

Editorial Elena Cattaneo - Italian newspaper La Repubblica, Saturday Insert "D"

August 5, 2023

Two stories to remember

Exactly 30 years ago, in what the New York Times described as "a rare example of scientific cooperation," the Huntington gene was discovered. It was 1993, and the Human Genome Project, which would lead to the first partial reading of our DNA in 2000, was in its early stages. Researchers from six laboratories in the United States, England, and Wales accomplished an extraordinary scientific feat: identifying the genetic basis of Huntington's Disease, an inherited neurodegenerative disorder. The discovery was published in the scientific journal *Cell* by the Huntington's Disease Collaborative Research Group. The significance of this achievement extends beyond science; it holds great social value.

In 1979, three geneticists, David Housman, Jim Gusella, and Marcy MacDonald, along with many colleagues, followed Nancy Wexler, a neuropsychologist and geneticist herself, to Venezuela, specifically the shores of Lake Maracaibo and villages with a high density of Huntington's patients. Wexler was convinced that in these remote places, where even today, 7 out of 1000 individuals are Huntington's patients (a rate up to 500 times higher than in Italy), she would find answers about the origin of the disease that affected her mother, grandfather, and some uncles. During their time in Venezuela, Housman, Gusella, and MacDonald had an idea: to "cut" the DNA obtained from blood samples from those populations and compare the genome fragments of healthy individuals with those of the affected ones. After numerous attempts, in 1983, they succeeded in isolating the DNA fragment present only in those showing symptoms of the disease: uncoordinated limb movements, altered facial expressions, depression, and psychiatric disorders. The gene responsible for Huntington's was near that fragment, consistently co-inherited with the disease. However, due to limited technology at that time, pinpointing the exact location, despite the proximity, remained as challenging as finding a needle on the highway between Rome and Milan. It took another ten years and thousands of DNA tests and comparisons to locate the Huntington gene finally. In 1993, Gusella informed Wexler that it had been identified at the apex of chromosome four. Since then, we also know that it is represented by a string of three letters, CAG (three of the four DNA bases, Cytosine, Adenosine, and Guanine), which repeat three by three. The disease inevitably appears when these triplets exceed 35 repetitions. This genetic "defect" was described as a sort of "molecular stutter."

In 1993, in the outskirts of El Difícil, Colombia, lived Dilia Oviedo, a 56-year-old woman, petite and elegant. She had married Valentin at a very young age, and together they had eleven children. For years, Dilia and Valentin were happy with their large family. Then, the disease started to manifest, first in Valentin, and then in nine of their children. Their seemingly fortunate life turned into a sentence. Symptoms also appeared in many of their grandchildren and great-grandchildren. I met Dilia in 2017 in Rome during the event "Hidden No More," where hundreds of Huntington's patients from Latin America and 25 other countries met with Pope Francis. By that time, she had already lost her husband and five children. Dilia, then eighty years old, confided that for a long time, she believed the disease only existed within her family, making them isolated and shunned by the community. Ridicule and segregation forced them to leave the village they had always lived in. Nevertheless, Dilia didn't give up. Despite extreme poverty, she turned her new home into a

"safe haven" for many afflicted family members who, when they began to show the first symptoms, were entrusted to her care. A few weeks ago, Dilia left this world.

We owe her gratitude for a life lived for others and for the future. It is our task to preserve her legacy. One way to do this is by continuing to remember her story alongside the scientific achievements of Nancy Wexler and the discovery of the gene. These are stories of determination and courage that are essential to understanding every aspect of Huntington's Disease, a "social" illness that, while telling the story of our species' evolution, teaches us the importance of erasing stigma and defending the values of acceptance and taking care of one another. Associations like Factor H (*) contribute to this effort, where the "H" stands for Huntington, but also for Humanity and Hope.

(*) To support people and families facing challenges similar to Dilia's, you can visit the Factor H Association's website: factor-h.org.

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