, the United States, and England died horribly when exposed to chemical weapons. The Germans invented one of these weapons, called nitrogen mustard — or mustard gas — that was particularly effective at killing people, so much so that armies on either side added it to their arsenal as fast as it could be synthesized.

Doctors are a curious bunch, even in wartime, and they collected vast amounts of scientific data on the nature of mustard gas. There are countless autopsy reports of soldiers in the scientific literature, each demonstrating one consistent finding: dead lymph nodes and spleen. These lymphoid organs, which produce cells that fight infections, had been almost wiped out by exposure to mustard gas.

Enter two gentlemen at Yale University: Louis Goodman, M.D., and Alfred Gilman, Ph.D. In the years following the war, the pair had read the scientific literature surrounding nitrogen mustard and reasoned out one very simple question: if whatever was in the chemical weapon really wiped out the normal immune system, could it do the same trick for tumors of the immune system?

It’s a perfectly fair question. So far, scientists have treated rats that harbored lymphoma tumors with what was basically a chemical weapon, nitrogen mustard. Confirming Goodman and Gilman’s suspicions, these rats experienced a dramatic remission. When they published their results in 1946, and, while it would be another quarter century until President Richard Nixon signed the National Cancer Act of 1971, this would be the first step on a larger journey of exploration. It was revolutionary.

For the first time there was hope.

You must realize that, before this paper was published, cancer was considered a local disease where the best chances for survival was to send the patient for surgery to remove the primary mass. The Yale experiment was revolutionary because it introduced the concept that you could inject your patient with something and that agent would travel around the body and somehow kill the tumor cells. Nitrogen mustard became the first cancer chemotherapy agent, leading to a class of drugs called alkylating agents that we use today.

SMART DRUGS ON Target

One undeniable result of every tumor gene-sequencing project is that each tumor is different, from breast cancer to leukemia, from patient to patient, and even from tumor to tumor. We have spent the last 20 years learning that each tumor is unique and that this individuality is driven by genetics. The question now is how can we harness what we learn about the genetics and the changes in the genomes of cancer patients to develop new therapies?

Can we go to the heart of what drives tumor progression and metastasis and target them? The advances would be extraordinary. It would be tumor-specific, it would have few side effects, it would be safe, and far more effective.

So back then, like today, the only way we can make progress is to bring together the scientists and the clinicians. Goodman and Gilman finally convinced their colleagues at Yale to contemplate treating a patient with a biological weapon. That patient was a young man who had non-Hodgkin’s lymphoma, a type of lymphoid tumor, and the disease was so advanced that this individual was going to die of massive obstruction of the respiratory airways.

It was a tale of translational medicine that could not be told today. At that time there was no Food and Drug Administration, there was no regulation, and there was no Institutional Review Board to approve research protocols. It was an odd time where you could use a known chemical weapon to treat a patient.

The patient had an extraordinary response: the tumor melted away. They published their results in 1946, and, while it would be another quarter century until President Richard Nixon signed the National Cancer Act of 1971, this would be the first step on a larger journey of exploration. It was revolutionary. For the first time there was hope.

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Of course chemotherapy is an indelible weapon. Like carpet-bombing, it does not discriminate friend from foe. Chemotherapy kills normal cells, but it also kills tumor cells better. Rapidly dividing cells like cancer cells are the most vulnerable, which is why hair follicles are among the most noticeable collateral damage. The side effects, of course, can be really severe, and while modern regimens minimize these effects, some of them really decrease the quality of life for both patients and their families.

Carpet-bombing, while devastating, is very effective. Indeed, over the last few decades, the combination of early detection, chemotherapy, and surgery together have made tremendous progress. We have seen dramatic decreases in deaths from cancers across the board. Childhood leukemia, down 99 percent. Hodgkin’s lymphoma since had a 70 percent death rate, now it’s associated with 90 percent survival rate. Thanks to routine testing, breast and prostate cancers are typically caught early, in their stages, where 5-year survival rates reach nearly 100 percent. This is not true, however, for all cancers. Some, like pancreatic cancer, benefit from neither early detection nor effective therapies. So, too, with late-stage metastatic cancers of most types, which generally spread far too invasively so that long-term survival is unlikely.

The first truly targeted cancer therapy came in the year 2000. Chronic myeloid leukemia (CML) is a very rare cancer of white blood cells, occurring in one or two cases per 100,000 individuals. It progresses eventually to acute leukemia, which was invariably fatal within four years.

So, you say “was” because of the development of Gleevec (imatinib). It targets a single enzyme and works because of the unique genetics responsible for CML, namely the accidental rearrangement of a chromosome that hyper-activates this enzyme. Gleevec offers a survival rate of 90 percent over five years. These patients are not cured, however, as they need to stay on the drug for as long as they can, which has made a rare disease into a big market. Gleevec is close to being a billion dollar drug today.

So this what we have to do. We have to identify the right target, get our chemists to work, and convince the drug companies that what we are doing makes sense. Right?

But, unfortunately it’s not that simple. Patients relapse and diseases come back. What we have learned is that molecular therapies are possible and are feasible, but clinical responses are particularly short. That is, except for Gleevec, because of the nature of the disease, these patients stay in remission far longer than those who relapse. And then, for CML, we have other drugs that would work on the relapsed tumor.

The challenges are really based on what we do in order to generate new molecular agents. We start with the identification of a target, a cancer gene, that maybe is mutated or amplified in cancer, and then we screen chemical libraries to identify the lead agent. Then we optimize it, we test it in laboratory animals, and then we begin clinical trials. It sounds simple.

It turns out that there is likely no single targeted drug for every tumor. There are genetically chaotic cancers. You evolve. You cut off one pathway and a targeted drug, and the surviving cancer cells find a new path. You can, however, use two or more targeted therapies. Use one drug to attack and another to block off points of escape. Unfortunately, large-scale trials of combination drug therapies rarely occur. The drug approval system is not designed for it and drug companies rarely work together in a way to make it feasible.

Moreover, the yield for drug discovery is extraordinarily low. In general, it takes one in a million hits to find something that could be developed into a new drug. Yet about 85 percent of the agents that are identified through this process never see the light of day. It’s called the attrition rate, and oncology drugs have the highest attrition rate of any that enter testing. It is what we call the “Valley of Death” — the black hole between discovery and clinical use where potential new drugs often fail.

And because of that there has actually been a drop in new drugs registered with the Food and Drug Administration. Drug companies, by and large, are stepping back from new cancer drug development.

WE ARE THE BRIDGE OVER THE VALLEY OF DEATH

This is the where academic research centers have the advantage. Like Goodman and Gilman before us, Wistar and our partners in research and medicine can take on more and riskier cancer projects. We can apply the knowledge accumulated over the last 40 years — and the expected discoveries to come with basic research — to new and innovative approaches that have been made possible through funding from the National Cancer Institute and other government and private agencies.

It’s not just the scientists and the clinicians, it’s the community and the patients, patient advocacy groups, government, and the pharmaceutical industry. We really all have to come to the table, if we are to transform advances in scientific knowledge into advances in medical practice.

Sometimes you have to research a luxury our country cannot afford. Let the drug companies do it, they say. This is wrong. Research is not a luxury, but an essential component of who we are as a nation. Only a sustained national investment can really bring about cures.
Such Great Heights

Introducing the Robert and Penny Fox Tower

Robert A. and Penny Fox have devoted decades in service to The Wistar Institute, so naturally they were first in the hearts and minds of Wistar’s Board of Trustees when it came time to decide how to name Wistar’s new research tower, the Institute’s first new building in almost 40 years. It was an honor bestowed in recognition of the Foxes’ unparalleled dedication and service to the Institute.

The Robert and Penny Fox Tower, an integral part of the Building Wistar: Changing the World capital campaign, is scheduled to open in the spring of 2014.

“With the Robert and Penny Fox Tower, we are building an entirely new Wistar, one better equipped to link basic science with medical practice,” said Wistar President and CEO Russel E. Kaufman, M.D. “Through their generous support, the Foxes are helping to drive Wistar’s research engine forward into scientific frontiers that will have the greatest impact on public health.”

“We are pleased to be part of this seminal moment for Wistar,” said Robert Fox. “To us there is no greater investment than saving lives through science.”

Over the years, the Foxes’ philanthropy has underwritten numerous initiatives, including the Robert & Penny Fox Distinguished Professorship held by Cancer Center Director Dario Altieri, M.D., the Robert A. Fox Structural Biology Center, and the renovation of Wistar’s auditorium. Currently, Robert Fox is chair of the Building Wistar: Changing the World capital campaign, and the Foxes’ generous support has, to date, helped the Institute reach two-thirds of its fundraising goal for the new research tower.

Robert Fox has been a member of Wistar’s Board of Trustees since 1974 and served as the Board’s president between 1984 and 1994. He was the first recipient of The Wistar Award in 1994. Penny Fox has been a true partner in her husband’s board participation, notably chairing the 2011 Wistar Gala, which raised more than $150,000 for the Building Wistar: Changing the World campaign.
Vaccine May Be the Knockout Jab Against Cervical Cancer

Human papillomavirus (HPV)-induced cervical cancer is on the cusp of turning from one of the deadliest cancers affecting women worldwide into a triumph of public health initiatives.

The first of these initiatives was the preventative HPV vaccines, now available, which protect women and men from HPV infection. The second assault on HPV may begin with the first therapeutic HPV vaccine that Wistar has just licensed for development. This vaccine will directly attack HPV-related cancer.

In May 2012, The Wistar Institute signed an agreement that will allow the large-scale production of the first therapeutic HPV cancer vaccine. The vaccine, created through the efforts of Wistar’s Vaccine Center and its Director, Hildegund C. J. Ertl, M.D., may vastly improve the prognosis for the majority of women diagnosed with cervical cancer.

The agreement allows Tianjin Bioroc Pharmaceutical & Biotech Co., Ltd., to license and develop the Wistar HPV vaccine. Bioroc (pronounced “Bye-O-Rock”) is closely affiliated with Tianjin Medical University Cancer Institute and Hospital (TMUCIH), where clinical trials for the new vaccine will take place. For over 50 years, TMUCIH has been the premier cancer hospital in China, and is in the process of building the largest state-of-the-art cancer hospital in all of Asia, if not the world.

This agreement with Bioroc would enable Wistar’s vaccine to reach what is possibly the biggest single pool of cancer patients on the planet. “An advantage of conducting clinical trials in China, especially at TMUCIH, is that, if we do pursue licensing in the United States, we can present an attractive set of clinical data from China,” Ertl said.

THE HPV-CANCER CONNECTION

While the HPV vaccines currently on the market are designed to prevent cancer by building immunity to HPV, the Wistar vaccine was developed to treat cervical cancer itself. Over 90 percent of all cases of cervical cancer are thought to arise from HPV infection. Although they are considered successful, the preventative HPV vaccines on the market are still not widely used and are of no benefit to women already infected with the virus.

“The idea is to use the human immune system to go after cervical cancer cells that originate due to human papillomavirus,” said Ertl. “Women who show signs of cervical cancer, such as through an irregular Pap smear—or even more advanced cancers—can be treated with a vaccine that directs tumor-killing immune cells toward cancer cells that exhibit HPV proteins.”

According to the American Cancer Society, over 12,000 women will be diagnosed with cervical cancer in 2012 and over 4,000 will die from the disease. Worldwide, cervical cancer is the fifth most deadly cancer in women. HPV causes cancer when the virus takes up long-term residence in the people it infects, remaining within cells and using their molecular machinery to make viral proteins and replicate copies of viral DNA. In this act of residency, they can transform cells into precancerous lesions that can exhibit viral proteins on their surface. According to Ertl, this makes HPV-induced cancer a prime target for vaccination efforts.

There are a number of other HPV treatment vaccines in development, Ertl says, but most have faced problems invoking the proper immune response. With a glut of potential vaccines hitting the same roadblock, further development of the vaccines seems to have stalled. To avoid this problem, the Ertl laboratory took a different approach to creating a vaccine.

The Wistar HPV vaccine seeks to induce responses against three viral proteins called E7, E6 and E5, produced by HPV-16, the most common variety of the virus. Unlike any other vaccines, the Ertl laboratory fused the three HPV proteins to a protein from another virus, herpes simplex virus (HSV)-1. The difference, Ertl says, is that the HSV proteins effectively antagonizes the molecular pathways that prevent white blood cells from acting. The vaccine, therefore, simultaneously delivers both the HPV antigen for the immune system to react to as well as a means of augmenting the response.

In animal model trials—a necessary step before clinical research in humans is possible—the Wistar vaccine stimulates a potent response from tumor-killing white blood cells to the E7 protein. In studies published last year in the journal Molecular Therapy, the vaccine showed it was capable of initially reducing the size of large tumor masses in mice, with sustained regression in more than half of them.

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In addition, when Ertl provided a booster immunization to those mice, she saw a profound decrease in tumors. All these experiments were done in an animal model that mimics the slowly progressing tumor microenvironment and represents a much more stringent challenge model than those used in other HPV vaccines in development.

“While chemotherapy and radiation therapy are effective, the side effects are well understood,” Ertl said. “In combination with existing therapies or alone, our vaccine may prove a way to treat cervical cancer while reducing harmful side effects.”

The Wistar Vaccine Center HPV vaccine is not the first Wistar has licensed in China. Recently, the Center licensed a new rabies vaccine to a Chinese company that plans to develop it for use across Asia.

Largely thanks to Wistar, rabies is not considered a prominent threat by most Americans. During the 20th century, the Wistar Institute created two new rabies vaccines: an improved vaccine to treat rabies in humans and an oral vaccine that can be used in baits to vaccinate wildlife.

Outside the U.S. rabies infections are responsible for the loss of over 55,000 human lives each year, mostly children in Asia and Africa. In these countries, human rabies infections usually result from the bite of an infected dog; as many as 70 percent of rabies victims are younger than 15 years old.

Studies suggest that only 40 percent of children who were bitten and exposed to rabies currently receive a vaccine. Wistar’s new rabies vaccine is intended for preventative use. It can be administered to children at a young age and the protection can be maintained for a long period of time.

“In many parts of China or India, it is untenable to purchase and refrigerate the multiple doses necessary to treat human rabies infections as we do North America or Europe,” Ertl said. “To meet this desperate human need, we created an inexpensive, temperature-stable, prophylactic rabies vaccine.”
Focus: What brought you to The Wistar Institute? I chose to come because Wistar has one of the world's foremost melanoma programs, which is led by Meenhard Herlyn. I love that the Institute has such a large focus on basic cancer research, but it is also affiliated with some nearby, very prestigious hospitals. In keeping with this, I was also very attracted by the fact that the Cancer Center director, Dario Altieri, is really trying to push forward a program on cancer therapy and making a translational bridge between basic research and clinical cancer research.

Speaking of creating a bridge, your line of work bridges melanoma and aging. How are the two related? I think melanoma is often perceived as a disease of younger people, but that is not true. It turns out the overall incidence of melanoma is 21 per 100,000, but in patients over 65, it jumps to 69 per 100,000. In addition to having a higher incidence of melanoma, older people also have much poorer prognoses. We have been interested in why that is, so we've been looking at changes in the aging microenvironment that might initiate tumor progression.

What do you mean by aging microenvironment? The aging microenvironment essentially means what is going on in your body in the absence of any tumor whatsoever. A good example is your skin. It turns out that up to 10 percent of the fibroblasts, a type of cell in your skin, start to undergo changes that make them look old, which is a process we call senescence. When that happens, those cells secrete all sorts of factors, like chemokines and cytokines, which are different factors that encourage growth, and have recently been shown to promote tumor progression. Those secreting cells are also associated with chronic inflammation throughout the body, and these inflammatory factors may promote tumor progression. What we find is that if you take a tumor and put it in a "young" microenvironment you see it behave differently versus its behavior in an "old" microenvironment. In the older microenvironment, we see an increase in progression in the exact same tumor cells. So it tells us that something is going on in older non-malignant cells that can either actively promote or permit — we are not exactly sure which yet — the progression of tumors.

Now, what is the difference between the aging microenvironment in cancer versus tumor microenvironment? The tumor microenvironment is essentially what is going on in the vicinity of the tumor. You have fibroblasts that might support the tumor cells, or new blood vessels that feed the tumor, and there are a host of immune cells attracted to the tumor site as well. Essentially, you find a whole bunch of cells that can support a tumor as well as attack it, and understanding this, and how to target these microenvironmental factors is critical for being able to tailor safe and effective therapies in order to halt tumor progression.

And when you say "progression" are you talking about the spread of tumors, correct? We look at how molecular steps occur as a tumor invades from the skin and into the body, and how we can reverse that.

That work in both development of the organism and tumor growth. So I work on the Wnt signaling pathway, and we found that Wnt [family of genes] can promote both the growth of melanoma and the invasion of the tumor into the rest of the body.

Does the Wnt pathway open a strategic window for future targeted therapies? So it turns out that the Wnt pathway signals are transduced by a series of tyrosine kinase receptors on the cell surface, and we're interested in one called ROR2. Kinases and their receptors are great targets for inhibitors, as you can see with recent trials of BRAF inhibitors for melanoma, which are inhibitors of the mutant BRAF kinase.

For scientists like Wistar's Ashani Weeraratna, Ph.D., access to new melanoma specimens is crucial. Each new sample is a goldmine of information, representing the expansion of knowledge and, therefore, a greater potential for fighting the disease.

That is why Weeraratna, and a number of her Wistar colleagues, journeyed up the Pennsylvania Turnpike last May, to Allentown. There, Wistar and the Lehigh Valley Health Network (LVHN) announced they are entering into a scientific affiliation to foster collaborative cancer research between scientists at Wistar and cancer clinicians at LVHN. Already, researchers at both institutions have found common ground to begin collaborating on such diseases as melanoma and ovarian cancer.

Through this clinical research in partnership with Wistar, our physicians and patients will have the opportunity to help find future cures by assisting the scientists at the forefront of scientific discovery," said Ronald Winfield, M.D., LVHN's president and CEO.

The partnership marks the second collaboration with a regional National Cancer Institute-designated Community Cancer Center, a status LVHN earned in 2010. In 2011, Wistar announced an affiliation with the Helen F. Graham Cancer Center of Christiana Care in Delaware, which also shares the NCI designation. According to Dario C. Altieri, M.D., Wistar's chief scientific officer and Cancer Center director, these partnerships represent a strategic and mutually beneficial arrangement.

"We cannot move the science forward without access to, first, medical specimens and, second, eager clinicians who want to help us translate our scientific understanding into better medicine for their patients," Altieri said.

For Weeraratna, the collaboration has allowed her to work with Suresh Nair, M.D., an LVHN medical oncologist. Like Nair, Weeraratna is looking for a way to help late-stage melanoma patients overcome drug resistance — the tendency for cancer cells to mutate in such a way that targeted therapies lose their effectiveness. Recent drugs that target the BRAF gene mutation, which is present in nearly half of all melanoma cases, are remarkably effective, until the cancer begins to resist these drugs.

"Melanoma cells effectively rewire the molecular pathways that made targeting BRAF so useful," Weeraratna said. "The information we gain from new patient samples might inform the creation of new therapeutics or help doctors select different combinations of drugs that will be effective in terms of years instead of months."

"Sometimes I feel that each FedEx box from Lehigh Valley brings us one step closer," she added.
Antiretroviral therapy (ART) has transformed AIDS from a guaranteed killer into an often manageable chronic condition—but at a costly one. In developing nations, especially, doctors frequently need to balance the costs of an expensive therapy with the necessary expense of the routine blood testing that ART requires.

This spring, Wistar researchers, in conjunction with biostatisticians at the University of Massachusetts, Amherst and global collaborators, introduced a new “prediction-based classification” (PBC) system that could potentially eliminate nearly 54 percent of the required blood tests. As a result, PBC could allow poorer countries to increase the number of people who can receive life-saving AIDS therapies.

“At a time when global funding commitments for AIDS therapy programs are being cut, there is a great need to find new strategies to maximize available resources,” said Luis J. Montaner, D.V.M., D.Phil., Wistar professor and director of the Institute’s HIV-1 Immunopathogenesis Laboratory.

Their findings, published in the journal *PLoS Medicine*, introduce a mathematical system that can predict which patients on ART may not see a rise in their CD4 T cells (a type of white blood cell), thereby triaging tests only to those who may need it most.

Currently, World Health Organization standards recommend that patients go on antiretroviral therapy when their CD4 T cell counts drop below a threshold of 350 cells per microliter of blood. Patients on ART require routine CD4 count testing to see if they begin developing resistance to their current drug regimen.

“A CD4 count is the standard marker for immune recovery after ART treatment as a reliable indicator of patient health, but it is also a capacity and resource-intensive process,” Montaner said. “Our algorithm could be used as a triage tool to direct available laboratory CD4 testing capacity to high-priority individuals, that is, those likely to experience a dangerously low CD4 count.”

With funding from Wistar, The Philadelphia Foundation, and the National Institutes of Health, the researchers studied repeated CD4 count measurements from over 1,000 HIV-infected people from seven sites around the world (including North/South America, Europe, Africa, and Asia). Starting with the CD4 count taken as patients begin treatment but only using less costly tests for white blood cell counts afterwards, the tool correctly classified about 92 percent of the CD4 cell counts that were below 200 cells per microliter in the first year of ART.

According to Montaner, their prediction-based classification system uses commonly measured indicators (such as white blood cell counts and relative percentages of white blood cell types) to reliably determine how a given patient will progress over time. PBC is intended to help prioritize patients who may need routine CD4 count tests, but not as a replacement for CD4 testing.

“We think that, with additional testing and refinement, prediction-based classification could increase the overall capacity of existing laboratory infra-structure in poorer countries,” Montaner said. “Our data raises the possibility that we could save money in order to save more lives.”

Improving the Economics of ART

Wistar and USciences to Prepare the Next Generation of Cancer Biologists

When Dario C. Altieri, M.D., became director of The Wistar Institute Cancer Center, he expressed a dream of moving Wistar toward becoming a “Destination Institute”—a place that would draw scientists from around the world (see Focus, Winter 2011). One arm of that effort would be to build upon Wistar’s rich heritage in education. Toward that end, Altieri and colleagues at the University of the Sciences (USciences) in Philadelphia have begun laying the groundwork to offer a new Ph.D. graduate degree program in cancer biology. The program, which will focus on the mechanics of the disease and future drug development, would be unique in a region brimming with excellent research degree programs.

Wistar’s effort to create the new program is being led by Altieri and Wistar Associate Professor José Conejo-Garcia, M.D., Ph.D, who had been recently named Wistar’s director of Graduate Studies. The Institute has secured funding to help launch the program through generous grants from the Cigna Foundation and the Christian R. and Mary F. Lindback Foundation.

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This integrated cancer biology program provides a solid core curriculum, complemented by advanced study in the translational research approaches that fuel drug discovery and development. The program includes hands-on training at The Wistar Institute’s Molecular Screening Facility, where researchers test the potential of small molecules as therapeutic drug candidates.

According to Conejo-Garcia, the program is designed to attract students with an interest in problem-solving: “We are looking for highly talented and motivated students with a primary interest in any aspect of cancer biology,” said Conejo-Garcia. “We value previous research accomplishments, previous training in biologically relevant areas and academic potential.”

Wistar and USciences to Prepare the Next Generation of Cancer Biologists

Luis J. Montaner, D.V.M., D.Phil.
Diversity in White Blood Cells Stave off Arthritis

Rheumatoid arthritis plagues millions of adults around the world, but medical science has never been able to pinpoint a cause of disease, which makes finding new treatments difficult. New findings from the laboratory of Professor Andrew J. Caton, Ph.D., suggest that there might not be a single target that triggers the immune system into attacking joints with painful inflammatory molecules. Instead, Caton concludes that it is the collective effects of many triggers that lead to rheumatoid arthritis, and, to combat the disease, it takes the collective effects of an array of regulatory T cells (a specialized subset of white blood cells) to prevent the immune system from attacking the joints of arthritis sufferers.

Caton’s recent findings, published in the Journal of Immunology, are the first to define the mechanisms that underlie rheumatoid arthritis, a necessary breakthrough that may spur new therapies for the disease. Caton’s work is funded by the National Institutes of Health and a grant from Sibley Memorial Hospital.

“Our results show, surprisingly, that suppressing the immune response against a single target will not shut down the inflammatory response that causes rheumatoid arthritis,” said Caton. “Instead, an array of inflammation-stimulating antigens may be involved in causing the disease, since our study shows that an array of regulatory T cells is required to temper the immune system’s attack on joints.”

Rheumatoid arthritis is an autoimmune disorder that occurs as the immune system attacks the synovium, the membrane that lines all the joints of the body. It is a common disorder that causes uncontrolled inflammation — resulting in pain and swelling — around the joints. It is thought that approximately one percent of the adult population, worldwide, suffers from rheumatoid arthritis.

According to Caton, their findings also point to a possible answer of why the immune system targets the joints in the first place. Regulatory T cells influence other types of T cells to produce a substance known as IL-17, and these cells often travel through the body’s lymphatic system where they then drain out into the joints.

“One idea is that the immune system isn’t deliberately attacking joints in patients with rheumatoid arthritis,” Caton said, “but the joint inflammation is a side effect of the natural tendency of these cells to accumulate in these areas of the body.”
The Epstein-Barr virus is a remarkable virus not only for its ubiquity (nearly every adult human on Earth has been infected by it) but also because of how it evolved to become, in a sense, part of us.

As a supplement to the EBV genome — the characterization of the virus’s genes — the atlas describes the epigenome — all the protein and chemical decorations added to the EBV DNA that get passed along to new copies of the EBV virus — and the transcriptome — the catalog of all the RNA transcripts created from EBV DNA, which are either coded into proteins or serve to regulate DNA directly. The project was funded through the National Institutes of Health and published in the journal Cell Host & Microbe.

“Epstein-Barr is a human tumor virus associated with many carcinomas and lymphomas and how it is regulated is something we need to understand in detail,” said Paul Lieberman, Ph.D., the McNeil Professor of Molecular Medicine and Translational Research and director of Wistar’s Center for Chemical Biology and Translational Medicine. “The EBV atlas is an instructive guide for how to analyze an entire, intact genome.”

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Aubrey Watkins, Ph.D., a member of Wistar’s Leadership Council, takes a tour of the temporary laboratory of Andrew Caton, Ph.D.

Wistar’s Louise Show, Ph.D., talks to visitors from the Pennsylvania Lung Cancer Partnership.

2012 Ching Jer Chern Memorial Award

The annual Chern award is given to the postdoctoral fellow who has written the most outstanding scientific paper in the previous year. This year the awardees were Haikun Wang, Ph.D., and Xiaoming Feng, Ph.D. from the laboratory of Hui Hu, Ph.D. The award was established in 1989 by June Chern in memory of her husband, Wistar scientist Ching Jer Chern, Ph.D. Each year, the Chern family also donates generously to Wistar, and this year the family gave over $17,000 to the Institute.

Host of WHYY’s Radio Times, Marty Moss-Coane, interviews Sam Kean for a Wistar Authors Series event.

Tea with Wistar making an impressive showing at the 2012 Running for Cover 5K.

Outstanding In Their Field: The Widener University women’s softball team, under the direction of head coach Fred Dohrmann (standing, r), raised $1,800 for Wistar’s Melanoma Research Center while overpowering Cabrini College in a doubleheader. The team chose the WRC for their annual fundraiser because of Dohrmann’s struggle with melanoma and to raise awareness of the disease.
focus: fall 2012

Wistar Hires Chief Operating Officer

In September of 2012, Wistar saw a new addition to the Institute’s administrative suite of offices in the form of Chief Operating Officer (COO) Alan Stiles. Stiles, a creative senior executive with a 25-year success in finance and business operations, is Wistar’s first COO.

In this role, Stiles will manage and direct the Institute’s non-scientific operations and provide leadership in planning for Wistar’s continued growth. His responsibilities will cover financial and grants management, human resources, information technology, procurement, facilities, technology transfer, communications, development and other areas of general administration.

“In short, Alan’s job is to ensure that Wistar runs smoothly and provides our researchers with an outstanding environment for the conduct of science,” said Wistar President and CEO Russell E. Kaufman, M.D. “As Wistar continues its expansion, growing its faculty, its programs, and building a new research facility for its scientists, we welcome someone of Alan’s professional caliber to ensure we remain an efficient and lean organization.”

Stiles has a long history with academic research, managing operations for the Howard Hughes Medical Institute, and overseeing administrative services at Baylor College of Medicine, the Salk Institute, University of California, San Diego, University of California, Los Angeles, and University of Texas Southwestern Medical Center, among others. Among his positions outside of academia, Stiles was Director of Administration for the Washington, D.C. office of McKinsey & Company.

ACGT Foundation Supports Innovative Ovarian Cancer Therapy

It has been an extraordinary time for Hui Hu, Ph.D., an assistant professor in Wistar’s Tumor Microenvironment and Metastasis Program. First, the publication of what may be a seminal discovery on T cell quiescence—a “standby mode” mechanism in white blood cells that tumors can manipulate to their advantage. Then, Hu received word of his first federal R01 grant—a gold standard for research funding and a necessary component of a successful laboratory career.

Now, Hu has received a three-year, $300,000 Young Investigator Award from ACGT — Alliance for Cancer Gene Therapy — to turn his theories on T cell biology into a viable ovarian cancer therapy. Top of his list of future successes, receiving the award was “like receiving an ice-cold beer after a hard day’s work,” said Hu.

ACGT is the only public charity in the nation exclusively funding cancer cell and gene therapy research. According to Margaret C. Cianci, executive director of ACGT, the Young Investigator Award is a peer-reviewed grant for tenure track assistant professors conducting innovative exploratory research, and Hu received outstanding comments from both reviewers and ACGT’s Scientific Advisory Council members.

“We are honored to support Dr. Hu’s innovative research for ovarian cancer, a cancer with very few treatment alternatives,” said Cianci. “Dr. Hu’s immunotherapy approach to ovarian cancer is considered both exciting and feasible.”

The award will allow the Hu laboratory to study the effectiveness of genetically manipulating tumor-reactive T cells in order to transfer them back into patients. This “adoptive T cell transfer therapy,” would enable a patient’s own immune system to attack tumors. The funding will allow Hu to collaborate with Jose Conejo-Garcia, M.D., Ph.D., a Wistar associate professor and co-leader of the Tumor Microenvironment and Metastasis Program, using Conejo-Garcia’s ovarian cancer models.

“Knowledge obtained from Dr. Hu’s studies could lead to the design of new therapeutic strategies that manipulate T cell activation against ovarian cancer, and possibly other autoimmune and infectious diseases,” Cianci said.

“Science means to discover something new,” Hu explained, “and the support from ACGT is coming in at such a crucial moment that it allows us to branch out to try something new. It is absolutely a wonderful feeling.”

Wistar has partnered with the Hu laboratory to study the effectiveness of genetically manipulating tumor-reactive T cells in order to transfer them back into patients. This “adoptive T cell transfer therapy,” would enable a patient’s own immune system to attack tumors. The funding will allow Hu to collaborate with Jose Conejo-Garcia, M.D., Ph.D., a Wistar associate professor and co-leader of the Tumor Microenvironment and Metastasis Program, using Conejo-Garcia’s ovarian cancer models.

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Zhang Bolsters Wistar’s Ovarian Cancer Research Ranks

In the Spring of 2012, Rugang Zhang, Ph.D., became the latest recipient to The Wistar Institute, as an associate professor in the Gene Expression and Regulation Program of The Wistar Institute Cancer Center. Zhang studies the molecular biology of ovarian cancer, and joins Wistar from the Fox Chase Cancer Center.

According to Zhang, he was attracted to Wistar’s collaborative and engaging environment. His expertise in ovarian cancer complements a growing collective of ovarian cancer researchers at the Institute. “It was an easy choice to come here,” Zhang said. “The science here at Wistar is exciting, and the University City biomedical research community is interactive and vibrant.”

Rugang’s experimental program is an ideal match to Wistar science as it combines the most rigorous, mechanistic research with disease-relevant approaches to better understanding tumor onset and progression in humans,” said Deirdre Altieri, M.D., chief scientific officer and director of the Institute’s Cancer Center. “His passion for cancer research is only matched by his utmost dedication to making a difference in understanding and better treating the disease in people.”

Born and educated in China, Zhang received his Ph.D. from the Institute of Biochemistry and Cell Biology, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences in 2002. He completed his post-doctoral training at the Institute for Cancer Research at Fox Chase Cancer Center, where he became an assistant professor in 2008.

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The Zhang laboratory studies the molecular events that underlie how normal mammalian cells age and how tumors cells evade the aging process in order to become cancerous. In particular, his laboratory is interested in how alterations in epigenetics — heritable changes that affect gene expression without changes in the underlying DNA sequence — help tumors evade the aging process.

According to Zhang, understanding these mechanisms could lead to novel strategies for developing cancer therapeutics by forcing tumor cells to age. His laboratory primarily focuses on ovarian cancer, which ranks first as the cause of death among gynecological cancers in the developed world.

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Donor Advised Funds Drive Charitable Giving

Daniel Wheeler first set up his Donor Advised Fund in 2006. “It was a timing issue,” he said. “We had some extra income that year. The Donor Advised Fund provided a means to spread out the donations while getting the tax benefit when we needed it.” Wheeler and his wife, Amy Fox, have made more than 50 donations through their fund in the last 12 years, including several to Wistar. He was introduced to Wistar’s work through his father-in-law, long time supporter, board member and current chair of the Building Wistar, Changing the World campaign, Robert A. Fox.

Andrew Swinney, President of The Philadelphia Foundation, suggests that the Donor Advised Fund is an excellent option for people who to be active philanthropically and are looking for an efficient, flexible vehicle. “The Donor Advised Fund came into being in 1969 following some of society’s most successful families and investment firms made them available,” Swinney said. “Today, many charitable organizations sponsor them as well. They have become a very successful way of giving.”

A Donor Advised Fund works this way. The donor makes a charitable gift in a lump sum to the fund. He or she can then take the full tax deduction for that money in that year — but the grants can be made over a period of years to different organizations in different amounts. Once the gift is made, the donor legally gives up control of the money to the sponsoring organization, but can advise or make recommendations on how and when it is used. While there are several limitations, the standard is for the gifts be made according to the donor’s recommendations. Donor Advised Funds are not legal entities and do not require any specific structure such as a board of directors.

“Some people see that lack of control as a negative,” said Wheeler, “but we have never had any problems. All of our donations have been made as requested.”

Donor Advised Funds cannot be used to honor pledges made to an organization, and the donor cannot derive any benefit from the gift. Gifts of this type, for example, are not appropriate for buying tickets to events.

“I have never seen our Donor Advised Fund as a substitute for other types of giving,” said Wheeler. “We use it to make smaller gifts, but continue to make other gifts as individuals, such as the pledge we made to Wistar’s building campaign.”

Swinney views the Donor Advised Fund not just as a convenient means of making donations over a period of years, but also a potential stepping stone to a larger commitment. “We like to think about this more relational. For people who are interested in building relationships with the organizations that they are supporting, we recommend considering establishing a private foundation or a foundation. That ensures that the donor is informed about the work being done there and more involved in its activities.”

For more information about these donor options at Wistar, contact Peter Coronado, Vice President of Institutional Development at corona@wistar.org or 215.898.3771.

Wistar Shares its Brains with London

As a net-exporter of scientific discovery, The Wistar Institute has never been shy to share its brains with the world. Recently, however, the world was privileged to see how very large our brains can be. This spring, the Wellcome Collection, a museum hall established in London by Wellcome Trust, included items from the Wistar archives in its latest exhibit, “Brains: The Mind as Matter.”

The exhibition explores what humans have done with and to brains in the name of medical intervention, scientific inquiry, cultural meaning and technological change. Items from the Wistar archives include articles from the early 20th Century documenting Wistar’s pioneering work on the relationship between brain size and intelligence (answer: there isn’t really any).

However, the showpiece from the Wistar collection is the teaching model pictured here, which was most likely purchased by Joseph Leidy, M.D., around 1850 while traveling through Paris. Leidy was curator of the Wistar and Horner collection at the University of Pennsylvania prior to its transfer to the Institute in 1894. The brain model, which is roughly 4-feet long, is color-coded by region to make it easy to use as a prop during lectures.

According to Wellcome, over 100,000 visitors toured the exhibit, the busiest event since the museum opened its exhibit space in 2007.

The Wistar Institute on Display at the Second Annual Philadelphia Science Festival

It is a celebration of science in a city with a rich scientific legacy and, in its second year, the Philadelphia Science Festival continues to grow. This spring, The Wistar Institute, a founding member of the festival, was featured prominently in events across the city during the festival’s two-week run.

Can you solve this clue? While his nameake biomedical research institute is in University City and his nameake vine, Wisteria, can be found flourishing all over Philadelphia, this physician and professor of anatomy hosted his famous scientific salons of the 1800s in Old City on a street named for a different botanical specimen. If you knew that Caspar Wistar, M.D.’s home is on the corner of Locust Street, then you would have been a great competitor in the Science Scavenger Hunt during this year’s Philadelphia Science Festival.

At the “Visualizing the Body Beautiful” exhibit held at the Philadelphia Academy of the Fine Arts, Wistar’s Nina Long, director of Library Services and Archivist, joined noted experts in medical and anatomical illustration. Long’s presentation followed the evolution from classical medical drawing to the modern form of the art.

Wistar’s premier event was “The Great Vaccine Debate,” a panel discussion held at The Academy of Natural Sciences, and featuring Hilldegund G.J. Erll, M.D., director of The Wistar Institute Vaccine Center, Paul A. Offit, M.D., director of the Vaccine Education Center at the Children’s Hospital of Philadelphia and Wistar adjunct professor, Jason Schwartz, M.B.E., A.M., associate fellow at the University of Pennsylvania Center for Bioethics, and author Mark Largent, Ph.D., whose book inspired the title for the event.

The festival culminated with the Science Carnival and again crowds flocked to Wistar’s booth on Logan Circle, where Wistar volunteers helped visitors explore the microscopic world that lives inside their cheeks.
The Wistar community has lost a respected colleague in H Fred Clark, D.V.M, Ph.D., who died this past May after a long illness. Clark was one of the mighty triumvirate of researchers, including Stanley Plotkin, M.D., and Paul Offit, M.D., who are chiefly responsible for the rotavirus vaccine RotaTeq®, which has made a tremendous difference in the health of children here in the U.S. and around the world.

The vaccine, which protects against the highly contagious virus was approved and became part of the recommended vaccine schedule for U.S. babies in 2006. It is used in 16 countries and is approved in 30 more. The vaccine was co-developed at Wistar and Children's Hospital of Philadelphia (CHOP) in the 1980s.

In a remembrance published this August in the journal *Human Vaccines and Immunotherapeutics*, Plotkin recounts that it was Clark’s innovative efforts in genetic reassortment — combining elements of human and bovine rotavirus — that helped make RotaTeq® a safe and effective vaccine. According to Plotkin, estimates at the time suggested that rotavirus killed 600,000 infants each year, worldwide.

Those who knew him remember Clark for his keen sense of ethics and his intellectual vigor. He was a man who knew he was working toward an urgent, greater good and he performed his work accordingly. In the obituary published in *The Philadelphia Inquirer*, Clark’s wife, Karen Clark, was quoted as saying her husband “was committed to social justice, as important to him as his scientific research.”

Wistar President and CEO Russel Kaufman, M.D., recalled, “Whenever I hear stories about Fred, what becomes apparent time and again is his sense of humor. He had a quiet wit that he could unleash with devastating impact when the need arose.”

In June 19, Wistar lost a longtime friend and supporter with the death of former Wistar board chair Kevin M. Tucker. Over the last three decades, Tucker was a strong leader and vital member of the Wistar community.

By any standard, Tucker led an extraordinary life of achievement. From humble beginnings as a beat cop in Rahway, New Jersey, he became a highly ranked and decorated agent in the United States Secret Service. His assignments took him from guarding Jacqueline Kennedy and her two children to protecting Pope John Paul II on his historic visit to Philadelphia in 1979. In Philadelphia, he may be best remembered in his transformative role as the Philadelphia Police Commissioner, rebuilding the police department following the tragedy of the MOVE conflict in 1985.

“Mr. Tucker was a vital part of the Institute serving as chair of our board from 1998 to 2005, and tirelessly advocating for cancer research. His guiding vision and steady hand helped lead the Institute through an era of shrinking federal research budgets and organizational changes,” said Wistar President and CEO, Russel E. Kaufman, M.D. “His strategic mind and vision helped set Wistar on its current path, but it was his kindness and his devotion in service to others that truly inspired.”

After his career in law enforcement, Tucker moved into the banking industry, from which he eventually retired as vice president at PNC Bank. This next phase of his life was dedicated to the service of others. He founded the Corporate Alliance for Drug Education and was deeply involved in organizations such as the Boy Scouts and the Police Athletic League — groups that all served to make a lasting difference in the lives of young men and women.

“Of course, we will always be grateful that, in 1992, a man of such wisdom and resourcefulness as Kevin Tucker joined The Wistar Institute Board of Managers,” Kaufman said. “Despite his illness in recent years, he maintained his active engagement on the board, and his presence at many special Wistar events, such as the groundbreaking for the new research building and the Annual Taxin Golf Classic, helped raise the spirits of all who attended.”

Fred Clark (1937-2012)

Kevin M. Tucker (1940-2012)
In appreciation of a rich history and in anticipation of a promising future

The Wistar Institute invites you to spend an evening reflecting on its 40 years of discovery as a National Cancer Institute-designated Cancer Center and the future of cancer research.

Thursday, November 15, 2012
6:00–8:00pm
WHYY Studios • 150 N. 6th St. • Philadelphia, Pennsylvania

Reception + Program + Video Screening

Kindly respond by November 9th by visiting wistar.org/40yrs-cancercenter
Inquiries: 215.898.3955 or specialevents@wistar.org

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