Researchers have discovered how abnormalities in microRNAs, a family of molecules that regulate expression of numerous genes, may contribute to the behavioral and neuronal deficits associated with schizophrenia.

The findings are illuminated in the journal *Nature Genetics* as Columbia University professors Maria Karayiorgou, M.D., and Joseph A. Gogos, M.D., Ph.D., explain how they uncovered a previously unknown alteration in the production of microRNAs.

The alterations appear to influence a chromosome known to be associated with schizophrenia.

"By digging further into this chromosome, we have been able to see at the gene expression level that abnormalities in microRNAs can be linked to the behavioral and cognitive deficits associated with the disease," says Karayiorgou.

The investigators modeled mice to have the same genetic deletion as the one observed in some individuals with schizophrenia and examined what happens in the expression of over 30,000 genes in specific areas of the brain.

The significance of this work is that it implicates a completely novel, previously unsuspected group of susceptibility genes and brings investigators a step closer to understanding the biological mechanisms of this disorder.

Implication of such a large family of genes (the most recent estimate puts the number of human microRNAs at at least 400 that influence the expression of as many as a third of all genes) could partly account for the genetic complexity associated with this devastating disorder and explain some of the difficulties that the researchers have encountered in their efforts to pinpoint individual genes.

"Our hope is that the more we know about the genes involved in schizophrenia, the more targeted treatment can be," said Dr. Gogos.

"Much in the way that cancer patients who have tested for a particular gene, such as BRAC1, can be tested and then treated with protocols designed specifically for them, we want to be able to know enough about the schizophrenic brain to target treatments to individual patients."

The next step for the researchers is to find the many genes whose expression is controlled by the identified deficient microRNAs, which could in turn be involved in the pathogenesis of schizophrenia. Much more study and identification of other genetic variants must be done to further illuminate the disease's genetic underpinnings, according to Drs. Karayiorgou and Gogos.

Source: Columbia University