Series: Molecular Medicine Institutions

The Wistar Institute

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Caspar Wistar, for whom the Wistar Institute is named, was a practicing Quaker and pacifist who would not fight during the Revolutionary War but chose instead to care for those who were injured. Following the war, he went to Edinburgh and earned a medical degree, for which he delivered a 44-page doctoral dissertation in perfect Latin.

In 1787 at the age of 26, Caspar began the practice of medicine in Philadelphia, where he became widely respected for his professional knowledge, deep compassion, and teaching skill. Twenty-one years later, he became Chair of the Anatomy Department at the University of Pennsylvania, succeeding his mentor and George Washington's physician, William Shippen.

Cultivated in the humanities as well as the sciences, Caspar had a breadth of knowledge and public speaking skills that lured medical students from around the country. He reached still more with his book on anatomy, the first standard American text in the field.

In 1816, two years before his death, Caspar appointed William Edmonds Horner, a young physician, to be caretaker of his teaching aides, which consisted of wooden models made by sculptor William Rush, and dried and wax-injected human limbs and organs. Horner enlarged the collection with his own skeletal materials and created the first anatomical museum in the United States, the Wistar and Horner Museum at the University of Pennsylvania.

Nine years after Caspar's death, his great-nephew, Isaac Jones Wistar, was born. Despite a restless and rebellious youth, Isaac grew up to become a Civil War general, Philadelphia lawyer, and cultural leader. At the age of 63, he was approached by the University of Pennsylvania's provost for help with the restoration of the Wistar and Horner Museum, which had been damaged over the years by fire and neglect. Recognizing the importance of the collection, Isaac paid for its repair and established around it an institution independent of, but with strong ties to, the University. His wish was to provide a setting for "searchers after new and original knowledge."

Over the years, Isaac contributed his fortune to the Institute's development, believing that he was "not constructing a mere plaything" for his time, but rather "an enduring monument for a far-stretching future." Unfortunately, because of emphasis on the museum, which had acquired more than 10,000 new specimens since its founding, the scientific research conducted at The Wistar Institute was largely ignored until after the turn of the century.

Under the guidance of Milton J. Greenman, named director of Wistar in 1905, the Institute finally began to fulfill Isaac's dream. Its first success came from the development of the Wistar rat, later trademarked the WISTARAT, the first standardized laboratory animal and an ideal vehicle for the study of the human nervous system. According to Institute records, these carefully bred albino rats were treated with great affection; they received a diet that included rice pudding or optional chocolate for dessert, and soothing violin music that caused them to click their teeth in approval. It is estimated that over half of today's laboratory rats are descendants of the original WISTARAT, which was bred and widely distributed from 1906 through the 1940s.

At that same time, University of Pennsylvania graduate students and young scientists from all over the world were given access to training in Wistar laboratories, and the publication and circulation of scientific journals became a major Wistar initiative. During World War I, when most of Europe was unable to print or purchase publications, the Wistar Institute Press sent out thousands of dollars worth of free scientific journals. By 1925, the Wistar Institute had become a center of American biology.

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Molecular Medicine, Volume 3, Number 4, April 1997 229-230

Not until the 1960s, however, was Wistar publicly recognized for its basic research when, under the direction of Hilary Koprowski, Wistar scientists developed vaccines against rabies and rubella. These vaccines were made possible by Leonard Hayflick's and Paul S. Moorhead's establishment of "WI-38" (for the Wistar scientists' 38th try), a cell line of cloned human cells that were genetically identical and flourished in a test tube. Studies showed that almost any virus introduced into the WI-38 cell line grew plentifully and, through laboratory manipulations, could be transformed into a vaccine that was safer than any using animal cells.

WI-38 also allowed Hayflick to make another significant discovery. Troubled by the question of whether aging begins in the cells or the tissues they make up, Hayflick cloned cells from fetal tissue and placed them in a petri dish. Freed from the responsibility of supporting a larger organism, the cells doubled again and again until, quite suddenly, they stopped. From then on, they behaved as if they were aging, implying that somewhere in the nanoviscera of each cell there may be a timer giving it only so much time to live.

Cancer research, begun in the 1940s when Warren H. Lewis, editor of *Gray's Anatomy*, and Margaret Reed Lewis joined the Wistar staff to further their work in cytology, also became a high priority. In 1972, in recognition of its significant achievements, Wistar was named one of the country's first Basic Science Cancer Centers by the National Cancer Institute. This designation, shared with only nine other U.S. institutions, has distinguished Wistar as a federally recognized center of excellence in the multifaceted study of cancer.

Over the past 20 years, Wistar's investigations into the causes and cures of cancer have focused on genetics and immunology, with Wistar scientists being among the first to develop monoclonal antibodies (MAbs), which detect and destroy cancer and other foreign cells. One Wistar-developed MAb, known as 17-1A, was recently put into clinical use in Germany to prevent metastasis in patients with surgically resected advanced colon carcinoma. Wistar scientists also have identified several genes associated with leukemias, lymphomas, childhood tumors like Wilms' tumor, and soft tissue sarcomas. One of Wistar's most prominent discoveries was the *bcl-2* gene, which alters in most lymphomas and is a key player in programmed cell death.

For the past several years, the Institute's immunology research has been driven by the desire to promote understanding of the ways in which the cytokine interleukin-12 (IL-12), discovered by Wistar scientist Giorgio Trinchieri, steers the immune response to specific antigens, including tumor antigens, and to develop new methodologies for vaccines, including cancer vaccines. One promising area of future research is on the adjuvant abilities of IL-12 to direct a cytotoxic response in conjunction with modern DNA or viral vaccination.

Under the leadership of Dr. Giovanni Rovera, The Wistar Institute currently has approximately 350 staff members, including around 130 doctoral-level scientists, and more than 40 laboratories grouped into four research programs: Molecular Genetics, Tumor Biology, Tumor Immunology, and Structural Biology. Although each laboratory focuses on specific research goals, the programs are flexible and allow for the cross-disciplinary interaction that innovative research demands. Also housed within the Institute are The Robert A. Fox Structural Biology Center and The Albert R. Taxin Brain Tumor Research Center.

Throughout its history, The Wistar Institute has pursued the dual mission of scientific research and education that Isaac Wistar began in honor of the great-uncle he had never known. Guided by its motto, Saving Lives Through Science[SM], it is armed for another century of combat against the major diseases of our time—cancer, AIDS, Alzheimer's, atherosclerosis, and countless viral and parasitic infections.