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A VISIONARY WHO LED A GENETIC REVOLUTION

by Elaine Woo, Times Staff Writer

When Milton Wexler's ex-wife lurched across a downtown Los Angeles street one day almost 40 years ago, a police officer called out to her, "Aren't you ashamed of drinking so early in the morning?"

But Leonore Wexler was not drunk.

She was showing the signs of Huntington's disease, the rare, incurable genetic disorder that had slowly killed her father and three brothers and several months earlier had claimed the life of folk singer Woody Guthrie.

She had believed the disease only afflicted men, but that afternoon a neurologist's examination confirmed that she had been wrong. Even worse, she knew that her two grown daughters with Milton — Alice and Nancy — had a 50-50 chance of facing the same fate.

The devastating news sent Milton Wexler — a lay psychoanalyst popular with actors and artists, including a then-budding architect named Frank Gehry — on a journey to the edge of a scientific frontier. He would emerge a hero.

Wexler, 98, who died of respiratory failure Friday at his Santa Monica home, ignored the scientific wisdom of the time and poured his energy into unlocking the mysteries of one of the most enigmatic and crippling of diseases, often described as a time bomb because the mental and physical havoc it wreaks typically does not surface until midlife.

In the early 1970s, after starting what is now the Hereditary Disease Foundation, he began to recruit bright young scientists willing to gamble on a longshot to workshops aimed at finding a cure. The freewheeling workshops — structured like the group therapy sessions Wexler ran in his Westside practice — stressed brainstorming and were unlike anything the scientists had ever experienced.

In 1983, after a decade of struggle in laboratories around the country, the scientists nurtured by Wexler — and later also by Nancy, a clinical psychologist — achieved the breakthrough few people believed possible: They found the genetic marker for Huntington's. In 1993, they located the gene itself.

Wife dies of the disease

These milestones in the genetics revolution did not help Leonore Wexler, who died of Huntington's on Mother's Day in 1978 — 10 years after her diagnosis. But they would have a profound impact on others.

Discovering the gene not only represented an enormous step toward finding a cure for Huntington's, but it demonstrated the feasibility of mapping the entire array of 30,000 human genes.

Wexler "proved it could be done," said Dr. Francis Collins, who was a junior professor at the University of Wisconsin when he joined Wexler's workshops in the mid-1980s. Collins helped develop the methods for identifying the genes responsible not only for Huntington's disease but for cystic fibrosis before leading the successful effort to complete the genome blueprint in 2003.

"The search for the Huntington's gene became the paradigm for all such gene hunts.... That all came out of that wonderful intellectual ferment that Milton and Nancy created," said Collins, now director of the government-supported National Human Genome Research Institute in Bethesda, MD.

Dr. Anne B. Young, a Harvard Medical School professor and chief of neurology at Massachusetts General Hospital, said Wexler was "a visionary.... He was the guru and the glue," who held together a project that many eminent scientists had deemed foolish.

"Today we have the gene. We have an inkling of what the gene does. It wouldn't have happened without Milton," Young said. "He was a catalyst for all of that."

Born in San Francisco but reared in New York City, Wexler entered Syracuse University at 16 and earned a law degree from New York University. But he hated practicing law and abandoned it in 1937 to get a doctorate inpsychology at Columbia University. He also studied under Theodor Reik, a Sigmund Freud disciple who helped legitimize the practice of psychoanalysis by non-physicians in the United States.

Wexler followed Reik's path and became one of the country's first lay psychoanalysts. After serving in the Navy during World War II, he joined the staff of the Menninger Foundation, a renowned psychiatric research and treatment center in Topeka, Kan., where his success treating schizophrenics gained attention. He gave his patients round-the-clock care, even taking a small group of them on vacation with his family so their treatment would not be interrupted.

"He was an organizing force in their life. A lot of people got better," Nancy Wexler said.

In 1951, he left Menninger and moved to Los Angeles to begin a more lucrative private practice that would enable him to help support his wife's brothers, who had been diagnosed with Huntington's the year before. He found success treating clients who were

well-known in Hollywood. He even shared a screenplay credit with director Blake Edwards, the husband of actress Julie Andrews, for the movie "The Man Who Loved Women."

Wexler also accepted many struggling artists into analysis and by the early 1960s treated them free in groups.

One of his patients was Gehry, who entered therapy because of personal and professional problems. Shy and intimidated by the high-powered movie industry figures, lawyers, writers and doctors in his group, he went two years without saying a word to them. One night the entire group stunned him with its criticism. They thought his silence meant he was judging them. Afterward, Gehry talked with Wexler and realized that his clients had formed the same impression, which explained his career difficulties.

"It was a defining moment," Gehry, who would go on to design such iconic buildings as Los Angeles' Disney Hall, said in an interview this week. "He was brilliant at the moment of truth."

Transferring the group therapy method of free association to solving the quandary of Huntington's was, Gehry added, "sheer genius."

Several principles guided the workshops. The priority was to encourage a free flow of bold ideas, so written lectures and slide presentations were banned because they stifled interaction. The groups were kept small — usually no more than 20 participants — with an emphasis on postdoctoral students and young scientists who were less likely to be bound by orthodoxy.

Wexler also invited established scientists — including Nobel laureate and DNA pioneer James Watson — who functioned as living encyclopedias across a wide range of disciplines. Scientists who ordinarily would not be in the same room together — geneticists who studied worms and flies side-by-side with neurologists and psychologists — shared thoughts.

Wexler "had an ability to bring together a room full of disparate people and basically remove the walls. He was a master of the creative," said David E. Housman, a Massachusetts Institute of Technology biologist who played a crucial role in the collaborative effort that led to the identification of the Huntington's gene.

As an added perk, Wexler's celebrity friends hosted parties for the scientists. "Us geek scientists were totally blown away that this was also part of the workshop scene," said Collins, who remembered Saturday night soirees with Andrews, Carol Burnett, Walter Matthau and Jack Lemmon.

The spirit of cooperation was so strong that when the scientists published their findings, the authorship was given to the Huntington's Disease Collaborative Research Group.

A family project

By then the effort had become a Wexler family project. Nancy, a professor at Columbia, recruited scientists, led workshops and collected blood samples in a remote village in Venezuela where what was believed to be the world's largest family with Huntington's disease lived. She succeeded her father as president of the foundation. Alice, a historian, wrote "Mapping Fate," a stirring 1995 memoir of her family's struggle.

When the Wexler daughters learned that they might have inherited their mother's defective gene, they decided not to have children. When the procedure for detecting the gene was developed, in part through their brave efforts, they chose not to undergo it, believing that testing positive could raise more questions than they could handle.

Their father agreed with their decision. They were the reason he got into the fight in the first place. "I became an activist because I was terribly selfish," he once said. "I was scared to death that one of my daughters would get it too."

Now in their 60s, they are his only survivors. So far, they have remained free of the disease.

A memorial service will be held at 7:30 p.m. Monday at the home of actress-writer Carrie Fisher. For directions and to RSVP, call (212) 543-5667.