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Scientists Discover First Gene for Tourette Syndrome

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A team of scientists has discovered the first gene mutation that may cause some cases of Tourette syndrome (TS), an inherited neuropsychiatric disorder known for involuntary muscle and vocal tics. The National Institute of Neurological Disorders and Stroke (NINDS), a part of the National Institutes of Health, provided funding for this research.

The team was led by NINDS grantee Matthew State, Ph.D., a geneticist at Yale School of Medicine. "We're delighted that our grant support to Dr. State contributed to the finding of the first gene for TS and hope for the speedy discovery of other genes that cause or contribute to this disorder," said Laura Mamounas, Ph.D., the NINDS program director for TS research. Findings appear in the October 14, 2005 issue of *Science.**

The gene, named SLITRK1, was found through genetic analysis of a boy with TS who was previously identified as having an "inversion" on chromosome 13 - a portion of the chromosome had an orientation opposite that of the normal chromosome. He was the only family member with TS and the inversion, suggesting that these two events were related.

The team then screened SLITRK1 (found near where the boy's chromosome was abnormal) in 174 patients with TS and discovered an abnormality in the coding sequence of the gene in one family. The researchers also identified a separate mutated gene sequence in two unrelated individuals with the disorder. None of these mutations were identified among several thousand unaffected control individuals. Additional testing in cell cultures showed changes in protein expression or function, confirming the finding of the mutated gene.

"We now have an important clue to examine Tourette syndrome on a molecular and cellular level. Confirming this, in even a small number of TS patients, will pave the way for a deeper understanding of the disease process and offer a potential target for the development of drugs to treat the disorder," said Dr. State.

The normal SLITRK1 gene is involved with the growth of nerve cells and how they connect with other neurons. The mutated gene was found in regions of the brain (basal ganglia, cortex, and frontal lobes) previously identified as being associated with TS. Several chromosomal regions with breaks had previously been identified as possible sites of a TS-causing gene.

TS occurs in people from all ethnic groups; males are affected about three to four times more often than females. It is almost always noticed first in childhood, with the average onset between the ages of 7 and 10 years. An estimated 200,000 Americans have the most severe form of TS, and as many as one in 100 have milder and less complex symptoms such as chronic motor or

vocal tics or transient tics of childhood. Most people with TS experience their worst symptoms in their early teens, with improvement occurring in the late teens and continuing into adulthood.

The research team included scientists in the Tourette Syndrome Association's International Consortium for TS Genetics. In March 2000, the NINDS awarded the Consortium a five-year grant for $8.5 million to study the genetic causes of the disorder.

The NINDS is the nation's leading funder of research on the brain and nervous system. More information about the NINDS and neurological disorders is available at **www.ninds.nih.gov**.

*Abelson JF, Kwan KY, O'Roak BJ, Baek DY, Stillman AA, Morgan TM, Mathews CA, Pauls DL, Raisin M-R, Gunel M, Davis NR, Ercan-Sencicek AG, Guez DH, Spertus JA, Leckman JF, Dure IV LS, Kurlan R, Singer HS, Gilbert DL, Farhi A, Louvi A, Lifton RP, Sestan N, State MW. "Sequence Variants in SLITRK1 Are Associated with Tourette's syndrome." *Science* , October 14, 2005, Vol. 310, No. 5746, pp. 317-320; DOI:10.1126/science.1116502.

-by Paul Girolami

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