Thoughts Out of Season

Occasional Reviews & Notes
Of Mutual Interest
Compiled by Tim Forward

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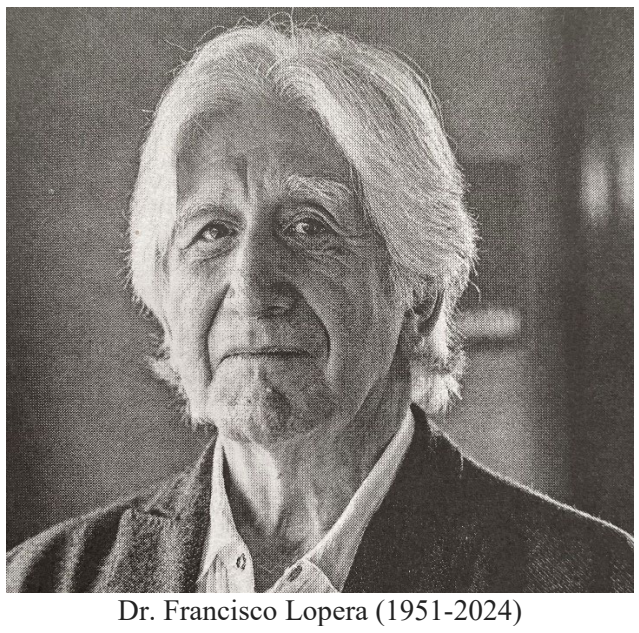

Dr. Francisco Lopera (1951-2024)

Dr. Francisco Lopera, 73 Neurologist and pioneer in Alzheimer's Research

September 14, 2024
By Pam Belluck
THE NEW YORK TIMES

Dr. Franscisco Lopera, a trailblazing neurologist who identified the world's largest extended family with Alzheimer's and spent decades working with them in his native Columbia, died on Tuesday at his home in Medellin. He was 73.

The cause was metastatic melanoma. His death was announced on social media by the neuroscience group at the University of Antioquia in Medellin, which Dr. Lopera led until last month, when he retired.

Dr Lopera, a professor at the University for nearly 40 years, made significant discoveries in the field of Alzheimer's. His work led to identifying the genetic cause of an extended family's disease, helped pioneer efforts to find drugs to prevent or delay symptoms and spearheaded discoveries of genetic mutations that appear to be able to forestall cognitive decline.

He also spent tremendous time and energy providing care and information to patients and their relatives. He identified about 6,000 members of the large clan in Medellin and mountain villages in northwest Columbia. An estimated 1,200 of them were born with a genetic mutation that causes Alzheimer's, with symptoms starting in their 40s and often causing death in their 60s.

He was very devoted to finding a cure for Alzheimer's and trying to stop the disease, but he also knew that there were "patients that were already facing the disease," said Ykeel Quiroz, a Columbian neuropsychologist and director of the Multicultural Alzheimer's Prevention Program at Massachusetts General Hospital who collaborated with Dr. Lopera and was among the many researchers he mentored.

Before Dr. Lopera's efforts began, people in the poverty-stricken and violence-scarred villages of Antioquia, the region where Dr. Lopera grew up, called the condition La Bobera: "the foolishness" or "the madness." According to superstitions, it was caused by witchcraft, by touching a mysterious tree, or from curses emanating from the statue of a Spanish colonial leader or an angry priest.

Those with the disease were shunned or hospitalized, Dr. Quiroz said. Now, because of Dr. Lopera's compassion and commitment to educating the family members, "they understand what the disease is," she said and "they are taking care of their patients."

Dr. Lopera began trying to identify the family's disease as a young doctor. In 1982, he saw a 47-year-old patient with memory loss and learned that the man's father, grandfather and seven other relatives had experienced the same symptoms, Dr. Lopera recalled in and interview The New York Times in 2010.

Determining the cause of the condition affecting the members of the extended family required analyzing the brains of patients after they died, but many people were uncomfortable with the idea of donating their brains to science.

Then, in 1995, he approached the relatives of a 56-year-old woman who belonged to the extended family after she died with dementia in the village of Angostura. Over the phone the relatives declined to donate her brain, and Dr. Lopera was also rebuffed when he sought help from the mayor, a priest and the local hospital director.

Nonetheless, Dr. Lopera and a pathologist drove to the village, joined the woman's family at her funeral and beseeched her 14 adult children.

All agreed, except for one son, a policeman linked to drug traffickers, who drunkenly demanded that Dr. Lopera pay 20 million pesos for the brain. Dr Lopera ultimately negotiated with the man for permission without payment, and the pathologist removed the woman's brain.

With the brain in formaldehyde in his hand luggage, the pathologist flew to Massachusetts, where Dr. Kenneth S. Kosik, a neuroscientist working with Dr. Lopera, detected plaques and tangles that he described as "textbook Alzheimer's."

Later, Dr. Lopera and Dr. Kosik identified a single genetic mutation - on the presenilin 1 gene on chromosome 14 – responsible for the cases of Alzheimer's in the extended family. Dr. Lopera called it the Paisa mutation, using the name for people from northwest Columbia.

"We now had a genetic explanation for the largest known family in the world with familial Alzheimer's." Dr. Kosik said. People who inherit one copy of that mutation, labeled E280A by scientist, are virtually guaranteed to develop cognitive decline in midlife.

The exact reasons and the timing for most cases of Alzheimer's are unclear, however the predictability and the distinct cause of the Columbian family's disease have presented an exceptional opportunity for research. Among other efforts, Dr. Lopera created a bank of more than 300 brains and a registry of members or the family.

He eventually helped lead a clinical trial of a drug given to members of the family before they developed symptoms. His research studies identified people with Paisa mutation who kept Alzheimer's at bay for years and determined that these individuals had other mutations that protected them form early-onset symptoms. These findings could yield clues for Alzheimer's treatments in the future.

Francisco Lopera Restrepo was born on June 10, 1951, in Aragón, Columbia, north of Medellin, the fourth of 13 children of Blanca Elena Restrepo and Luis Emilio Lopera, who owned a corner shop. He grew up in nearby Yarmal and was often called by the nickname Pacho.

Survivors include his wife Claramonika Urbe and their daughter Karina.