Gene discovered that causes brain lesions among Hispanics

For Martha Valdivia, the only certainty about her blackouts were the scary questions that always followed:
How did she end up on the other side of the store? What did she say or do during those lost five minutes? "I used to think it was all in my head," Valdivia said with a laugh. "Actually, it is all in my head."

Sort of. Researchers at Barrow Neurological Institute have concluded that it's all in her genes - one particular gene that causes a brain lesion that leads to Valdivia's seizures. And they think they can both develop therapies to eliminate the seizures and create tests to detect the same problem, which seems more prevalent in Hispanic families than in others.

Barrow researchers say it's a gene called KRITl that causes cerebral cavernous malformations, or clumps of capillaries inside the brain that can lead to seizures, migraines and hemorrhages.

The Barrow study is part of the Human Genome Project, a nationwide effort to have a "working draft" of the genetic code by mid-2000. It also is part of St..Joseph's Hospital, and Medical Center's efforts to expand its role in genetic research. Eric Johnson, molecular genetics chief at Barrow, plans to open a clinic to test people who want to know whether they are genetically at risk for such conditions as cystic fibrosis or certain types of muscular dystrophy. The hospital got into the gene hunt after its physicians realized they were treating a large number of patients - many times from the same Hispanic families for the brain lesions. The cerebral lesions occur in about one out of every 250 people. But in 40 percent of the cases, they go undetected, sometimes with deadly consequences. U.S. Olympic track star Florence Griffith Joyner died last year after she suffered a lesion-caused seizure and suffocated in her sleep.

Frequently, people can have multiple lesions, ranging in size from a BB to a half-dollar, said Dr. Joseph Zabramski of Barrow. But, they don't cause problems because of their size or their location in the brain. It was Zabramski who thought genetics could be behind the large number of families with the lesions. As researchers started asking questions, they found stronger family ties. In 1994, Zabramski, with the help of a state grant, looked at six large Hispanic families. Researchers tracked down family members and persuaded them to get an MRI. Fifty percent of the family members had lesions. He then took his work to Johnson, who has a background in neurogenetics and pharmacology.

They knew that the gene that was responsible was on chromosome 7. But then the search was on, said Zabramski who likened it to trying to find a "John P. Smith" in the United States. By placing it on Chromosome 7, they knew what state it was in. "But," he said, "it's a very populated state. Through statistical analysis, blood tests of patients, computer modeling and mapping, Barrow and other researcher across the country tried to locate the gene. At times, they would compare 18-by 24-inch sheets of film, similar to X-rays, to check for gene mutations."We ran down several blind alleys," Johnson said. "There were four to six times when we were sure we had nailed the gene. We'd get on the Internet and there would be all of us buzzing, and it would turn out to be false." Now that they've found it, researchers will try to figure out what the gene does. Are the lesions caused because the gene is stuck on overdrive? Or is it simply not working? Zabramski hopes to have answers in several years.

Another question to be answered is why Hispanics show more signs of inheriting the risk. Johnson thinks the malformations could have occurred centuries ago and been carried through bloodlines since. Meanwhile, researchers are encouraging families to come in for testing. Previously, patients suspected of having the lesions, would have to go in for MRI's, a costly and claustrophobic procedure. Now a blood test can do the work.

Valdivia is urging her family to get tested, but it's a difficult sales job. Sometimes, people just don't want to know, she said. For her, it was the unknown that was so unnerving about her seizures. Not only did she not know when she would have them, doctors couldn't pinpoint why she was having them or what medications would alleviate them.

After surgery last year, Valdivia's seizures went from several a day to five or six within the past year. She cut her medication drastically. After so long of not knowing. I can't believe they have figured out anything about this," she said. "It's just amazing."