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Research Team Narrows Search for Diabetes Gene

After sifting through the human genome for more than two years, researchers have found a gene that may make people susceptible to non-insulin-dependent diabetes mellitus (NIDDM), or type II diabetes.

A team of 33 scientists reported in the June, 1996, issue of *Nature Genetics* that they've roughly located NIDDM1, a gene that has a major effect on NIDDM in Mexican Americans. Now they must isolate the gene, which lies on chromosome 2.

"I believe that a gene found by my research team may be part of a new group of genes involved in regulating blood glucose levels."

— Graeme Bell

"This is the crucial first step toward finding a gene that is a major contributor to the common forms of this extremely prevalent disease," said Graeme Bell, a Howard Hughes Medical Institute investigator at the University of Chicago and senior author of the report.

NIDDM affects an estimated 15 million people in the United States. Heredity plays a role in NIDDM, but finding the responsible genes has proved difficult. Researchers need to gather large, multi-generational families for NIDDM genetic studies. Bell's team hit on the idea of using "affected sibling pairs"—adult brothers and sisters with NIDDM—as a way around recruiting extended families for DNA tests.

Craig Hanis and colleagues at the University of Texas Houston Human Genetic Center collected blood samples from 330 pairs of Mexican-American adult siblings, all with NIDDM. The study's participants hail from Starr County, Texas, which has the highest number of diabetes-related deaths of any county in Texas. U.T. Houston researchers have studied inhabitants of Starr County in long-term genetic and epidemiologic studies of diabetes since the late 1970s.

With blood samples in hand, four research centers screened the entire genome: Bell's HHMI/University of Chicago team; the U.T. Houston group;

Patrick Concannon and colleagues at the Virginia Mason Research Center in Seattle; and Richard Spielman's team at the University of Pennsylvania. Nancy Cox of the University of Chicago did the statistical analysis of the genetic data.

For 30 months, each team combed through nearly 500 DNA markers from each study participant. DNA markers are small fragments of DNA that vary from person to person. In the end, one marker on chromosome 2 stood out as the most likely candidate.

"We now believe that late-onset NIDDM in Mexican Americans results from the action of at least one relatively major susceptibility gene on chromosome 2," said Hanis. The research could lead to a whole new group of diabetes genes. Eventually, Hanis said, researchers hope to learn how these genes interact with environmental factors to trigger diabetes.