Wistar Names a Director

Lessons from Structure

Renewing History
From the Director

On June 10 of this year, Russel E. Kaufman, M.D., will become the next director and CEO of The Wistar Institute. I want to extend a warm welcome and all best wishes to Dr. Kaufman as he takes the helm of the Institute. I have been so proud to serve for the greater part of my career in science.

An accomplished clinician, researcher, and administrator, Dr. Kaufman comes to Wistar as a top officer from the Duke University Health System with research interests in the genetics of blood disease and cancer, as detailed on pages 4-5 of this issue of Focus. Dr. Kaufman’s vision for the Institute’s scientific future is grounded in the principle upon which the Institute was founded, that advances in medicine are possible only through an understanding of basic biological processes.

During the lifetime of Institute namesake Caspar Wistar, insight into basic biological processes came as a result of close anatomical observations. Wistar’s lectures on the subject were supported by teaching models prepared by his friend, the sculptor William Rush. As described on pages 8-9, preserving the Rush models and all of the Institute’s heritage has become a dedicated pursuit for Wistar’s archivist, Nina Long, whose efforts have recently been recognized by a major grant from the William Penn Foundation.

Today, little is as fundamental in understanding biology as knowing the three-dimensional architecture of biologically active molecules. Wistar professor Roger M. Burnett, Ph.D., is one of the world’s experts in structural biology, and his work with adenoviruses is now considered classic in the field, as explained on pages 6-7.

Also noted in this issue is the debt of deep gratitude Wistar owes to Herbert Kean, M.D., a long-time friend of the Institute, who through his great generosity has established the Herbert Kean, M.D., Family Professorship. This gift will allow a selected member of the Institute to pursue, unencumbered, the kinds of innovative scientific ideas that lead to the medical breakthroughs of the future, thereby continuing the legacy upon which we were founded.

In closing, I would like to thank Wistar’s Board of Managers, the many friends of the Institute, and its scientific and support staff for their patience, advice, and wisdom during my tenure as acting director and CEO. We have all worked closely to guarantee the continuing health of the Institute and maintain a consistently vibrant and productive scientific environment. Once again, thanks to all my friends and colleagues for your help and for allowing me one more opportunity to serve The Wistar Institute.

Clayton A. Buck, Ph.D.
Professor and Acting Director & CEO

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Ensuring Tomorrow’s Science:
Herbert Kean, M.D., Family Professorship Established

By Franklin Hoke

On April 16, friends and family of Herbert Kean, M.D., gathered at The Wistar Institute to celebrate the establishment of the Herbert Kean, M.D., Family Professorship. The evening reception and dinner honored Dr. Kean for his philanthropic vision and contributions toward the continuing vitality of Wistar research.

The newly endowed chair, made possible by a generous gift from Dr. Kean, a Philadelphia surgeon, businessman, and philanthropist, will enable Wistar to recruit an unusually talented new researcher to the Institute’s faculty or, alternatively, to recognize the accomplishments of a distinguished member of its current scientific staff. The professorship will provide the researcher selected with the resources necessary to pursue freely the types of bold, high-risk ideas that can lead to major advances in medicine. An international search for the first holder of the professorship will begin later this year.

“The Kean Family Professorship will provide the resources to make it possible for a gifted investigator to follow his or her best scientific insights wherever they may lead,” says Frank J. Rauscher III, Ph.D., who provided guests at the April 16 event with an overview of the Institute. Rauscher is deputy director of the Wistar Institute Cancer Center and leader of Wistar’s molecular genetics program. “This kind of freedom leads to the most innovative thinking and, potentially, to research advances that will make a positive difference in tomorrow’s medicine. It is clear that Dr. Kean understands the importance of supporting unfettered basic science, and the Institute is most appreciative of his vision and generosity.”

“In establishing the Kean Family Professorship, my aim is to make it easier for a talented scientist to come into the laboratory each day and work in an unencumbered way,” says Dr. Kean. “I want that researcher to be free to think big and concentrate on making the kinds of significant discoveries that will be needed to end cancer and other diseases.”

At the reception, friends and family praised Dr. Kean for the generosity of spirit exemplified by his gift to The Wistar Institute. Robert A. Fox, a member of Wistar’s Board of Managers and chairman and CEO of the investment firm R.A.F. Industries Inc., welcomed the Kean family and their guests. Dr. Kean’s boyhood friend and lifelong friend Joseph M. Field, founder, chairman, and CEO of Entercom Communications Corp., spoke, as did Dr. Kean’s wife, the Honorable Joyce S. Kean, and his son, Jon S. Kean. Wistar Board members Vincent G. Bell, Jr., and Harold M. Davis presented Dr. Kean with a framed calligraphic plaque of the text of a resolution in his honor passed by the Board at its April 5 meeting. At dinner, Dr. Kean’s long-time friend Sarle Cohen, M.D.,

(continued on page 14)
Looking to the future, what are the most promising scientific directions in which to lead The Wistar Institute? In which emerging research areas will Wistar leadership and expertise prove most influential?

Russel E. Kaufman, M.D., is developing his views on these questions, and as Wistar’s newly appointed director and CEO, he’ll have the chance to put his ideas into action in the coming years. Approved as the 110-year-old Institute’s seventh director at the April 5 meeting of the Board of Managers, Kaufman will assume his duties on June 10.

“As the first new leader to come from outside Wistar since 1957, Dr. Kaufman is in an unparalleled position to bring a fresh perspective to the Institute and set ambitious goals for the future,” says Kevin M. Tucker, president of the Board. “His administrative ability and extensive experience in both the laboratory and the clinic combine to make him the right person to continue the Institute’s legacy of improving human health through basic research.”

“I’m excited to be given the opportunity to shape the direction of cancer research at one of the finest basic research institutions in the country,” Kaufman says. “The Wistar Institute has a great tradition and outstanding scientists, and it resides in a rich intellectual environment in Philadelphia. Also, as an independent basic science center, Wistar is well positioned to respond quickly to new opportunities in cancer research and is able to sharply focus its efforts to attack and understand problems in cancer biology.”

In coming to Wistar, Kaufman, 56, leaves the post of vice dean for education and academic affairs for the Duke University School of Medicine and associate vice chancellor for academic affairs for the Duke University Health System. He was also a professor of medicine and biochemistry at Duke, with research interests focused on the genetics of blood diseases and cancer. He plans to move his laboratory to Wistar and continue his research.

Among the areas in which Kaufman envisions Wistar scientists taking a lead role are functional genomics, proteomics, stem-cell biology, and pharmacogenetics. Functional genomics works with the estimated 35,000 genes in the human genome to create precise genetic fingerprints of tumors and other tissues, healthy or diseased. Those several-thousand genes can produce up to a million proteins in the body, and proteomics aims to identify the subset of these proteins present in any given tissue. Stem cells are cells able, in theory, to replace damaged or diseased cells anywhere in the body. Pharmacogenetics is the study of how genetic profiles of patients might predict their individualized responses to specific drug therapies.
All are young fields with largely unrealized but enormous potential to advance medicine. All are areas in which Wistar researchers have begun to make their marks and where the Institute is poised to extend those contributions.

Kaufman indicates that as Wistar scientists establish new collaborations both inside and outside the Institute, other areas of research may emerge as offering similar promise. He expects to initiate several key faculty recruitment efforts and notes that these processes frequently identify scientists who can add new dimensions to existing areas of strength—molecular genetics and gene regulation, for example—or start completely new programs. The faculty can expect to be intensely involved in both recruitment and the shaping of programs, he adds.

Kaufman also says that new DNA-based vaccine technologies are likely to be important in the fight against many viral diseases, including HIV, HPV (the cause of cervical cancer), and smallpox and other potential bioterror agents. In this and other immune-system research, he sees opportunity and a possible return to Wistar's historical strengths in infectious diseases studies and vaccine development. These areas also offer the prospect of pursuing so-called translational studies, research that builds bridges between basic and clinical research to improve patient care in the near term.

With long-standing interests in both basic and applied cancer research, Kaufman has served as a scientific advisor in these areas to the National Institutes of Health, the American Cancer Society, and a number of other organizations. He has received awards for his work from the March of Dimes, the Arthritis Foundation, and others. He was named a Scholar of the Leukemia & Lymphoma Society of America, one of that organization's most prestigious awards. He was also tapped as one of the first Searle Scholars. The Searle Scholars Program supports top-flight academic research in biomedicine and chemistry.

Kaufman has extensive experience in national leadership roles in research and medical organizations. He served as president of the Association of Subspecialty Professors and chair of the Association of Hematology and Oncology Program Directors. He has been active in many internal medicine organizations, including the American Board of Internal Medicine and the Federated Council of Internal Medicine. He has served on several task-forces at the Association of American Medical Colleges.

At Ohio State University, Kaufman majored in zoology and biochemistry, graduating with a B.S. in 1968. He attended Ohio State University's College of Medicine and was awarded his M.D. in 1973, after which he moved to Duke University Medical Center for his medical residency, beginning a long affiliation with Duke, as a clinician, researcher, and administrator.

At Duke, he led a restructuring of its clinical research infrastructure, which has been acknowledged as a national model. He is often called upon by national organizations to participate in discussions concerning human-subject protections in clinical trials and the need for appropriate balances between academic and commercial interests to maintain the integrity of the research process.

Kaufman emphasizes the importance of community and private support of The Wistar Institute and is looking forward to developing many new friendships and relationships in the Philadelphia area. An avid golfer, he is eager to participate in the 2002 Albert R. Taxin Golf Classic to be held June 17 at the Green Valley Country Club in Lafayette Hill, PA, to benefit the Albert R. Taxin Brain Tumor Research Center at Wistar.

He has strong personal and professional ties with many physicians and scientists in Philadelphia and anticipates building on those relationships. As an internal medicine specialist, he has had the opportunity to work closely with Arthur Rubenstein, M.B., B.Ch., executive vice president of the University of Pennsylvania and dean of Penn's School of Medicine.

Kaufman and his wife, Jane, have two grown children. Jane Kaufman, M.S.N., is a clinical assistant professor in the School of Nursing at the University of North Carolina, Chapel Hill, and a nurse practitioner. Their son, Jonathan, now employed at Deutsche Bank, graduated from the University of Pennsylvania in 1999. Their daughter, Emily, graduated from Washington University in St. Louis in 2001 and now works at Genzyme Corp. in Boston. The Kaufmans are looking forward to the rich entertainment and dining opportunities of Philadelphia.

"After a long search during which we interviewed many candidates, we are delighted to welcome a physician, research scientist, and administrator with Dr. Kaufman's unique skills to The Wistar Institute," says Robert A. Fox, a member and former president of Wistar's Board and head of the Institute's search committee for a director. Mr. Fox is also chairman and CEO of the investment firm R.A.F. Industries Inc. "As director, Dr. Kaufman's vision for the future of cancer research, which springs from his broad experience in both the clinic and the laboratory, will ensure that Wistar remains at the leading edge of biomedical science."

Wistar professor Clayton A. Buck, Ph.D., who has served as acting director and CEO since Giovanni Rovera, M.D., stepped down in September 2000, sees in Kaufman's new directorship an opportunity for The Wistar Institute to align itself with some of the profound shifts in scientific thinking that have emerged in the past few years.

"The sequencing of the human genome has opened exciting and potentially important new fields of biomedical science," Buck says. "Russel Kaufman has his finger on the pulse of these changes, and I fully expect his tenure as director to be one of confident, bold guidance to ensure that The Wistar Institute remains among the leading institutions of its kind in the world."
Structural biology, the study of the form and function of biological molecules, is part biochemistry, part engineering, and part good puzzle solving. It seems that, for structural researchers, the ability to think big hinges on the ability to picture small.

For the past 35 years, Wistar structural biologist Roger M. Burnett, Ph.D., has been filling in the big picture surrounding some of the smallest biological structures: viruses. His findings have lead to new ways of imaging viruses and have fueled research into using viruses as molecular tools for medicine. In the process, he has refined the way he views molecular structures and developed a deeper appreciation of the ingenuity of evolution. He has also trained many promising scientists in his laboratory.

“I am fascinated with how we can make something so tiny into something concrete simply by making a model of it to see how it works,” says Burnett, a professor in Wistar’s structural biology program. “This satisfies the two parts of me, as I can see it from both the computational and the biological side of things.”

Burnett began his science career as an undergraduate in physics at the University of London, England. Like most students, Burnett was unsure of his future direction and toyed with the idea of pursuing a career in medicine. Fortunately, he gained a mentor in Michael G. Rossmann, Ph.D., who recruited Burnett into the X-ray crystallography program at Purdue University and began his transformation into a life sciences researcher.

Crystallography is one of the laboratory techniques that helped usher in modern biology. When a crystallized molecule is exposed to X-rays, the electrons surrounding each atom in the molecule scatter, forming a lattice-like pattern specific to the crystal. When Watson and Crick uncovered the structure of DNA, for example, they relied on crystallographic data. By the time that Burnett finished his postdoctoral work, however, the need for crystallographers had waned in the United States. In 1975, he found a position at the University of Basel, Switzerland, where he put his education to work trying to solve the structure of adeno virus.

“Then as now, adeno virus served as a starting point for trying to understand the fundamental principles of viral construction,” says Burnett. “The more you know about the structure of the virus, the better off you are in trying to figure out how to control it.”

By itself, adeno virus is not among the more glamorous disease-causing agents. Unlike hantavirus or Ebola, it's not an especially dangerous virus, but it is a common one. In humans, it can cause respiratory infections; conjunctivitis, an ailment that commonly arises in the form of pink eye; and enteric dysentery, an intestinal disease which, despite an available therapy, is a leading cause of death by dehydration in children of third-world countries.

Burnett would spend the next 15 years divining the structure of the virus capsid, the protective shell that surrounds the viral DNA. Computers, of course, were a huge aid to making this possible. The ability to process data faster meant that jobs that Burnett once considered impossible his graduate students could now do in a few hours.

“It is amazing. You think that, eventually, there will be a limit,” says Burnett,
The molecular hexon models that Burnett proudly displays in his office are crude replications of the real things, he admits. Hexons do not piece together like a lock and key, but are guided into place by gentle interactions on the atomic level not yet completely understood. "The structure of an adenovirus is just a starting point," says Burnett. "We continue to gain insight on how they assemble, disassemble, and function."

Even as his laboratory prepared to publish their definitive findings on the structure of adenovirus, Burnett began to look at the larger implications of his research. In the early 1990s, he helped organize a series of "viral assembly" meetings, bringing together structural biologists to share information across the specialized discipline. It was at those meetings where Burnett struck up a working relationship with Dennis H. Bamford, Ph.D., a professor at the University of Helsinki, Finland. Bamford was interested in bacteriophages, viruses that infected bacteria, specifically, the PRD1 bacteriophage.

First discovered in the sewers beneath Kalamazoo, Michigan, PRD1 has a natural affinity for the bacteria E. coli. As with adenovirus, researchers hope that bacteriophages can be subverted to protect against disease like an antibiotic, capable of identifying and destroying infectious bacteria.

Unlike adenoviruses, the capsid structure of PRD1 was anchored firmly in an internal membrane. What surprised Burnett and his colleagues, however, as they teased out the PRD1 structure, was an overwhelming feeling of déjà vu: side-by-side, the two viruses shared an uncanny similarity and a near protein-for-protein homology.

"It turned out that the adenovirus work done in the Burnett lab was invaluable in realizing the similarities between adenovirus and PRD1," says Bamford, "It has also led to a new idea in virus evolution."

Although adenoviruses and bacteriophages prey on separate branches of the tree of life, their shared structure strongly implies a shared heritage. Somehow, well before the earliest multi-cellular creatures broke off from their single-celled brethren, viruses had evolved a system that worked, one they still rely upon.

Curiosity is what drove Burnett to science to begin with, and the never-ending supply of new challenges is certainly what keeps him in the game. These days, however, Burnett is paying more attention to the talented team of young researchers that he has assembled in his Wistar laboratory. Their hard work and dedication are what drive the laboratory, and Burnett takes their mutual commitment seriously.

"Mentoring made a tremendous difference in my career early on," says Burnett. "These days I get just as much—if not more—satisfaction helping students blossom in the field as I do taking part in the science itself."
Founded in 1892, Wistar has evolved from its beginnings as an anatomical teaching and research museum to its present-day status as an international leader in biomedical research.

To preserve the Institute's unique history for future generations, Wistar has redoubled its efforts in recent years to care for the many important artifacts and specimens it possesses. Leading the way has been Nina Long, M.L.S., Wistar's director of library services, archivist, and curator of the Wistar Museum Collections.

“Our collections have a lot of value, not only to the Institute, in terms of knowing where we’ve come from, but also to academics and other researchers,” Long says. “We’ve been working not only to conserve our collections, but also to make more of our materials available to researchers and to the public via exhibits. After all, the Wistar collections were originally teaching collections,” she notes.

At the heart of Wistar's holdings are the Wistar Museum Collections, the anatomical specimens and models around which The Wistar Institute was founded. Dr. Caspar Wistar, the Institute's namesake, was a prominent Philadelphia physician who became chair of anatomy at the University of Pennsylvania in 1808. To augment his medical lectures, Caspar Wistar began a collection of dried, wax-injected, and preserved human specimens. These collections enabled physicians and students to compare biological structures in states of health and disease, the dominant method of biomedical study in that era.

By the late 1880s, however, the collection had fallen into disrepair. Isaac Jones Wistar, the great nephew of the late Caspar Wistar and a Philadelphia civic leader, proposed the creation of an independent Institute for the serious study of biology with his great uncle's teaching collection as its centerpiece. He funded an endowment and research building for The Wistar Institute of Anatomy and Biology, and the University of Pennsylvania contributed the museum collections to the new Wistar Institute in 1892.

During the 20th century, biomedical research experienced a permanent shift away from the comparison of anatomical structures to the hypothesis-driven experiments around which science is centered today. Accordingly, Wistar began to devote increasing resources to its laboratories while maintaining its museum collections.

Long took responsibility for the collections in 1996 to oversee Wistar's compliance with the Native American Graves Protection and Repatriation Act. The legislation required that certain artifacts and human remains be returned to the appropriate Native American tribes.

Long, who had headed Wistar's library since 1992, was tapped to lead the inventory of Wistar's collections necessitated by the legislation because of her experience as a librarian in cataloging and organizing collections. She also had curatorial experi-
ence and training, having worked with archival materials in her previous position at Episcopal Hospital in Philadelphia and completed a certificate program at the Modern Archives Institute in Washington, D.C. Long worked with a team of physical anthropologists and a conservator to reorganize Wistar’s museum collection and create a computerized catalog. She also began putting together small rotating exhibits of Wistar specimens in the Institute’s atrium display cases.

Now Long is working on the most significant exhibit at Wistar in decades: a display in the Institute’s atrium of anatomical models by William Rush, the first native-born professional sculptor in the nation. Caspar Wistar commissioned Rush to make oversized models of structures in the human body in wood and papier-mâché to use as teaching aids. In Wistar’s day, medical courses were taught in large amphitheaters, and Rush’s models made it possible for students sitting in the furthest rows to see the biological structures Wistar lectured on. Today, The Wistar Institute has the only known examples of these Rush models. Among its holdings are a partial jawbone with teeth and a sphenoid bone, a wedge-shaped compound bone of the skull.

Yale art history professor Alexander Nemerov, Ph.D., consulted the Rush models during a visit to Wistar as he researched his 2001 book, The Body of Raphaelle Peale. According to Long, Nemerov urged her to seek funding for an exhibit of the models due to their uniqueness and importance as historical artifacts.

“Some of these models have been on display in art museums, but we feel that one advantage we have here at Wistar is that the models can be displayed in their own milieu, so to speak,” Long says. “They were made for teaching, research, and medicine, and that’s what we do. We also feel that we can reach a different audience, because we want to promote this exhibit not only to the art history and medical museum worlds but also to our West Philadelphia neighborhood, community groups, and those involved in the history of science.”

“A SCIENTIFIC RESEARCH INSTITUTE LIKE WISTAR CAN MAKE A MAJOR CONTRIBUTION TO THE CULTURAL LIFE OF THE PHILADELPHIA COMMUNITY.”

Long has been working with Wistar’s foundation relations associate Gloria Pugliese to secure funding for the exhibit, with very favorable results. Initially Long and Pugliese obtained $5,000 from the Bay Foundation in New York for the conservation of the models and an additional $5,000 from the Pennsylvania Historical and Museum Commission for the creation of the exhibit. Then in April, the William Penn Foundation awarded Wistar a grant of $44,600 for the exhibit.

“One of our strongest arguments to the William Penn Foundation was the idea that a scientific research institute without an arts and humanities focus or mission can make a major contribution to the cultural life of the Philadelphia community through such an exhibit, which will be free and open to the public,” Long says.


In addition to caring for the Rush models, anatomical specimens, and other items from the Wistar Museum Collections, Long has also taken on responsibility for the Wistar Archives. The collection includes manuscripts and books, correspondence and other personal effects of Institute founder Isaac J. Wistar and his family, works of art donated by the Wistar family, and the official historical records of the Institute. Some highlights: a first-edition Call of the Wild by Jack London; an oil painting by noted portrait artist Thomas Sully; and a silver cup that belonged to early abolitionist Benjamin Lay.

Perhaps the most significant items in the Wistar Archives are the Civil War memorabilia and letters of Isaac J. Wistar, who served as a brigadier general on the Union side. These materials figured prominently in The History of Edward Baker’s California Regiment, a 2001 book by Gary G. Lash, Ph.D., of Fredonia State University College in New York.

“The Wistar Archives were of great value to me in doing my research,” says Lash, who adds that Long was among the most helpful archivists he dealt with for his project. His book included photographs from Wistar’s collection and never-before published sketches by an artist who was a member of the unit later killed in battle.

Lash typifies the user of Wistar’s historical materials—an academic researcher, usually working on a book or article. Long also gets some requests from those outside of academia, particularly people interested in Wistar’s Civil War records.

Most librarians spend their working hours with books and databases, but on any given day, Long’s work may put her in contact with valuable historical documents, significant sculptures like the Rush models, even preserved human organs. Her position requires a good deal of curiosity and flexibility, and perhaps a sense of humor, but Long would have it no other way. “It’s a job unlike that of any other librarian in the city,” she says. “It’s definitely interesting.”

Facing page: Nina Long showing a labyrinth of the human inner ear and the Rush model of the same structure.
New Findings on Spinal-Cord Injury

Severe injury to the spinal cord can lead to paralysis or other severe disabilities, and subsequent recovery is often minimal. Accordingly, the factors that inhibit recovery have been a major research focus in recent years. Might there be ways to promote regeneration of the cells in the spinal cord or otherwise encourage a restoration of function following injury?

A recent study conducted in mice by researchers at The Wistar Institute suggests that the key to recovery from severe spinal-cord injury may lie in limiting the scarring process that generally follows such an injury, rather than in an enhanced regenerative capacity.

In mice where the ability of inflammatory cells to reach the injury site was physically limited, the Wistar scientists found in their experiments that the formation of scar tissue at the site was also limited. Without the physical barrier of scar tissue to impede their progress, neurons on both sides of the injury site were able to grow and reestablish connections with each other over a period of two to three weeks, leading to substantial recovery of function. A report on the study appeared in the February 1 issue of the Journal of Neuroscience Research.

"The problem in recovery from spinal-cord injury appears to be the scar tissue that forms in response to injury," says Wistar professor Ellen Heber-Katz, Ph.D., senior author on the study. "The scar response eliminates the ability of the neuronal cells to grow. The scar stops that potential in its tracks. It's an absolute physical block. We found, however, that if you prevent the scar tissue from forming, the mice recover from their injuries."

To prevent the formation of scar tissue at the site of injury to the spinal cord, the researchers were careful to maintain the integrity of the dura, the protective membrane that encloses the spinal cord. This had the effect of preventing the inflammatory cells that would normally migrate to the injury site from being able to reach the site. These are also the cells responsible for initiating scar formation.

The Wistar study shows that physically preventing scar tissue from forming can open the way for recovery from spinal-cord injury, according to Heber-Katz. The research also suggests that drugs able to biochemically block scar-tissue formation immediately following such an injury might have a similarly beneficial effect. Perhaps most tantalizing is the possibility raised by the findings that therapies designed to eliminate existing scar tissue at the site of past injuries might also be helpful.

National Public Radio, the National Post (Ottawa, Canada), and other news organizations reported on the research.

In addition to senior author Heber-Katz, the remaining authors on the Journal of Neuroscience Research study are lead author Alexander Seitz, M.D., and co-author Elsa Aglow, both also at The Wistar Institute.

The research has been generously funded from its inception by the G. Harold and Leila Y. Mathers Charitable Foundation, a private foundation based in Mount Kisco, NY. Recently, the work has also received substantial funding from the F.M. Kirby Foundation in Morristown, NJ, and the National Institutes of Health.

How a Hardy Virus Survives

Epstein-Barr virus (EBV) infects almost every person worldwide at some point in life. Once infection occurs, the virus usually survives in the host forever, lying dormant and causing no symptoms. Occasionally, however, this latent EBV reactivates and contributes to certain human cancers, among them Burkitt's lymphoma, nasopharyngeal carcinoma, and Hodgkin's disease.

Now, in a finding that could potentially guide development of new therapeutics against EBV-associated cancers, a study from The Wistar Institute reveals the unexpected mechanism for how EBV survives inside its host for so long.

Once settled in the host cell nucleus, the EBV genome uses a system of cellular proteins to preserve genome stability, the researchers discovered, similar to the proteins at the ends of human chromosomes called telomeres. In both the virus genome and the human chromosome, these proteins are key to survival. When the researchers inhibited the telomeric protein
complexes associated with EBV, the latent virus genome became unstable and was eventually lost from the cell. A report on the research appeared in the March issue of Molec Cell.

The finding was particularly surprising because the structures of the virus genome and the human genome are so different: the virus genome is circular while the human genome is linear.

“It turns out that it doesn’t matter whether the proteins bind to the end of a linear chromosome or exist independently on a circular chromosome—the basic function is the same,” says study senior author Paul M. Lieberman, Ph.D., an associate professor at The Wistar Institute. “Those telomeric proteins are telling the cell not to destroy the viral DNA, and biologically, that’s very interesting.”

There may also be medical implications, Lieberman notes.

“In malignancies where EBV is known to be a contributing agent, inactivating the mechanism by which the virus maintains its genome could inhibit tumor cell growth,” Lieberman says. “Such a therapeutic approach might also be effective against EBV and other related members of the herpes virus family, although this remains to be shown.”

Reuters Health, The Scientist, The Lancet, and other media outlets carried news of the research.

In addition to senior author Lieberman, the remaining co-authors on the Molecular Cell study are Zhong Deng, Larissa Lezina, Chi-ju Chen, Svetlana Shitivelband, and Wingkan So, all at The Wistar Institute.

The research was supported by grants from the National Institutes of Health, the Leukemia & Lymphoma Society of America, and the American Cancer Society, and the Leukemia & Lymphoma Society of America.

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**New Grant Awards**

The Wistar Institute and its scientists continue to compete successfully for grants to support research and programs. Below is a list of recent awards.

### Private Grants

**American Foundation for AIDS Research**
- Aguialdo Pinto, Ph.D., laboratory of Hildegund C.J. Ertl, M.D., “A Combination Vaccine to HIV-1,” two-year grant of $99,000.
- **The Barra Foundation**
  - The Wistar Institute, community outreach programs, $2,500.
- **The Breast Cancer Research Foundation**
  - Ramini Shiekhattar, Ph.D., “Targeting Breast Cancer through Elucidation of BRCA1 Function,” one-year grant of $200,000.
- **Dolfeinger-McMahon Foundation**
  - The Wistar Institute, scientific lecture series, $2,500.
- **Meyer and Stephanie Eglin Foundation**
  - The Wistar Institute, scientific equipment, $40,000.
- **The Emerald Foundation**
  - Steven B. McMahon, Ph.D., “Characterization of N-MYC Coactivator Complexes in the Childhood Cancer Neuroblastoma,” one-year grant of $50,000.
- **The Hassel Foundation**
  - The Wistar Institute, training programs, $30,000.
- **F. M. Kirby Foundation, Inc.**
  - Ellen Heber-Katz, Ph.D., “New Model for Central Nervous System Regeneration,” one-year renewal grant of $250,000.

### Government Grants

**National Cancer Institute**
- Ronen Marmorstein, Ph.D., “Structure/Function of Human Papillomavirus Oncoproteins,” five-year grant of $1.95 million.
- **National Heart, Lung, and Blood Institute**
  - David W. Speicher, Ph.D., “Membrane Proteins of Normal & Abnormal Red Cells,” five-year grant of $2.12 million.
- **National Institute of General Medical Sciences**
  - Paul M. Lieberman, Ph.D., “Functions of the General Coactivator p160,” four-year grant of $1.23 million.
  - Ronen Marmorstein, Ph.D., “Structure and Function of DNA-Regulatory Proteins,” four-year grant of $1.05 million.
- **Pennsylvania Department of Community and Economic Development**
  - The Wistar Institute, Opportunity Grant Program, $400,000.

**Pennsylvania Department of Health**
- The Wistar Institute, Commonwealth Universal Research Enhancement program, $1,397,012.

**U.S. Army Medical Research Acquisition Activity**
- William C. Ho, Laboratory of Ronen Marmorstein, Ph.D., “Structural Basis for Pharmacological Rescue of Mutant p53 with Small Molecule Compounds,” Predoctoral Breast Cancer Award, three-year grant of $66,000.
- Marc Holbert, laboratory of Ronen Marmorstein, Ph.D., “Structural Studies of the BRCA1-Associated Human SWI/SNF Complex,” Predoctoral Breast Cancer Award, three-year grant of $66,000.

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Information on Wistar technologies available for licensing can be found on the Institute’s Web site, www.wistar.upenn.edu, under “Technology Transfer.”
Plotkin Honored

Wistar emeritus professor Stanley A. Plotkin, M.D., developer of the rubella vaccine and an expert adviser to government and industry, was awarded the 2002 Sabin Gold Medal. The award, given by the Sabin Vaccine Institute in New Canaan, CT, recognized Plotkin as a “scientist and humanitarian” for his work on a range of vaccines, including polio, rabies, varicella, and cytomegalovirus. Plotkin received his award on May 7 in Baltimore.

Also The Philadelphia Inquirer featured Plotkin in a January article discussing his development of the rubella vaccine. The article noted that rubella, which once infected tens of thousands of people a year and caused numerous birth defects, is on the verge of being eliminated in the U.S. thanks to Plotkin’s vaccine.

Rauscher Says . . .

Frank J. Rauscher III, Ph.D., deputy director of The Wistar Institute Cancer Center, was tapped for expert commentary by reporters during the April meeting of the American Association for Cancer Research in San Francisco.

The Associated Press and Reuters looked to Rauscher for his view of a study presented at the AACR meeting, which suggested that a pill long used to treat dry mouth might help protect against lung cancer in lifelong smokers. “It’s an intriguing, promising finding in a small patient population,” Rauscher said. The AP story was picked up by a number of news organizations, including the Milwaukee Journal Sentinel, The Atlanta Journal-Constitution, the Rocky Mountain News (Denver), and The Canadian Press.

Rauscher also gave a live interview on KGO Radio 810 AM in San Francisco.

State Grant for Wistar Scientist

Wistar professor Hildegund C.J. Ertl, M.D., received a grant from Pennsylvania’s income tax check-off program for breast and cervical cancer research. Pennsylvania First Lady Kathy Schweiker.

Hail to the (Former) Chief

The American Association for Cancer Research (AACR) honored President George H.W. Bush in March with its prestigious Public Service Award in recognition of his “active and unstinting support for cancer research.” On hand at the award ceremony in College Station, Texas, was Frank J. Rauscher III, Ph.D., deputy director of The Wistar Institute Cancer Center. Rauscher is editor-in-chief of the AACR’s journal, Cancer Research, the most frequently cited cancer journal in the world.

Rauscher joined AACR President Waun Ki Hong, M.D., and CEO Margaret Foti, Ph.D., in presenting President Bush with an award plaque and a framed copy of the February 15 issue of Cancer Research, which featured President Bush on the cover.

Since leaving the Oval Office, President Bush has continued to be a strong ally to the cancer research community. He is chair of the Board of Directors of the University of Texas M.D. Anderson Cancer Center, and he and his wife, Mrs. Barbara Bush, are co-chairs of the National Dialogue on Cancer, a collaborative forum of the leaders of key national cancer organizations and others who share the goal of eliminating cancer as a major public health problem.
Schweiker announced the grants at a press conference on the University of Pennsylvania campus in April.

Ertl received the maximum award amount of $35,000 to study “Vaccine Prevention of HPV-16 Associated Cancer.”

The grants were made possible by Pennsylvania taxpayers who donated a portion of their income-tax refunds to the Breast and Cervical Cancer Research Fund.

In addition to Mrs. Schweiker, the press conference was attended by Pennsylvania Secretary of Health Robert S. Zimmerman Jr. and Pat Halpin-Murphy, president and founder of the Pennsylvania Breast Cancer Coalition.

Wistar Teams Up With Morphotek

The Wistar Institute and Morphotek Inc. announced in February a collaborative research agreement to develop improved monoclonal antibodies. Under the terms of the agreement, Morphotek, a Philadelphia-area biotechnology company, will apply its patented process to monoclonal antibodies from Wistar to develop second-generation antibodies with greater utility for the diagnosis and treatment of cancer and other diseases.

“The collaboration with Morphotek is an excellent opportunity for Wistar to add value to our portfolio of monoclonal antibodies,” says Meryle J. Melnicoff, Ph.D., director of business development for Wistar.

The Philadelphia Inquirer, BioWorld Today, and other news organizations reported on the collaboration.

Take a Swing

Golf for a good cause at the 2002 Albert R. Taxin Golf Classic, Monday, June 17, at the Green Valley Country Club. Now in its seventh year, the annual tournament has raised nearly $500,000 for Wistar’s Albert R. Taxin Brain Tumor Research Center. Interested golfers or volunteers can call 215-898-3930 for more information.

The tournament is made possible through the generous support of sponsors including Mellon Private Asset Group; David Cutler Group; Cozen & O’Connor; R.A.F. Industries; PNC Bank; Charlap & Miller; and the Taxin family.

News and Notes

- Nina Long, the Institute’s director of library services, archivist, and curator of The Wistar Museum Collections, has been elected chair of the Philadelphia Chapter of the Medical Library Association, which has a membership of 170 medical librarians from the Greater Delaware Valley area. Her term commences in 2003. Long has also been appointed to the board for the Southeast Chapter of the Pennsylvania Library Association, which has a membership of 170 medical librarians from the greater Delaware Valley area. Her term on the board began in January and continues for two years.

- The Biomedical Technician Training Program, jointly founded by The Wistar Institute and Community College of Philadelphia, was named a finalist in the “Workforce Development” category of the Bellwether Awards, which honor innovative programs at community colleges. Wistar welcomed its third class of biomedical-technician trainees in May.

Live at Wistar: NPR

National Public Radio has chosen The Wistar Institute as the ongoing venue for its “Justice Talking” program. Since January, the program has been taped in Wistar’s Joseph N. Grossman, M.D., Auditorium. The show features vigorous debates before a live audience on a wide range of legal controversies in current affairs.

By providing the venue for “Justice Talking,” the Institute carries forward the spirit of its namesake, Caspar Wistar, who hosted frequent gatherings at his home for leading intellectuals to engage in debates of the important issues of the day.

Recent topics debated on “Justice Talking” include the privatization of public schools, assisted suicide, and military tribunals, among many others. Additional information about the program is available at www.justicetalking.com.

NPR’s “Justice Talking” team: Top, Kathryn Kolbert, Kara McGuirk, and Julie M. Drizin; bottom, Gary Kalman, Margot Adler, and Erin Mooney.
Herbert Kean, M.D., Family Professorship Established

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chairman of The Hassel Foundation, addressed the guests, as did the Honorable Edward R. Becker, Chief Judge, U.S. Court of Appeals for the Third Circuit, another close friend.

A lifelong Philadelphia resident, Dr. Kean graduated from the University of Pennsylvania in 1952. He attended Hahnemann Medical School and was awarded his M.D. in 1956. He served his internship at Hahnemann Hospital in 1956-57 and his residency at Jefferson Hospital from 1957 to 1960. From 1960 until his retirement in 1999, Dr. Kean was in private practice as an ear, nose, and throat clinician and surgeon, and he was board certified in otolaryngology and facial plastic and reconstructive surgery. At the time of his retirement, he was an attending physician at Thomas Jefferson Hospital and a clinical professor in otolaryngology at Thomas Jefferson Medical College. Among many others, his professional society memberships included the Philadelphia County Medical Society, the American College of Surgeons, and the American Board of Otolaryngology.

Today, he is chairman of the public health committee of the Philadelphia County Medical Society, working to extend health-care access to underserved Philadelphia residents. He is a board member of Singing City, a Philadelphia-based choral ensemble. Dr. Kean is also a member of the board of Entercom Communications Corp.

The Herbert Kean, M.D., Family Professorship honors the members of Dr. Kean’s family, among whom are his wife Joyce, his daughter Marjorie, and his son Jon. The professorship also recognizes Dr. Kean’s first wife, Jeannette, who died of breast cancer in 1989. When Jeannette’s death was imminent, Dr. Kean arranged to fund a laboratory in her honor at the Institute, beginning a pattern of giving to...
Wistar that has continued to the present with the establishment of the Kean Family Professorship.

"Over the years, I just made it a habit to make gifts to The Wistar Institute to honor or memorialize friends," says Dr. Kean. "Many of my friends, in turn, adopted the same tradition."

Recently, he felt the desire to do more, to make a more significant gift. He traces the increase in his philanthropic urge to a serious accident—a broken neck—in Mexico City on October 9, 1999, that left him temporarily paralyzed and facing an extended course of convalescence and physical therapy. He found, too, that he would not be able to return to his work as a surgeon: "I was involuntarily retired," he says.

"During the course of my recovery, I saw so much," he recalls. "I saw much of the sadness of incapacity— I felt it myself, for a time— but I also saw the good being done by caring people. And I thought, 'I'm going to do more to help people.'"

That aspiration led to the establishment of the Kean Family Professorship, which promises to enhance the research capabilities of The Wistar Institute in perpetuity.

"The Kean Family Professorship will allow The Wistar Institute to recruit or retain an outstanding investigator who will have the unrestricted flexibility to pursue the novel scientific ideas that he or she believes will prove most promising in the fight against disease," says Clayton A. Buck, Ph.D., professor and acting director & CEO of The Wistar Institute. "We at the Institute are grateful to Dr. Kean for his philanthropic leadership in support of Wistar's basic science mission."

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Please mail this form to: Development Office, The Wistar Institute, 3601 Spruce Street, Suite 242, Philadelphia, PA 19104-4268. If paying by credit card, you can expedite your gift by calling (215) 898-3930.

The official registration and financial information of The Wistar Institute of Anatomy and Biology may be obtained from the Pennsylvania Department of State by calling, toll-free within Pennsylvania, (800) 732-0999. Registration does not imply endorsement.
For 35 years, Roger M. Burnett has been filling in the big picture surrounding some of the smallest biological structures: viruses.

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