

Researchers confirm multiple genes robustly contribute to schizophrenia risk in replication study

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Multiple genes contribute to risk for schizophrenia and appear to function in pathways related to transmission of signals in the brain and immunity, according to an international study led by Virginia Commonwealth University School of Pharmacy researchers.

By better understanding the molecular and [biological mechanisms](#) involved with schizophrenia, scientists hope to use this new genetic information to one day develop and design drugs that are more efficacious and have fewer side effects.

In a study published online in the April issue of *JAMA Psychiatry*, the [JAMA](#) Network journal, researchers used a comprehensive and unique approach to robustly identify genes and biological processes conferring risk for schizophrenia.

The researchers first used 21,953 subjects to examine over a million genetic markers. They then systematically collected results from other kinds of biological schizophrenia studies and combined all these results using a novel data integration approach.

The most promising [genetic markers](#) were tested again in a large collection of families with [schizophrenia patients](#), a design that avoids pitfalls that have plagued [genetic studies](#) of schizophrenia in the past. The genes they identified after this comprehensive approach were found

to have involvement in [brain function](#), nerve cell development and immune response.

"Now that we have genes that are robustly associated with schizophrenia, we can begin to design much more specific experiments to understand how disruption of these genes may affect [brain development](#) and function," said principal investigator Edwin van den Oord, Ph.D., professor and director of the Center for Biomarker Research and Personalized Medicine in the Department of Pharmacotherapy and Outcomes Science at the VCU School of Pharmacy.

"Also, some of these genes provide excellent targets for the development of [new drugs](#)," he said.

One specific laboratory experiment currently underway at VCU to better understand the function of one of these genes, TCF4, is being led by Joseph McClay, Ph.D., a co-author on the study and assistant professor and laboratory director in the VCU Center for Biomarker Research and Personalized Medicine. TCF4 works by switching on other genes in the brain. McClay and colleagues are conducting a National Institutes of Health-funded study to determine all genes that are under the control of TCF4. By mapping the entire network, they aim to better understand how disruptions to TCF4 increase risk for schizophrenia.

"Our results also suggest that the novel data integration approach used in this study is a promising tool that potentially can be of great value in studies of a large variety of complex genetic disorders," said lead author Karolina A. Aberg, Ph.D., research assistant professor and laboratory co-director of the Center for Biomarker Research and Personalized Medicine in the VCU School of Pharmacy.

Provided by Virginia Commonwealth University

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