

GENETIC BREAKTHROUGH YIELDS CLUE TO TS

Yale University Investigator Makes Critical Discovery

In what is being called a significant breakthrough in understanding the genetic underpinnings of Tourette Syndrome, researchers have identified a gene mutation that appears to lead to this neurological disorder in some individuals.

A paper published in *Science* (October 14, 2005) reported findings by a team led by Dr. Matthew State, Assistant Professor of Child Psychiatry and Genetics, Yale University School of Medicine and Child Study Center.* Pursuing genetic analysis of one boy with TS with a known chromosomal abnormality, the group was able to pinpoint a gene on Chromosome 13 that is associated with some forms of TS. The gene is expressed in the brain's cortex and basal ganglia—the same regions previously implicated in causing TS symptoms. When functioning normally, it is involved with neuron growth in these regions. Two additional rare abnormalities in the gene were identified in other affected individuals.

Dr. State's group was able to then confirm their findings in a number of ways: by performing several additional tests on non-affected relatives (the initial mutation was not found), and by determining that none of the abnormalities identified in patients were present in many thousands of chromosomes from unaffected individuals. Additional testing in cell cultures showed that the genetic changes identified altered protein function or expression. Taken together, these converging results suggest that this gene is associated with some forms of TS in some families.

TSA has provided substantial funding for a significant number of TS genetic studies for over two decades. It now appears that after many years of pursuit, a critical discovery has been made.

The Association and its Board of Directors have already moved quickly and approved additional support to continue this work.

Last year, Dr. State was awarded the TSA Early Career Research Award for his work in identifying the genes involved in TS. At that time, TSA funding also was awarded to Nenad Sestan, M.D., Ph.D. a co-author on the paper. With this recent TSA funding, Drs. State, Sestan and colleagues will now pursue the development and investigation of a mutant mouse where the suspect gene has been inactivated. Such a "knock out" mouse will allow the team to examine the impact of this gene mutation on normal brain development.

"While not a cure, TSA's funding of this effort is not only a logical 'next small step,' but it is also potentially a 'giant leap' in the broader field of TS science, and

especially for the long-standing efforts by scientists to identify the causes of, and improved treatments for this disorder," said Dr. Neal Swerdlow, Chair of TSA's Scientific Advisory Board and neuropsychiatrist at the University of California, San Diego, School of Medicine.

Through newsletter articles and subsequent advertising for families with known chromosomal abnormalities, TSA was able to locate and then refer the family that proved critical to this study to Dr. Carol Mathews (UCSD) who did a comprehensive assessment of the family. She in turn forwarded that information on to Dr. David Pauls (MGH) who knew that Dr. State's

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TS Segment on Oprah

Kids Talk about TS and Promote the HBO/TSA Documentary

Colin Shoff, Amanda Shirey and Jasper Bledsoe appeared on the November 8 *Oprah Winfrey Show* to talk about life with Tourette Syndrome and the HBO/TSA documentary *I Have Tourette's but Tourettes Doesn't Have Me*—which premiered on November 12. The children and their mothers were flown to Chicago for the interviews where they faced the daunting challenge of appearing before an attentive studio audience and viewers around the world.

Oprah asked the three mothers sitting in the front row when they realized their children were different and also showed clips from the documentary.

The Oprah Winfrey Show is watched by an estimated 21 million viewers a week in the United States and is also aired in 109 countries around the world. The scale of the talk show's reach dwarfs nearly every other opportunity to promote TS awareness. The campaign continued with nationally televised interviews on the *CBS Early Show*, *Paula Zahn Now*, and *The Insider*.

The children's appearances on *Oprah* and other television shows helped TSA achieve an extraordinary audience for the premiere of the documentary.

