

Immunity, signaling genes may be linked to schizophrenia

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The secret to schizophrenia, psychiatry's most abiding mystery, may lie in the DNA associated with the body's immune system, according to a genome-wide study published online Tuesday.

The analysis of variations in nearly 150,000 DNA samples identified 108 regions that strongly correlate with the highly heritable disorder, which is marked by psychotic episodes and cognitive deficits.

Many of the areas of DNA identified by the study either include a functioning gene or are close to one, including those previously associated with [schizophrenia](#) and other psychiatric disorders, according to the study published online Tuesday in the journal *Nature*.

Though far from producing a "smoking gun," the findings provide substantial support for a genetic root to the disorder and greatly narrow the search for genes that may cause the disease, the authors said.

"The fact that we were able to detect [genetic risk factors](#) on this massive scale shows that schizophrenia can be tackled by the same approaches that have already transformed our understanding of other diseases," the study's senior author, Michael O'Donovan, director of the Institute of Psychological Medicine and Clinical Neurosciences at Cardiff University, said in a statement.

The most significant association involves an area on chromosome six that harbors genes associated with the cellular mechanism that flags

foreign invaders so that the body's immune system can attack them. All of the anti-psychotic drugs used to treat symptoms of schizophrenia target that system, known as the major histocompatibility complex.

Other suspect areas of the genome include coding associated with signal transmission of neurons and with reception of the [neurotransmitter dopamine](#). Researchers have long suspected that schizophrenia is rooted in abnormal signaling involving dopamine.

The work was led by a multi-national consortium of dozens of scientists who have been investigating the roots of [psychiatric disorders](#) through genome-wide association studies, which identify variations in [genetic code](#) that are associated with disease. It was funded by the National Institute of Mental Health and Broad Institute, a biomedical research organization that partners with the Massachusetts Institute of Technology, and Harvard University and its affiliated hospitals.

The same consortium last year highlighted genetic risk factors common to autism, bipolar disorder, attention deficit hyperactivity disorder, major depression and schizophrenia. Other studies have identified about 30 areas of genetic code associated with schizophrenia.

Researchers not involved in the study praised its findings even as they cautioned that hope of a genetic key to the disease has been dashed before. Identifying an area of the genome associated with the disease is not the same as finding a specific gene, and far from identifying the biomechanical process behind the disease, said Jonathan Flint, an Oxford University geneticist who was a co-author of a separate opinion on the study in the journal *Nature*.

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