EXPEDITION WISTAR

EXPLORING THE FRONTIERS OF BIOMEDICINE

THE WISTAR INSTITUTE ANNUAL REPORT 2010

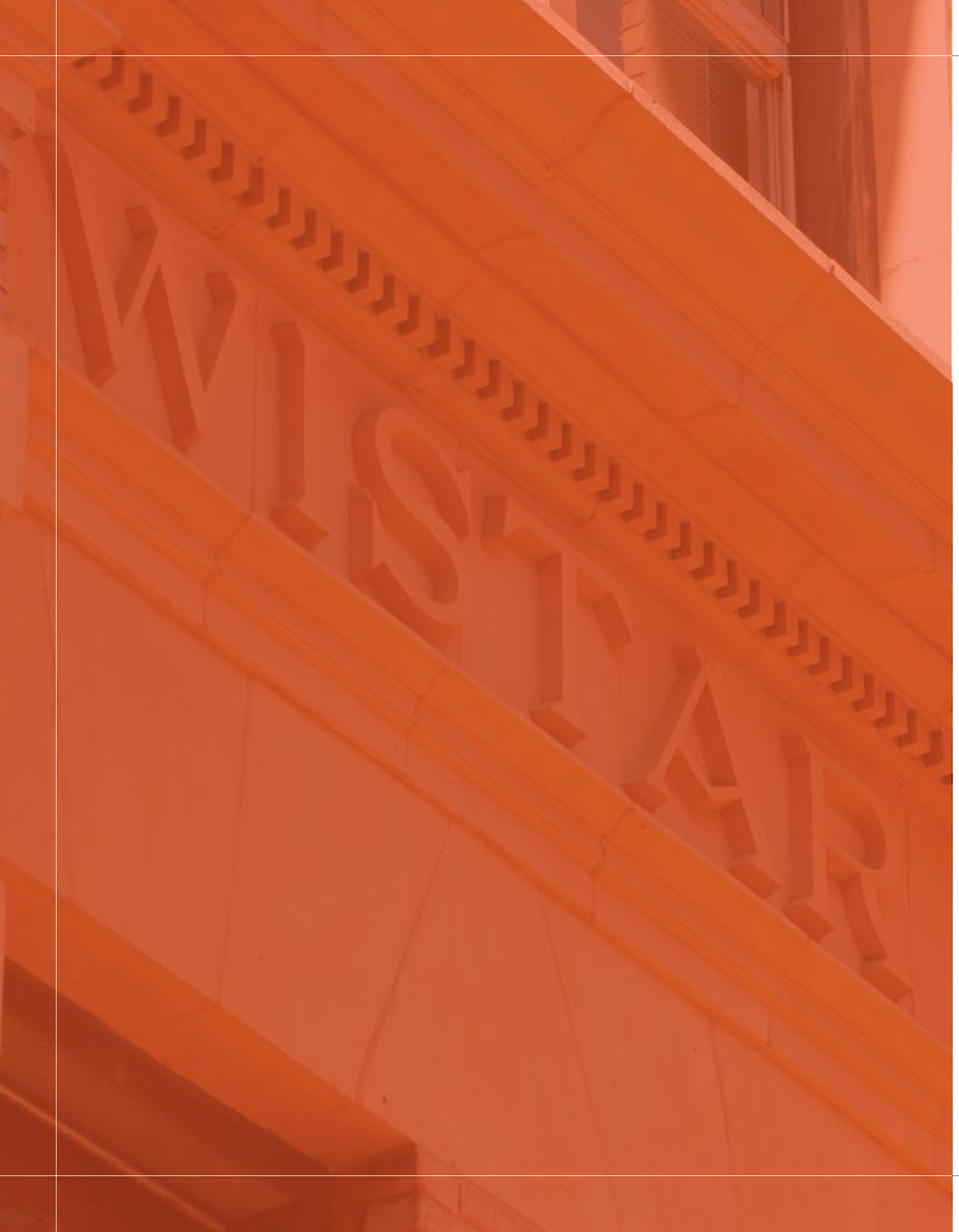
In the years ahead, I believe many of us will look back on 2010 as a seminal moment in the history of the Institute, a year in which we embarked on a journey that changed the face, and the future, of Wistar.

Following the course set forth in our strategic plan, we began expanding our research faculty by recruiting a new Cancer Center director and other talented faculty members. We completed preparations for the Institute's first major expansion project in almost 30 years, and we laid the groundwork for a capital campaign to support our ambitious agenda. These critical steps will enable us to expand our research into new scientific directions, the emerging frontiers of biomedical research.

This exploration of emerging scientific frontiers is not unlike the great expeditions — Christopher Columbus' search for a better spice trade route, Lewis and Clarke's journey to chart the American frontier, Neil Armstrong's first steps on the surface of the moon. Wistar scientists start with a goal — an AIDS vaccine, for instance, or a cure for melanoma. Stoked by the adventurous spirit of the explorer and the inquisitive nature of the scientist we launch our own expeditions into the frontier to understand the intricacies of human biology, health and disease. We reach important milestones along the way and gather new ideas and perspectives through collaborations with our colleagues. It is the tantalizing promise of the major discovery — Columbus' New World, Armstrong's giant leap for mankind — that spurs us on.

Expedition Wistar has launched. I invite you to join us on our fantastic journey into the frontiers of biomedical research.

Russel E. Kaufman, M.D.
President and CEO



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The shortest distance between two points is a straight line. But the nature of biomedical research is rarely so straightforward. It is more a winding path, with many forks in the road. Some lead to disappointing dead ends. Others wind off in surprising and promising new directions never imagined at the outset of the experiment.

It is the desire to take risks and explore the frontiers that distinguishes the great leaders in science. From clarity of vision and deep curiosity to follow that obscure fork in the road come the scientific breakthroughs that benefit humankind.

A great research institute distinguishes itself by charting a course that supports its intellectual risk-takers with tools and resources and an exceptional environment in which to pursue scientific research. This has been the hallmark of The Wistar Institute, from its inception in 1892 to today.

Exploring with gusto the frontiers of biomedical research has long been the tradition here. A steady hand at the helm guides the enterprise.

Under the leadership of President and CEO Russel E. Kaufman, M.D., Wistar has set a strategic plan for expansion of the Institute — its faculty, the scope of its research programs and its facilities.

At the top of the agenda is a considerable expansion of the faculty. The opportunity to strategically diversify Wistar's faculty will allow us to match current strengths with new and complementary expertise in emerging fields of discovery, such as the study of the tumor microenvironment, or the role of RNA in gene expression and regulation. The expansion will ramp up the activity and capacity of every team working on genetics, vaccines and cancer research.

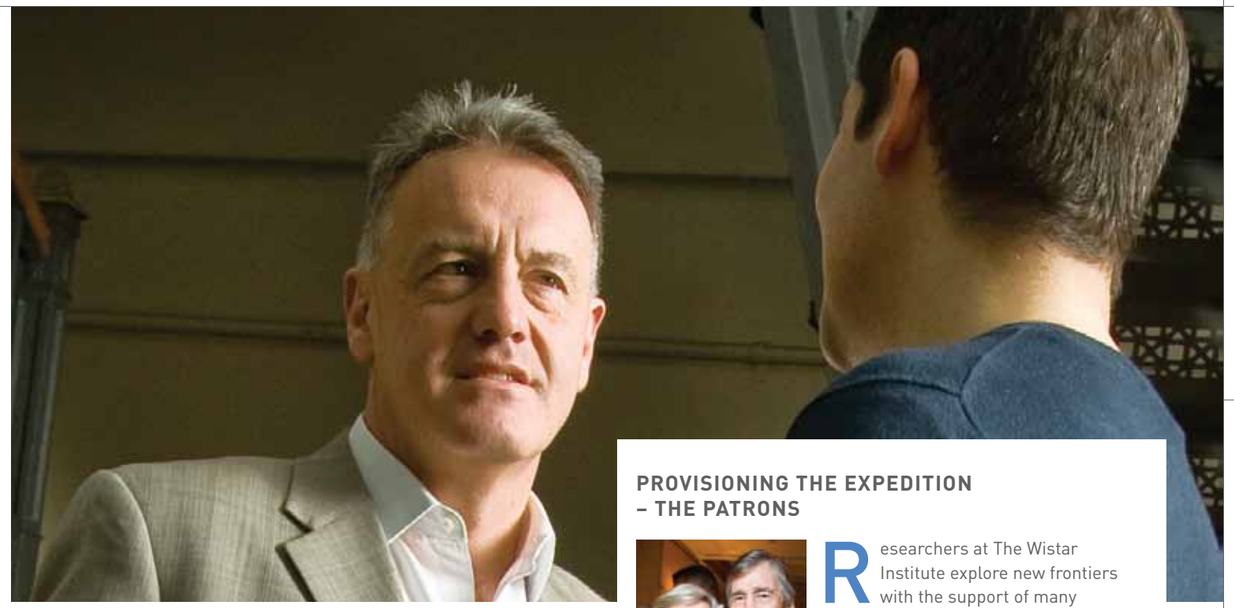
Leading the faculty and targeted recruitments and setting overall research direction is the charge of the new chief scientific officer and director of The Wistar Institute Cancer Center.

Dario C. Altieri, M.D., Robert and Penny Fox Distinguished Professor, joined Wistar in July, 2010 with a deep appreciation for the role of basic research as an engine for clinical innovation.

Altieri arrived at a time when Wistar's leadership had embarked on another visionary path — its first major physical expansion in decades. At a point in time ripe with potential for major breakthroughs in genomic research, the Institute was constrained by aging facilities designed for 20th-century science. Today's brand of Wistar science requires space and infrastructure to foster work that is both multidisciplinary and collaborative.

Plans call for the construction of a seven-story research tower which features vast, open laboratory space. Multidisciplinary teams of researchers will work in these laboratories where open floor plans will facilitate the kinds of interactions that spark creativity and innovation. The new building will take Wistar's intellectually rich environment to a whole new level.

The crew is assembling, the ship is under construction, we are provisioning the expedition. The Wistar Institute stands poised at the leading edge, ready to follow the next fork in the path to a new world of discovery. ■



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Wistar Cancer Center Director Dario Altieri confers with a colleague.

PROVISIONING THE EXPEDITION – THE PATRONS

Researchers at The Wistar Institute explore new frontiers with the support of many generous individuals. With their passionate commitment to the Institute, two in particular rise above: Robert and Penny Fox.

The Foxes' support of Wistar stretches back to the 1970s, when Bob joined the Board of Trustees. His vision and leadership as president of the Board from 1984 to 1994 helped lay a strong foundation for future growth of the Institute to its present position as an international leader in biomedical research.

"Bob Fox's support for Wistar has been not only generous, but consistent," said Wistar Board Chairman Brian Dovey. "He has been instrumental in putting the Institute on the road to becoming a truly top-tier research organization."

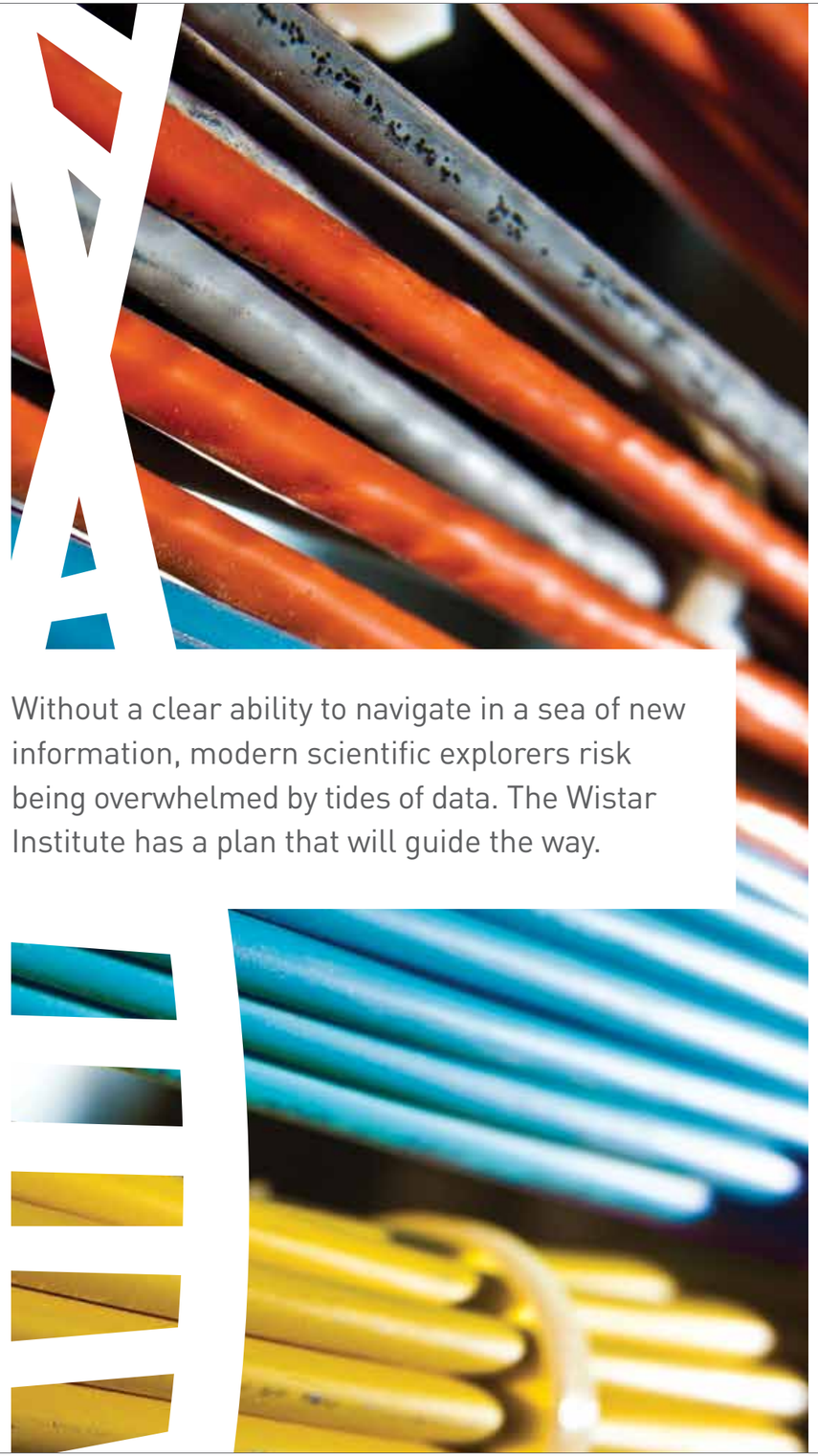
The Foxes are the most generous donors to The Wistar Institute since its founding in 1892, making major contributions to Wistar in support of capital campaigns, and funding special projects, such as the 1991 auditorium renovation which was named in honor of Penny's father, Joseph N. Grossman, M.D.

In 1995, they established The Robert A. Fox Structural Biology Center to support research into the structure and function of key biological molecules. The gift demonstrates both altruism and foresight; Wistar's structural biologists today are making important discoveries that provide the framework for developing new drugs for treating cancer and other diseases of aging.

In 2006, the Foxes funded the Robert and Penny Fox Distinguished Professorship to support a world-class cancer researcher. The Fox Professorship was used to recruit the new director of The Wistar Institute Cancer Center, Dario C. Altieri, M.D.

Their generosity continues. Always with an eye on the future, Bob will burnish his imprint on the Institute as chair of the five-year *Building Wistar, Changing the World* capital campaign to fund construction of the new research tower.

VOYAGE to the Bottom of the ‘Omes



Without a clear ability to navigate in a sea of new information, modern scientific explorers risk being overwhelmed by tides of data. The Wistar Institute has a plan that will guide the way.

In 2000, when the first draft of the human genome was published, the Human Genome Project was promoted as an atlas for charting the course of human health. It quickly became clear, however, that science had only scratched the surface of the complexity that underlies genetics. As any explorer knows, the potential payoffs of discovery are vast, yet the risk of getting lost is an ever-present danger.

Without a clear ability to navigate in a sea of new information, modern scientific explorers risk being overwhelmed by tides of data. The Wistar Institute has a plan that will guide the way.

“The payoffs to understanding the human genome continue to unfold with every new discovery or personalized therapeutic treatment,” said Russel E. Kaufman, M.D., Wistar president and CEO. “In recent years, Wistar has made bold investments in technologies and Centers that will enable scientists to sift and sort through enormous sets of research data to create more precise therapeutics and a deeper understanding of human biology.”

According to Kaufman, focused recruitment and the Institute’s desire to drive scientific discovery to medical reality has enabled Wistar to create team-based, technology-driven research initiatives. These are the Center for Systems and Computational Biology (CSCB) and the Center for Chemical Biology and Translational Medicine (CCBTM).

The CSCB combines advanced gene sequencing systems, generations beyond the platforms used a mere 15 years ago at the outset of the Human Genome Project, with racks of computer servers capable of sorting and analyzing complicated data sets.

The CCBTM, a partnership with University of the Sciences in Philadelphia (USciences), combines USciences’ expertise in medicinal chemistry and pharmacology with Wistar’s strengths in basic science and its $1.1 million Molecular Screening Facility. The facility, capable of screening over 150,000 candidate molecules at once, allows the CCBTM to find therapeutic targets with potential inhibitors to disease-causing proteins, which can then be further refined into usable drugs.

“The two centers complement each other nicely, by design,” Kaufman said. “The CSCB is in the business of discovering new targets of therapeutic interest while the CCBTM is in the business of hitting those targets.”

THERE’S NO PLACE LIKE THE ‘OMES

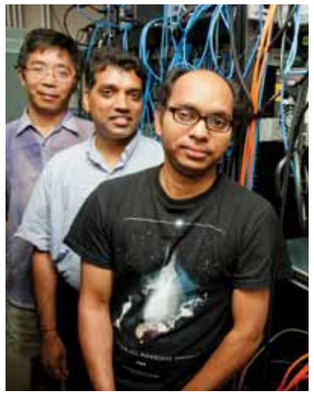
“It was not until the Human Genome Project that the average person was aware of the genome — the sum total of genes written into our DNA,” said David W. Speicher, Ph.D., Wistar professor and director of the Wistar CSCB. “The genome alone, pundits speculated, would have a profound effect on our understanding of genetic disorders and our susceptibility to disease. And they were right, but only to a certain extent.”

As we learned more about the human genome and those of other animals, Speicher says, we found that it was essential to learn more about how our cells use the genome.

And so they emerged: the ‘Omes, layer after layer of additional information.

There is the proteome (the sum total of proteins and protein variations that DNA encodes); the transcriptome (the sum total of all the RNA transcripts written from DNA); the promoterome (the sum total of “gene promoter” locations — sites on DNA where the cellular machinery promotes transcription); the epigenome (the sum total of the many ways molecules can influence genetics without altering DNA sequences); and many more, culminating in, perhaps, what is referred to as the interactome (the sum total of the interactions amid all of the other ‘omes).

“Scientists are good at generating data, almost too good, in fact, as our ability to produce data about the genome and its associated functions has far outstripped our ability to make sense of it,” said Ramana Davuluri, Ph.D., Philadelphia Healthcare Trust Professor. “Finding interactions and putting information into a real world context — this is what bioinformatics is about, this is how we make sense of our data.”



Ramana Davuluri, Ph.D. (center) and colleagues mine vast sets of genetic data for clues in their search for new therapies.

In 2010, Davuluri, associate director of the CSCB and director of computational biology, spearheaded the creation of The Mammalian Promoter Database (MPromDb) which integrates the genome sequencing data generated at Wistar with publicly available data on human and mouse genomics. MPromDb pinpoints known promoters and predicts where new ones are likely to be found. "With this information, researchers can design personalized diagnostics and therapeutics or delve deeper into the study of gene regulation than previously thought possible," Davuluri explained.

Through the CSCB, Wistar scientists can take complicated sets of data and boil them down to their essential nature, highlighting distinct points amid these tangled, interrelated genetic systems where therapeutic treatments will have the most effect.

The ultimate result will be improved targeted drugs; better biomarkers that will enable efficient tests for disease diagnosis, patient prognosis and predictions for a patient's response to treatment; and a deeper understanding of the biology of life.

FOUND IN TRANSLATION

If the CSCB represents the ability of Wistar to make sense of complicated biological processes, the Center for Chemical Biology and Translational Medicine represents the ability of Wistar to put this information to use. The primary goals of the Center are to develop and use small molecules to study and probe the biology of living systems. This approach is expected to identify new chemical agents that can be developed to work against biological targets — such as genes and proteins — known to be involved in human disease.

Using the capabilities of Wistar's Molecular Screening Facility, CCBTM molecular biologists can identify and characterize new molecules and compounds that hold the most promise for developing into therapeutic drugs for cancer and other diseases. Such compounds will then be "handed off" to computational and medicinal chemists at USciences for further refinement into potential new drugs.

In 2010, USciences and Wistar named Wistar Institute principal investigator Paul M. Lieberman, Ph.D., an expert in gene expression and regulation, as the McNeil Professor of Molecular Medicine and Translational Research. His task is to steer the exploration into uncharted waters of drug discovery, allowing the CCBTM to find new therapeutics based on emerging scientific data.

"We are here at the cusp of drug discovery, the moment where we can custom design novel drugs to hit novel molecular targets," said Lieberman. "While the pharmaceutical industry may have an interest in producing new therapies, they do not have the capability or interest in assuming the risk of 'early phase' drug discovery work."

With high risk, Lieberman says, come high rewards. And as Wistar delves deeper into genomics and its related disciplines, there will be no shortage of new places to explore. ■

Staking a Claim IN MELANOMA

The most aggressive, deadly form of skin cancer is where Wistar has planted its flag. This is where Wistar has staked territory and declared, "This disease ends here."

Meenhard Herlyn, D.V.M., D.Sc., (center) and colleagues search for a cure for melanoma.

In the history of The Wistar Institute, 2010 will be seen as a watershed year in the fight against melanoma. It marks the establishment of Wistar's Melanoma Research Center (MRC), an effort that reflects decades of research excellence and relationship building at Wistar. It is an effort guided by Wistar's team-based philosophy, leveraging the expertise of researchers here and across the world to prevent, detect and — most importantly — vanquish metastatic melanoma.

Coinciding with the birth of the Center are the first clinical trials of vemurafenib, a targeted anti-melanoma therapy whose origins can be traced to research conducted at Wistar and whose eventual refinement and success may depend on research currently underway here. (See story, p. 13)

The MRC is directed by Meenhard Herlyn, D.V.M., D.Sc., who, as a Wistar professor, has maintained what is possibly the world's largest laboratory effort against melanoma. Since the 1970s, Herlyn has steadily built an impressive body of knowledge about the nature of melanoma tumors — from the genes that drive them to the way they react with the surrounding tissues of the body. In that time, Herlyn has built an almost equally impressive set of relationships among physicians, other researchers, the pharmaceutical industry, and advocacy groups that act on behalf of melanoma patients and their families.

"The MRC is the formalization of what we have had here for many years, both in terms of the scientific research program and the ties we have built to the greater melanoma community," said Herlyn. "The scientific tools and technologies have finally caught up with our aspirations, so now we need to channel our energies into driving basic science into clinical applications."

"Among cancers, melanoma presents its own unique set of challenges," Herlyn said. "Yet the lessons we learn in defeating or preventing melanoma will provide a platform to fighting almost every cancer."

WHY MELANOMA?

Melanoma is managing to defy the overall trend in declining cancer rates. Melanoma affects 68,000 Americans each year and will kill 8,600, two figures that have doubled over the last 30 years. At its earliest stages, melanoma can be effectively cured surgically, but at its later stages it is a persistent, defiant tumor that easily spreads and develops resistance against any therapy.

"The hallmark of melanoma is its tenacity," Herlyn said. "Each melanoma tumor is a highly-efficient engine of evolution, using and manipulating every gene at its disposal in order to thrive."

In 2010, Herlyn and his colleagues redefined the biology of melanoma with the discovery of what they term "dynamic stemness." In recent years, cancer researchers have pointed to so-called cancer stem cells as the source for drug resistance and the inevitable return of certain tumors. Cancer stem cells, like the stem cells that drive fetal development, serve as the source for other cancer cells.

The Herlyn laboratory's discovery upends the entire notion of cancer stem cells, at least as they apply to melanoma. They found that all melanoma cells equally harbor cancer stem cell potential and are capable of inducing new tumors, not just individual cells. Any cell that survives a given therapy has the ability to resurrect a tumor. Dynamic stemness, they say, means that 100 percent of a tumor must be destroyed in order to kill melanoma.

"A targeted therapy that kills 99.9 percent of a melanoma tumor still misses the mark," Herlyn said. "The way forward is through combination therapies — identifying and striking multiple targets in a way that will completely destroy the tumor, denying it an opportunity to regenerate."

Jessie Villanueva, Ph.D.

Mizuho Kalabis, Ph.D.

Ashani Weeraratna, Ph.D.

According to Herlyn, the key to killing melanoma through targeted therapies is a complete understanding of the active genes and their relationships to one another. The signals that tell melanoma cells to grow and divide travel down pathways, cascades of protein interactions that, in normal cells, work in careful balance to ensure a cell behaves in a controlled, orderly fashion. All cancer cells manipulate these pathways to ensure their own survival.

If you block one pathway with a therapeutic, it will encourage the survival of melanoma cells that use alternate pathways, Herlyn says. A priority of the Herlyn laboratory over the last 35 years has been defining the genes that drive melanoma cell growth and understanding how they interact with each other to promote melanoma cell survival. His laboratory and that of his wife and colleague Dorothee Herlyn, D.V.M, D.Sc., who retired from Wistar in 2010, conducted the early genetic research that led to a number of therapeutics in development, including BRAF inhibitors (see story on page 13).

"There are currently a number of drugs in the pipeline that work on separate chemical pathways within melanoma cells, but the biggest obstacle to using these drugs synergistically is convincing the drug companies and the drug regulators that this makes sense," Herlyn said. "This is where the Melanoma Research Center will make a huge difference."

THE WISTAR INSTITUTE MELANOMA RESEARCH CENTER

The MRC combines Wistar's home-grown knowledge and tools with the talents of researchers across the Institute. In addition to the Herlyn laboratory, the MRC includes the laboratory of David W. Speicher, Ph.D., whose expertise in advanced screening methods will uncover new clinical indicators, known as biomarkers, that will enable doctors to better diagnose patients and chart their course of therapy. The structural biology laboratory of Ronen Marmorstein, Ph.D., uses an advanced understanding of the physical makeup of proteins to build new therapeutics against melanoma. They are joined by new Wistar principal investigators including Ashani Weeraratna, Ph.D., who arrived at Wistar from the National Cancer Institute in 2011, and Jessie Villanueva, Ph.D., who trained in the Herlyn laboratory and was promoted in 2011 to the rank of assistant professor.

In addition to the body of melanoma knowledge generated at Wistar, chief among the MRC's tools is the so-called "artificial skin" invented and refined in the Herlyn laboratory. Human cells grown in the laboratory do not typically behave like cells that grow in actual humans. Instead, they form a thin layer on a petri dish. Real cells live in three dimensions, they interact with their own kind and with cells in the surrounding tissue, which they rely upon for both nourishment and information. Artificial skin is a three-dimensional cell culturing system that recreates the natural microenvironment of melanoma cells to the best of current technical ability.

The result is a much more realistic look at tumor behavior, both in terms of how melanoma cells function and how they respond to new drugs or combinations of drugs.

However, scientific resources and technical expertise alone will not drive the next generation of melanoma therapeutics. Major advances in this field will require another asset that is unique to Wistar: relationships.

As an independent academic biomedical research organization, Wistar stands apart from both the worlds of clinical medicine and pharmaceutical development, yet it can muster scientific resources available to neither. Wistar can champion the sort of dialogue demanded by patient advocacy organizations, such as the Melanoma Research Foundation and The Noreen O'Neill Foundation for Melanoma Research.

"Combining all of our resources is what is going to defeat melanoma," Herlyn said. "We have built the tools, we have gathered the talent and — perhaps most importantly — we have the will to see it done." ■

A MOST PROMISING DISCOVERY

In the early part of 2010, clinical trial results of the next best hope for advanced melanoma, PLX4032, a drug also known as vemurafenib, were announced. The drug targets a specific mutation in the BRAF gene that has been found to be involved in a subset of inoperable melanomas.

Reports of the drug trial described shrinking tumors and improved health. Yet seven months after therapy began the tumors returned and resumed growing. Wistar scientists were involved in the early stages of research that linked BRAF mutations to melanoma and, through their involvement with the drug's maker, Plexxikon, Wistar Melanoma Research Center scientists continue to explore strategies for killing melanoma by inhibiting BRAF.

Using data from the trial, including patient samples, Wistar scientists explained why patients relapsed: the tumor learned to signal around the blocked gene by adjusting its molecular wiring. They have also shown how to overcome resistance by simultaneously targeting multiple signaling pathways.

"Cells are complex machines that work, essentially, through chains of biochemical reactions that we refer to as signaling pathways," said Jessie Villanueva, Ph.D., senior author on the study and an assistant professor working with Herlyn. "Knocking out mutant BRAF shuts a major pathway down, but if some cells can use an alternate pathway, then they can survive."

To find out which alternate pathways the drug-resistant cells use, Villanueva and her colleagues looked for signs of increased activation among proteins along the pathways BRAF uses, as well as other pathways. Their hunt turned up two paths that worked together to aid survival. First, they found that resistant cells used a protein similar to BRAF to carry the signal down the chain. Second, they found these cells received an additional boost from the IGF-1 receptor, a protein that sits on the surface of cells and sends signals that prevent cells from being killed. The resistant cells re-route the signal around BRAF by switching to an alternate protein (CRAF or ARAF), which promotes tumor cell growth, while IGF-1R signaling promotes survival of the resistant cells.

Fortunately, there are a number of compounds in clinical development that could block signals along both these pathways. So-called MEK inhibitors target a protein along the same pathway as BRAF, and IGF-1 receptor inhibitors (and inhibitors of PI3K, a protein that is activated by the IGF-1 receptor pathway) block the cancer-enabling survival signal. As predicted, a combination of these two inhibitors killed BRAF-resistant melanoma cells in the laboratory.

Moreover, tissue samples from patients in the PLX4032 trial — taken both before treatment and after they developed resistance — showed how the presence of numerous IGF-1 receptors coincided with drug resistance.

"Tumors are efficient engines of evolution — they are going to find a way around most treatments, so we want to kill all the malignant cells from the very beginning," said Villanueva. "By targeting both pathways simultaneously you hit these cells with two punches from which they cannot recover."

"If you do this at the outset of treatment, we reason, it will prevent melanoma survival and hopefully improve patient outcomes," Villanueva added.

2010

YEAR IN REVIEW

Lighting Up the Dark

WISTAR SCIENTISTS UNCOVER NEW ROLES FOR RNA

Despite substantial progress in decoding the genome, scientists estimate that fully 95 percent of our DNA represents dark, unknown territory. But studies by researchers at The Wistar Institute have shed new light on the genetic unknown with a pair of discoveries showing that some forms of RNA can actually promote gene expression, while others allow a well known virus to evade the body's immune system.

These findings join a growing body of evidence that the classic central dogma of genetics — that chromosomal DNA is transcribed into RNA, which is then translated by the cell into proteins — is still incomplete. In recent years, scientists have found that not all transcribed RNA molecules become translated into proteins. In fact, studies have shown that whole swathes of the genome are transcribed for unknown reasons.

These non-coding RNAs are small molecules that do not produce proteins and were once thought of as little more than evolutionary leftovers that littered the genome but did nothing of any importance. As it turns out, non-coding RNAs are now seen as central players in the need to maintain better control over the genome. There are several different types of non-coding RNA, including microRNA.

In the first study, published in the journal *Cell*, Wistar scientists found that long non-coding RNA actually promotes gene expression. These molecules may represent so-called gene enhancer elements — short regions of DNA that can increase gene transcription. While scientists have known about gene enhancers for decades, there has been no consensus about how these enhancers might work.

In the study, the Wistar researchers pinpointed 3,000 long non-coding RNAs and estimate that there could be a total of between 10,000 to 12,000 long non-coding RNA sequences within our DNA; this number is comparable to the 20,000 genes that are known to encode proteins. Most long non-coding RNAs are in DNA near genes known to be important to both stem cells and cancer. This also suggests that targeting these non-coding RNAs may represent a novel strategy in slowing cancer growth.

"We're very excited because this is a new discovery about the very nature of human DNA — a new class of genetic object and a new layer of genetic regulation," said Ramin Shiekhattar, Ph.D., Wistar's Herbert Kean, M.D., Family Professor and senior author of the study. "These long non-coding RNA sequences may account for the activity of enhancer elements, which have been well-studied but never quite characterized."

The scientists mapped the non-coding RNA sites within the genome, and found that non-coding RNA tended to be located near genes that influence how stem cells change into other cell types. Shiekhattar and his colleagues then developed new assays to screen cell cultures for these non-coding RNA sequences, and discovered that they were found extensively in a variety of cell types.

"We know long non-coding RNAs can promote gene expression, but now we need to know how they do it," Shiekhattar said, "which is precisely the object of our ongoing research plan."

The second study describes how viral microRNA — small segments of RNA that can suppress the effects of gene activity — allows the Epstein-Barr virus to hide within cells and evade the body's immune system. While most commonly associated with mononucleosis, Epstein-Barr virus has been linked to many diseases that affect people long after the initial infection takes place, including some forms of cancer.

In the study, published in the *Journal of Biological Chemistry*, scientists at The Wistar Institute show how the virus uses microRNA encoded among its own genes to create an elaborate timing mechanism that allows it to

quietly persist until an opportune moment to reproduce en masse. In particular, a viral microRNA called BART6 keeps the virus in a latent state by preventing the host cell from creating its own microRNA as part of normal gene regulation.

Wistar scientists believe their new findings may one day enable physicians to flush the virus out of hiding, allowing a healthy immune system to finally rid the body of it.

"Epstein-Barr infection is marked by a period of active infection and replication — the lytic stage — where it causes acute disease, but it can also remain latent, and later emerge as an effective cancer-causing agent," said Kazuko Nishikura, Ph.D., a professor in Wistar's Gene Expression and Regulation program and senior author of the study. "It's a strategy that allows the virus to survive our initial immune response and await conditions, such as weakened immunity, to reemerge."

These findings suggest that Epstein-Barr virus and humans have been engaged in what amounts to an intense microRNA arms race, where the virus evolved microRNA that specifically exploits the human host cell's own microRNA machinery. The result is a complex feedback mechanism that can be tipped into inciting cancer if the human immune system is weakened by age or HIV/AIDS infection, for example.

The research adds to a growing body of evidence that suggests that microRNA activity has a real and potent effect on health, Nishikura says. MicroRNAs are among a host of objects encoded within our DNA that help regulate how genes are read — or "expressed" — by our cells in the form of proteins. More than 1,000 so-called microRNAs are known to science, for example, and their effect on silencing genes has been well described.

MicroRNAs suppress gene activity by knocking out messenger RNA, molecules that convey genetic instructions to the cell's protein-making machinery. In effect, microRNA suppression of messenger RNA is akin to the diner manager who fires the only waiter in the middle of a shift — your order may have been placed, but the cheeseburger you asked for may never make it to your table.

"Epstein-Barr virus uses microRNA to achieve a balance between suppressing genes and promoting genes," Nishikura said. "Although it may be some time before we can manipulate microRNA as a part of patient care, these findings do offer evidence that one day we may be able to use some of the same tools our cells use to regulate gene activity." ■

Above: Kazuko Nishikura, Ph.D.
Left: Ramin Shiekhattar, Ph.D.


Ellen Heber-Katz, Ph.D.

A Single Gene Regulates Tissue Regeneration in Mammals

From a chance observation over a decade ago, Wistar scientists have identified a gene they believe may regulate tissue regeneration in mammals. The absence of this gene, called p21, confers a healing potential in mice long thought to have been lost through evolution. A study published in the *Proceedings of the National Academy of Sciences* demonstrates that mice lacking the p21 gene regain the ability to regenerate lost or damaged tissue.

According to the Wistar study, the loss of p21 causes the cells of these mice to behave more like embryonic stem cells than adult mammalian cells, and their findings provide solid evidence linking tissue regeneration to the control of cell division.

"Much like a newt that has lost a limb, these mice will replace missing or damaged tissue with healthy tissue that lacks any sign of scarring," said the project's lead scientist Ellen Heber-Katz, Ph.D., a professor in Wistar's Molecular and Cellular Oncogenesis program. "Perhaps, one day we'll be able to accelerate healing in humans by temporarily inactivating the p21 gene."

Heber-Katz and her colleagues first encountered the p21 mystery in 1996 when a particular mouse strain in an autoimmunity study had holes pierced in their ears as identification markers. A few weeks later, investigators discovered that the ear holes had closed without a trace. While the initial experiment was ruined, it led the researchers in a more potent direction — the discovery of the p21 gene and its role in tissue regeneration. ■

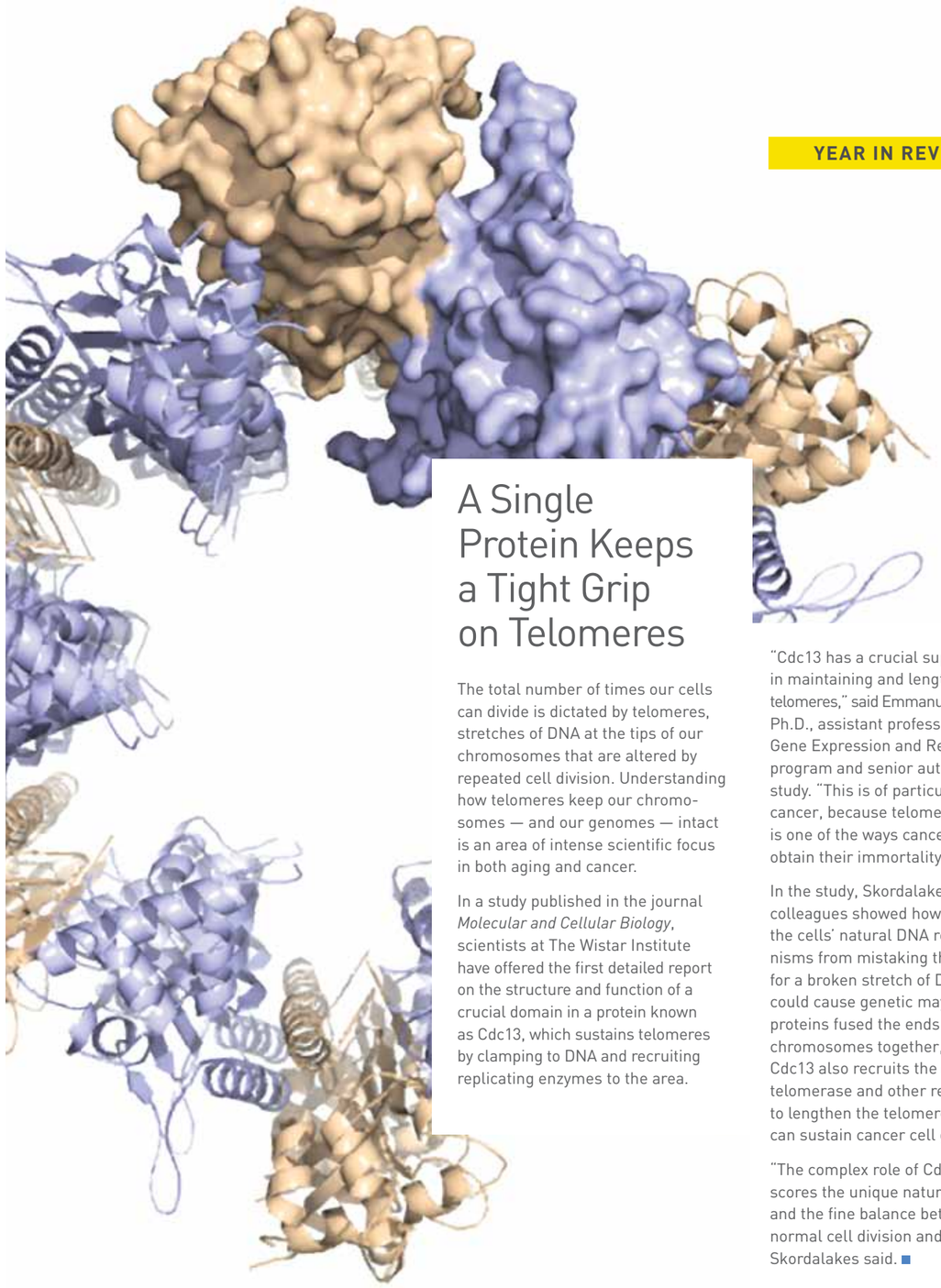
Wistar Scientists Show That Genome Structure Helps Regulate Gene Function

The interrelationship of our genes is now accepted as integral to life but as researchers at The Wistar Institute have discovered, many of these complex genetic associations may be explained in part by the three-dimensional structure of the genome itself. Their study, published as a featured article in the journal *Nucleic Acids Research*, is the first to combine microscopy with advanced genomic sequencing techniques to create a novel way to visualize both the genome and the movement of the molecules that act on it.

A cell's DNA spends the vast majority of its lifetime in a tangled clump of chromosomes, which positions groups of related genes near to each other, exposing them to the cell's gene-controlling machinery. This structure, the researchers say, is not merely the shape of the genome, but also a key to how it actually works.

"When the chromosomes come together, they fold into positions that bring genes from different chromosomes near each other," said Ken-ichi Noma, Ph.D., an assistant professor in Wistar's Gene Expression and Regulation program and senior author of the study. "This positioning allows the processes that dictate how and when genes are read to operate efficiently on multiple genes at once."

This structure is not just the accidental result of chemical attractions within and among the chromosomes — although that is certainly a part of the larger whole — but an arrangement guided by other molecules in the cell to create a mega-structure that dictates genetic function. ■



A Single Protein Keeps a Tight Grip on Telomeres

The total number of times our cells can divide is dictated by telomeres, stretches of DNA at the tips of our chromosomes that are altered by repeated cell division. Understanding how telomeres keep our chromosomes — and our genomes — intact is an area of intense scientific focus in both aging and cancer.

In a study published in the journal *Molecular and Cellular Biology*, scientists at The Wistar Institute have offered the first detailed report on the structure and function of a crucial domain in a protein known as Cdc13, which sustains telomeres by clamping to DNA and recruiting replicating enzymes to the area.

"Cdc13 has a crucial support role in maintaining and lengthening telomeres," said Emmanuel Skordalakes, Ph.D., assistant professor in Wistar's Gene Expression and Regulation program and senior author of the study. "This is of particular interest in cancer, because telomere lengthening is one of the ways cancer cells obtain their immortality."

In the study, Skordalakes and his colleagues showed how Cdc13 keeps the cells' natural DNA repair mechanisms from mistaking the telomere for a broken stretch of DNA, which could cause genetic mayhem if repair proteins fused the ends of two chromosomes together, for example. Cdc13 also recruits the enzyme telomerase and other related proteins to lengthen the telomeres, which can sustain cancer cell growth.

"The complex role of Cdc13 underscores the unique nature of telomeres and the fine balance between normal cell division and cancer," Skordalakes said. ■

NUMBER OF EMPLOYEES:	NUMBER OF POST-DOCTORAL FELLOWS:	NUMBER OF PRE-DOCTORAL TRAINEES:
422	65	32
NUMBER OF LABORATORIES:	**NUMBER OF VISITING SCIENTISTS:**	**NUMBER OF COUNTRIES* OF ORIGIN REPRESENTED:**
28	18	33

Patents Issued

U.S. PATENT NO. 7,666,983

Peptides and Peptidomimetics with Structural Similarity to Human p53 that Activate p53 Function

FILED: 03/09/2007

ISSUED: 02/23/2010

INVENTORS: Thanos Halazonetis, Wolfgang Hartwig

U.S. PATENT NO. 7,674,468

Treatment of Cancer Using HSV Mutant

FILED: 06/13/2005

ISSUED: 03/09/2010

INVENTORS: Nigel W. Fraser, Bruce P. Randazzo, Susanne M. Brown, Alasdair R. Maclean

U.S. PATENT NO. 7,691,976

BRAF35 Protein and BRCA2/BRAF35 Complex and Methods of Use

FILED: 11/13/2001

ISSUED: 04/06/2010

INVENTOR: Ramin Shiekhattar

U.S. PATENT NO. 7,811,993

Methods and Compositions for Treating Melanoma

FILED: 06/28/2006

ISSUED: 10/12/2010

INVENTORS: Dorothee Herlyn, Rajasekharan Somasundaram, Laszlo Otvos

U.S. PATENT NO. 7,740,860

Composition and Method for Preventing or Treating a Virus Infection

FILED: 03/13/2006

ISSUED: 06/22/2010

INVENTORS: Walter Gerhard, Laszlo Otvos

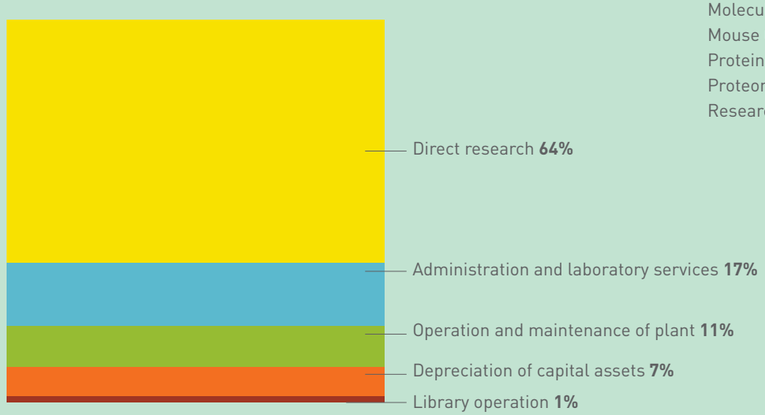
*Algeria, Austria, Bahamas, Belarus, Brazil, Canada, China, Colombia, Croatia, Cuba, Denmark, Ireland, France, Germany, Ghana, Greece, Hungary, India, Italy, Japan, Kenya, Korea, Peru, Poland, Romania, Russia, Singapore, Sri Lanka, Taiwan, Trinidad, United Kingdom, United States, Vietnam

Sources of Funds

Federal grant funding	$36,968,000	51%
Foundation and other private funding	3,893,000	5%
State funding	2,758,000	4%
Corporate-sponsored research	183,000	0%
Unrestricted contributions	568,000	1%
Capital campaign contributions	7,267,000	10%
Technology transfer	13,223,000	18%
Total return from invested funds	7,742,000	11%
	$72,602,000	**100%**

Uses of Funds

Direct research	$36,255,000	64%
Administration and laboratory services	9,744,000	17%
Operation and maintenance of plant	6,250,000	11%
Library operation	423,000	1%
Depreciation of capital assets	3,730,000	7%
	$56,402,000	**100%**



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The Albert R. Taxin Brain Tumor Research Center

The Center for Chemical Biology and Translational Medicine

The Center for Systems and Computational Biology

The Robert A. Fox Structural Biology Center

The Wistar Institute Cancer Center

The Wistar Institute Melanoma Research Center

The Wistar Institute Vaccine Center

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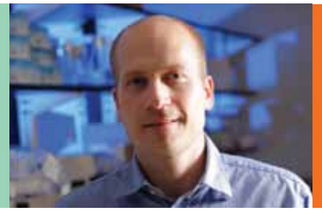
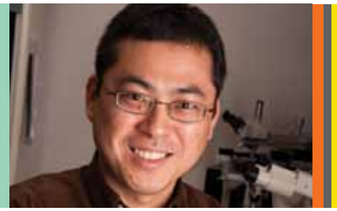
José Conejo-Garcia, M.D., Ph.D.



Scott Hensley, Ph.D.

Qihong Huang, M.D., Ph.D.

Susan Janicki, Ph.D.



Ken-ichi Noma, Ph.D.

LOOKING AHEAD

Talented new recruits join a world-class faculty in pursuit of the scientific frontier.

Wistar Investigators Gear Up for the Voyage Ahead

When setting off on a voyage of discovery, explorers need to gain their sea legs. It is a period of adjustment marked by uncertainty and no small measure of jittery nerves. The same could be said about scientists seeking federal funding, particularly the coveted National Institutes of Health (NIH) Research Project Grant — or R01, as it is commonly known.

In an era of dwindling federal financial resources, competition for grants is intense. Wistar laboratory leaders — like those at most nonprofit research organizations — need to be self-sufficient in funding their research programs, and an R01 grant is the ultimate goal for most practicing scientists.

In 2010, a number of Wistar's junior faculty members, including Qihong Huang, M.D., Ph.D., Susan Janicki, Ph.D., Joseph Kissil, Ph.D., and Ken-ichi Noma, Ph.D., achieved their first R01 grants. It is an astounding feat considering that only about one in five R01 grant applications succeeded in 2010, nationwide, among both junior and senior investigators.

"The funding climate right now is terrible, just terrible, and the competition is fierce," said Janicki, an assistant professor in Wistar's Molecular and Cellular Oncogenesis program. "I felt an overwhelming sense of relief when my grant came through, but it is incredibly difficult to do cutting-edge work when the support mechanisms favor safety and routine."

New Researchers Join the Adventure

2010 saw the addition of two faculty members in The Wistar Institute Cancer Center's Immunology program: José Conejo-Garcia, M.D., Ph.D., who joined Wistar from Dartmouth College; and Scott Hensley, Ph.D., previously a researcher at the National Institute of Allergy and Infectious Diseases of the NIH. Both researchers have academic roots in Philadelphia and Hensley worked at Wistar as a doctoral student.

Hensley is an expert on the seasonal variability of the flu. He has distinguished himself in immunology circles for his work on antigenic drift, the technical term for the evolutionary changes that make the outer coating of the influenza virus such a moving target for public health researchers. His expertise will augment The Wistar Institute Vaccine Center's efforts to create a "universal" flu shot — a single vaccine that may one day replace annual vaccinations.

Conejo-Garcia studies how certain white blood cells called vascular leukocytes promote the growth of ovarian cancers. His laboratory has demonstrated that withdrawing these "vascular leukocytes" results in the collapse of the blood system supporting ovarian cancers in mice, and enhances the effects of standard chemotherapy. His goal though, is to not just target these cells, but also to transform them, using vascular leukocytes as "nanocarriers," to carry genetic material to cancer cells. Once ingested, these genes can then be used to boost the immune system against established tumors and silence the activity of leukocytes that are suppressing immune activity in the tumor.

"I was very excited to come to Wistar," Conejo-Garcia said. "Here, I am able to reconnect with my old mentors and collaborators. My research is also becoming progressively more translational in nature so I wanted to be close to the huge biomedical community in Philadelphia."

The Institute Eyes New Recruits

As part of its broader strategic vision, The Wistar Institute is bolstering its capacity for innovative science by strategically recruiting new faculty who will complement Wistar's current roster of scientists.

"The way forward now is to build teams of investigators with widely different sets of knowledge and expertise," said Dario Altieri, M.D., professor and chief scientific officer at The Wistar Institute. "We want our scientists to feel the complete freedom of discovery and to pursue their ideas, of course, but the challenge is that we must work together."

In the first half of 2011, the recruitment of Ashani Weeraratna, Ph.D., and Jessie Villanueva, Ph.D. (both of whom were named assistant professors in The Wistar Cancer Center's Molecular and Cellular Oncogenesis program), will specifically strengthen Wistar's melanoma research efforts and broaden the research portfolio. Biostatistician Qin Liu, M.D., Ph.D., also joins Wistar's faculty in 2011 as an associate professor in the Molecular and Cellular Oncogenesis program. It is her expertise in biostatistics which will enhance Wistar research overall by supporting intra-institutional collaborations at all academic levels, and enabling scientists to find correlations between genes, disease and individual patient health in ways that may inform physicians outside of Wistar in treating cancer and other diseases.

WISTAR SCIENCE SAVES LIVES

THINK ABOUT THOSE FOUR WORDS FOR A MOMENT. WHAT DO THEY REALLY MEAN?

They mean generations of healthy children will never know the threat of German measles or rotavirus infection, thanks to vaccines developed by Wistar.

They refer to the millions of people beating cancer each year thanks to new, specialized drugs that are based on cancer biology and genetics discoveries that originated in Wistar's labs.

These words speak to countless others who benefit from Wistar's research into the fundamental processes underlying human growth and development, health and disease. From this basic knowledge, Wistar researchers work to create vaccines that protect against infectious diseases and new preventive, diagnostic and therapeutic strategies against cancer.

The simple fact is, Wistar research has a tremendous impact on all of our lives.

In early 2010 the Board of Trustees unanimously endorsed a five-year strategic plan for the Institute that calls for growth and expansion of the scientific faculty, the laboratories and buildings in which they work, and the areas of research they pursue.

These plans are now in motion and the momentum is building. It is an exciting time at Wistar, and I am proud to be part of an institution that is making such important and lasting contributions to improving public health.

If you're a friend of Wistar, you understand how Wistar science saves lives. On behalf of the Institute and its researchers, thank you for your generous support. If you're not already familiar with the great work that goes on behind the doors at 3601 Spruce Street, I invite you in to join us on our journey of discovery.

Brian H. Dovey
Chair, Board of Trustees

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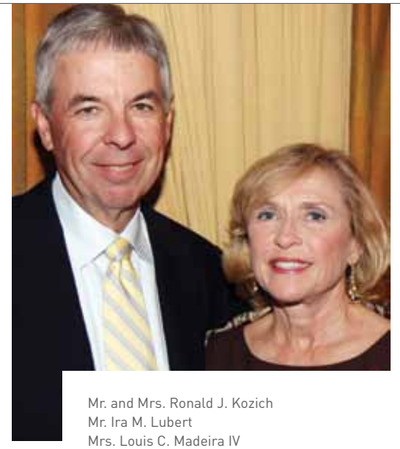
Above, left: The Wistar Institute recruited Dario C. Altieri, M.D., as the new Wistar Institute Cancer Center Director. At a reception welcoming Altieri to Wistar are Leadership Council member Sharon Kestenbaum, Board of Trustees Co-Vice Chair Richard Horowitz, and Trustee Tony Schneider.

Above, right: Wistar President and CEO Russel E. Kaufman, M.D., and Board of Trustees Secretary Maida Milone at the Altieri welcome reception.

Opposite, left: Wistar Trustee Doug Briggs and his wife, Peggy, at a gathering of Wistar supporters in Palm Beach, Florida

Opposite, right: (left to right) Paula Zelazek, Wistar Trustee Kevin Tucker and his wife, Judy, met Wistar scientists at a gathering of friends and supporters in Palm Beach, Florida.



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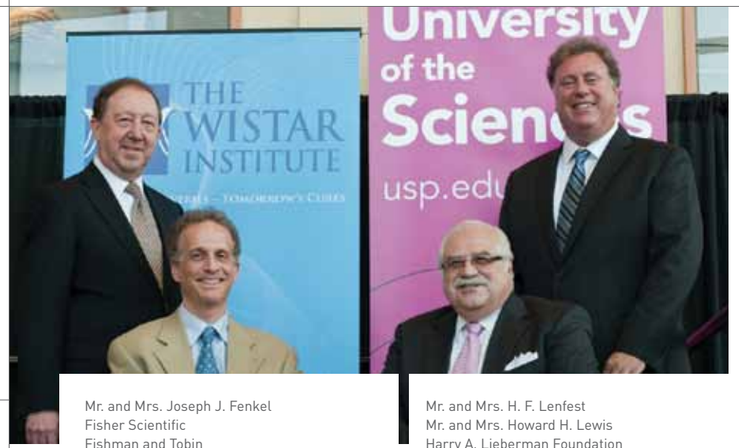

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Above, left: Paul M. Lieberman, Ph.D., (seated left) assumed the McNeil Professorship at a ceremony at University of the Sciences. Presenting the chair are (standing left) Wistar President and CEO Russel E. Kaufman, M.D.; USciences Provost Russel J. DiGate, Ph.D. (standing right) and USciences President Philip P. Gerbino, Pharm.D.

Above, right: Wistar supporters Fran Tobin (center) and Sharon and Joseph Kestenbaum at the Albert R. Taxin Golf & Bridge Classic.

Opposite: David Schultz, Ph.D., leads a tour of the Institute's Molecular Screening Facility at a Wistar "Open House" special event.

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Above, left: Penny Fox, Marjorie Silverman and Janet Kronfeld hit the links at the 2010 Albert R. Taxin Golf and Bridge Classic, which raised more than $110,000 to advance brain tumor research at the Albert R. Taxin Brain Tumor Research Center at The Wistar Institute.

Above, right: Wistar Librarian and Archivist Nina Long shares objects from the Institute's archival collections with guests during a Wistar "Open House" special event.

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Above, left: Rebecca Skloot, author of The Immortal Life of Henrietta Lacks *greets guests and signs books at an Authors Series event.*

Above, right: Richard Weisberg (left) and Sam Dennis check in at the 2010 Albert R. Taxin Golf and Bridge Classic at Green Valley Country Club in Lafayette Hill.

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Above, left: Leadership Council Vice-chair Keith Gaspard examines objects from the Institute's archival collections. More than 30 friends and supporters visited during a Wistar open house for tours of the Institute and an update on the "State of Wistar."

Above, right: Hitting the back nine at the 2010 Taxin Golf and Bridge Classic are (left to right) Bill Reulbach, Jay Reynolds, Mark Rauch and Wistar Trustee and Leadership Council Chair Daniel Wheeler.

A Close Encounter with Melanoma

In 2003, at age 87, Mrs. Helen T. "Patsy" Madeira spotted an unusual mole on her leg. It was about this same time that she received a research report in the mail from The Wistar Institute, illustrating some of the facts about melanoma, the deadliest form of skin cancer. Madeira promptly made an appointment to see her dermatologist, who took a biopsy of the mole and returned a diagnosis of Stage 1 melanoma. The mole was removed and she has been NED (No Evidence of Disease) ever since.

Madeira is grateful to Wistar for providing her with the information she credits with saving her life. A regular contributor to Wistar's annual fund for 10 years prior to her melanoma diagnosis, following her recovery she more than doubled her support. "Wistar saved my life. It may not be a hospital with doctors and nurses, but had I not read my mail that day, I probably would not be here right now," said Madeira. She also understands the value of an institution like Wistar and the importance of its research. "We are fortunate to have Wistar in Philadelphia, but it's truly a global gem. Their research impacts people all over the world."

Born in 1916, Madeira has been witness to numerous medical advances in her lifetime, from the discovery of penicillin to the end of the polio epidemic. However, it is 21st-century science and the Human Genome Project, in particular, that amaze her more than any of these previous discoveries. Completed the same year Madeira received her cancer diagnosis, the Human Genome Project has made it possible to discover and diagnose the major genome variations that cause cancer and to select patients for gene-targeted therapies.

One dramatic example of this effort at "personalized medicine" was the first trial in 2010 of PLX4032, a BRAF inhibitor designed to kill tumors in patients whose lesions demonstrate a mutation in the BRAF gene. (Early work at Wistar on BRAF paved the way for the drug's creation.) The initial results demonstrated shrinkage of the tumors and improved health, but seven months later the lesions returned and resumed growing. Despite this set-back, the trial has greatly enhanced our knowledge of how cancer operates and Wistar scientists are currently researching combination therapies to overcome this drug resistance.

It gives Madeira hope for other patients who receive an advanced-stage melanoma diagnosis. "I know I was lucky to have found my melanoma when I did," she said. "For many the prognosis is not so good. But, with Wistar and other scientists working on this problem, each day we move closer to a cure."

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In honor of William Albert's special birthday
Mr. and Mrs. Harold Schaeffer

In hopes of James Brody's speedy recovery
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Mr. and Mrs. Robert Gamberg

In honor of the Peter Corrado family
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and Ms. Denise DiPangrazio

In honor of Arnold Dresner's 80th birthday
Mr. and Mrs. Gilbert Tucker

In honor of Marlene Dubin's birthday
Albert Ominsky, Esquire and Ms. Paula Dresnin

In honor of Robert Fox's birthday
Mrs. Charlotte Rosenthal
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In honor of Gerald Gushner's 80th birthday
Mr. and Mrs. Joseph L. Garde
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Mr. and Mrs. Harold Schaeffer

In hopes of Gerald Gushner's speedy recovery
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In hopes of Dr. Don Hockman's speedy recovery
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Mr. and Mrs. Bernard Zolot

In honor of Robert Miller's 80th birthday
Mr. and Mrs. Mark R. Frazin

In honor of Ann K. Noonan
Ms. Lyda Robison

In honor of Sandy Reichlin's special birthday
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In hopes of Harvey Sicherman's speedy recovery
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In honor of Dr. and Mrs. Stanley Steinberg's 60th Anniversary
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Mr. and Mrs. Irwin Govberg

In honor of Jean Taxin
Judy, Mark, and Sarah Frazin

In honor of Fran Tobin
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In honor of Fran and Sylvan Tobin
Mr. and Mrs. Harvey S. Kronfeld
Ms. Ronnie L. Pleet

In honor of Kevin Tucker
Mr. Terry Samway

In honor of Jim Vanderwaal
Mr. Jay Rosenbluth

* Deceased

"A Date with a Plate" Event Benefits Melanoma Research

Most of us while eating at home or dining out do not pay much attention to how a table is set — that is, not just the way our tableware is placed but also the color palette of the linens, and other finer details. In 2008, Wistar contributors Sharyn Berman and Judi Goodman attended an event that embraced table setting as an art form and were inspired to develop a similar program in the Philadelphia area to help raise money for local causes.

Their first table-setting fundraiser, titled "A Date with a Plate" was held later that year and met with great success among the local community, drawing more than 500 guests. The beneficiary was The Noreen O'Neill Foundation for Melanoma Research (NOFMR), an organization that is committed to raising awareness about melanoma and funding research into increased prevention, early detection, and new treatments.

Wistar has long been a recipient of funding from the NOFMR, which holds an annual "Running for Cover" 5K Run/Walk to benefit the Institute's Melanoma Research Center.

In 2009, Berman and Goodman formalized their charitable giving efforts by founding the IMAJNZ Foundation. Their "A Date with a Plate" has been expanded into a two-day gala event. The 2010 event was held May 4-5 at the Phoenixville Foundry. Once again, the beneficiary was the NOFMR for its programs supporting the Wistar Melanoma Research Center.

On Day One, guests were invited to enjoy cocktails and hors d'oeuvres, followed by a walking dinner tour of unique place settings designed by area event professionals including Beautiful Blooms, Evantine Design and Neiman Marcus, as well as private collectors and table décor enthusiasts. Stephen Starr Events provided the catering. Day Two featured a "Second Helping" luncheon, a series of lectures and both live and silent auctions. The special guest presenters were Shaun Rowen, Director of Education for Jo Malone Fragrance; lifestyle expert Eddie Ross (Martha Stewart, House Beautiful, HG TV); and Wistar scientist Ellen Puré, Ph.D., who gave a talk on the significance of melanoma awareness in the prevention and early detection of this deadly disease.

The event was another success and, in October 2010, the Wistar Melanoma Research Center was awarded a $200,000 grant from the NOFMR to develop targeted therapies for melanoma patients with collaborators at the University of Pennsylvania. More than 85 percent of the grant funding was made possible by "A Date with a Plate." The rest came from the NOFMR's 5th annual "Running for Cover," which took place in June.

The Wistar Institute is grateful to Berman and Goodman and the IMAJNZ Foundation's committee members for making melanoma research a priority in their unique fundraising efforts. Please Save the Dates for the third "A Date with a Plate" — May 8 & 9, 2012!

Above: Seated at "A Date with a Plate" (left to right) are the event's chairs, Judi Goodman and Sharyn Berman, and Kate O'Neill, President of The Noreen O'Neill Foundation for Melanoma Research.

IN MEMORY OF...

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Mr. and Mrs. Leonard A. Jackowski

In memory of Howard Adoni
Mr. and Mrs. Leonard A. Jackowski

In memory of Marlene Arronson
Mr. and Mrs. Bernard Zolot

In memory of Carol Avella
Mr. and Mrs. Kevin M. Tucker

In memory of Deena Baird
Mrs. Eileen Baird

In memory of Vincent Bell
Mr. and Mrs. Frank G. Binswanger, Jr.
Mr. and Mrs. Harold Schaeffer

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Mr. and Mrs. Stanley D. Ginsburg
Ruth and Richard Horowitz
Meryle J. Melnicoff, Ph.D.
Doris Taxin and Jack Stievelman

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In memory of Robert G. Blount
Mr. and Mrs. Richard Schatz

In memory of Cletus Bernard Boeshart, M.D.
Gloria Marin Darthea Sharples, Ph.D.

In memory of Moe Brenda
Dr. and Mrs. Jerome I. Flicker

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In memory of Todd Brunswick
Penny and Robert Fox

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In memory of Christopher M. Davis
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In memory of Edna Drachman
Ruth and Richard Horowitz

In memory of Hermann Durst
Mr. and Mrs. Matt Cohen

In memory of my beloved Jerry
Ms. Roni L. Feierstein

In memory of David Feldman's father
Mr. and Mrs. Harold Schaeffer

In memory of Ervin Feltoon
Dr. and Mrs. Jerome I. Flicker

In memory of Selma Fishman
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In memory of Pam Friedrich
Mr. and Mrs. Joseph H. Friedrich

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In memory of Richard Gagné
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Ms. Linda Hirsch

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Mrs. Eileen Baird

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Mrs. Eileen Baird

In memory of Phyllis Gutman
Mr. and Mrs. Irwin Govberg
Mr. and Mrs. Sylvan M. Tobin
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Mr. and Mrs. Edward Edelstein

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Ms. E. K. Pomerantz

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Mr. and Mrs. Harold Schaeffer

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In memory of Mary Kilroy-Pogach's sister-in-law Ildiko
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Ms. Nora Pincus Schwarz

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Mr. and Mrs. C. Lawrence Rutstein

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Mr. and Mrs. Harold Schaeffer

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Ms. Mindy Fink Dickerman
Mr. and Mrs. William A. Don
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Ms. Mona Yudkoff

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Mr. Robert C. Schmitt

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Mrs. Eileen Baird
Mr. and Mrs. Harold Schaeffer

In memory of Ed Silvers
Mr. and Mrs. Bernard Zolot

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Mr. and Mrs. Ronald J. Kozich

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Mr. Joseph F. Grusemeyer

In memory of Lee Smith
Mr. and Mrs. Richard Schatz

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In memory of Marion Strassburger
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In memory of Kenneth Sweet's daughter Alison
Mr. and Mrs. Harold Schaeffer

In memory of Sissy Tecce's mother
Mr. and Mrs. Harold Schaeffer

In memory of Catherine Foley Tucker
Mr. and Mrs. Anthony Dent
Penny and Robert Fox
Mr. John Hammond
Mrs. Judith Lea
Mr. and Mrs. Eugene Metzger

In memory of Nancy Urlik
Ms. Jane Laffend
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Above, left: Helen Pearson (second from left), chief features editor at Nature, won the 2010 Wistar Institute Science Journalism Award for her article titled "One Gene, Twenty Years," which investigates research advances and obstacles since the discovery of the cystic fibrosis gene in 1989. Honoring Pearson at an awards reception at Wistar are (left to right) SJA judge Bijal Trivedi, Daniel Wheeler and Russel E. Kaufman, M.D.

Above, right: Fore! At the 2010 Taxin Golf Classic (left to right) Jack Stievelman, Doris Taxin, Gabi and Mitchell Mandell.

Focus on the Brain – The Tobin Kestenbaum Family Professorship

Long-time supporters of The Wistar Institute Sylvan and Fran Tobin, and their daughter and son-in-law Sharon and Joseph Kestenbaum, were looking for a way to make a major impact with their philanthropy. Motivated by a keen interest in research to find cures for Alzheimer's disease and brain tumors, the family made a generous gift to establish the Tobin Kestenbaum Family Professorship in Neuroscience.

Endowed professorships — also called endowed chairs — enable Wistar to stay at the leading edge of biomedical research because they give the Institute the ability to recruit and retain excellent scientists to complement its world-class faculty. The philanthropic support also provides these researchers with the freedom to pursue the kind of bold, high-concept research that can lead to major advances in medicine.

The Tobin Kestenbaum Family Professorship will support a scientist who studies the brain, whether his or her research interest is in brain tumors, Alzheimer's disease, Parkinson's disease, or one of many other neurological disorders that affect tens of thousands of people each year. The family has a particular interest in this area, in part, because of Sylvan Tobin's battle with a brain tumor and Joseph Kestenbaum's mother's affliction with Alzheimer's disease.

"Sylvan and I find Wistar's dedication to pure research the best opportunity to conquer neurological diseases. Given the chance to continue their research, Wistar scientists will find cures," said Fran Tobin.

The Tobins and Kestenbaums examined the management, leadership and scientific strengths of the Institute before deciding to commit to the professorship. "We believe that the management of Wistar under Russel Kaufman is outstanding, and they have a very active and caring board," said Joseph Kestenbaum. "We have met many of the dedicated scientists at Wistar and found that they are focused on bringing real solutions to some of the more disturbing medical issues facing mankind."

The Tobin and Kestenbaum families are long-standing friends and supporters of The Wistar Institute. Fran Tobin and Sharon Kestenbaum have been instrumental in the success of the Institute's annual golf and bridge tournament. Fran coordinates the event as event co-chair, and Sharon co-chairs the silent auction fund-raiser. Since its inception in 1995, the event has raised $1.3 million to support brain tumor research at The Wistar Institute Albert R. Taxin Brain Tumor Research Center, where researchers are studying brain tumors at the molecular level to develop better targeted therapies.

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Above, left: Leroy Kean takes a very close look at melanoma cells during opening day celebrations at Wistar's new Melanoma Research Center.

Above, right: Ramana Davuluri, Ph.D., (left) associate director of the Center for Systems and Computational Biology at Wistar, was named the Philadelphia Healthcare Trust Professor. Joining Davuluri at the presentation of chairs ceremony are Wistar President and CEO Russel E. Kaufman, M.D., and Bernard J. Korman, Chairman of the Philadelphia Healthcare Trust.

The Wistar Institute's board of trustees gained four new members in 2010.

GAIL WALKER HEARN, Ph.D., is a biology professor at Drexel University in Philadelphia and founder of the Bioko Biodiversity Protection Program, a wildlife conservation program for rare species of primates, sea turtles and large vertebrates on Bioko Island in Equatorial Guinea, Africa. Hearn serves on the boards of the Academy of Natural Sciences, First Hospital Foundation, Penn Medicine and Pennsylvania Hospital.

VINCENT PRICE, Ph.D., is provost of the University of Pennsylvania and the Steven H. Chaffee Term Professor of Communication at the Annenberg School for Communication in Philadelphia. Price has published extensively on the topics of mass communication and public opinion, social influence processes and political communication. His book, *Public Opinion*, has been translated and published in five languages. Former editor-in-chief of *Public Opinion Quarterly*, the leading journal of public opinion research, he has delivered more than 100 presentations at universities and colloquia around the world.

MILTON "TONY" S. SCHNEIDER is the founder and principal of The Glenville Group, a real estate development and investment firm in Plymouth Meeting, Pennsylvania. Schneider is a member of the National Advisory Board of the Barbara and Edward Netter Center for Community Partnerships at the University of Pennsylvania. He is president of the Anti-Defamation League Foundation and serves as a member of the League's National Executive Committee. Schneider also serves on the board of directors of the Jewish Federation of Greater Philadelphia.

EDWARD ZIFF, Ph.D., is a professor of biochemistry and neuroscience at New York University where he maintains an active research laboratory in the department of biochemistry at the School of Medicine. His lab studies the regulation of AMPA receptors which are found at excitatory synapses in the central nervous system. While at NYU, Ziff spent 13 years as an investigator of the Howard Hughes Medical Institute, discovering a class of genes that are rapidly activated by extracellular signals. He is chair of The Wistar Institute External Scientific Advisory Committee, of which he has been a member for more than 20 years.

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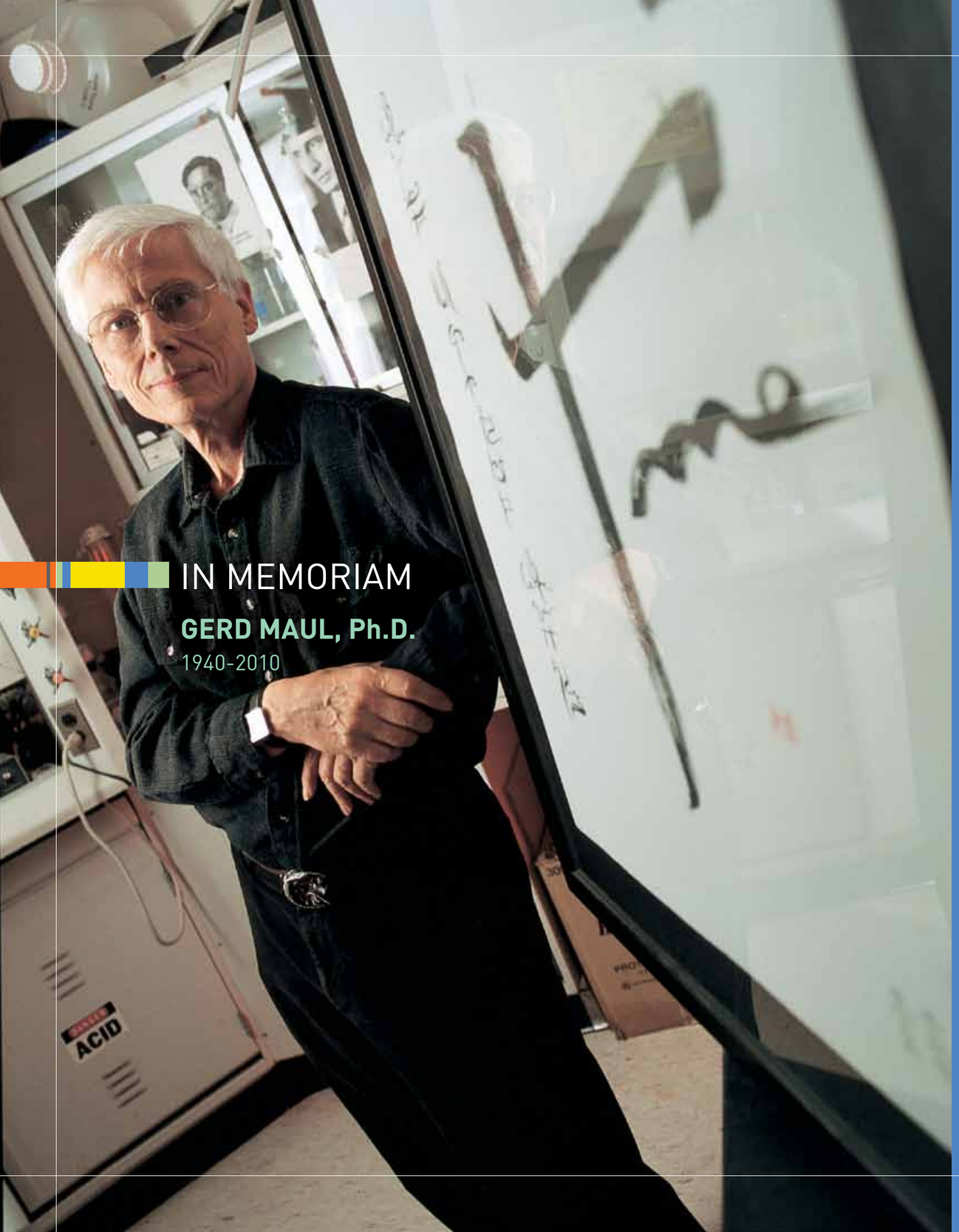

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