

Does immune dysfunction contribute to schizophrenia?

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A new study reinforces the finding that a region of the genome involved in immune system function, called the major histocompatibility complex (MHC), is involved in the genetic susceptibility to schizophrenia.

Schizophrenia is among the most disabling [psychiatric disorders](#). Approximately 80% of the risk for developing schizophrenia is heritable, but there has been slow progress in identifying [genetic variation](#) that contributes to the risk for schizophrenia.

The current paper contributes to this growing literature by identifying variants of genes that influence the function of the immune system which may contribute to the heritable risk for schizophrenia.

Two large, international, collaborating groups of scientists – the Wellcome Trust Case Control Consortium 2 and the Irish Schizophrenia Genomics Consortium – conducted this new study.

They first performed what is called a discovery scan, where they analyzed over 6 million genetic variants in [schizophrenia patients](#) and controls from Ireland. This allowed them to compile a list of variants that showed the strongest association signals with schizophrenia.

They then performed similar work in an independent sample of 13,195 cases and 31,021 controls from around the world in order to search for the same top 'hits'. This wealth of data was provided by the international schizophrenia genetics community. This replication work is an important

scientific strategy, particularly in the field of genetics, to strengthen and support the original findings.

Using these multiple datasets and approaches, their findings lend further support for the involvement of the [MHC genes](#) in schizophrenia susceptibility. "In this large collaborative effort, we have replicated evidence for specific risk and protective alleles at the MHC locus - a critical step teasing apart the [genetic risk](#) mechanisms involved," commented Dr. Aiden Corvin, one of the lead authors and a professor at Trinity College Dublin. "However, pinpointing specific risk genes or [alleles](#) has been challenging because this is a region of great genomic variation within and between populations."

These genetic findings also highlight an important gap in our understanding of the biology of schizophrenia. There is a long history of interest in immunologic contribution to schizophrenia including wide ranging observations linking viral infection, gluten sensitivity, changes in cytokine levels in blood and cerebrospinal fluid, and other factors to schizophrenia.

"Despite this, we have relatively little understanding how alterations in immune function are involved in the etiology and pathophysiology of this disorder," commented Dr. John Krystal, Editor of *Biological Psychiatry*. "Immunologic studies in schizophrenia that illuminate the nature of the contribution of variation in immune system genes to schizophrenia will be an important new direction in schizophrenia research."

More information: The article is "Genome-wide association study implicates HLA-C*01:02 as a risk factor at the MHC locus in schizophrenia" by Irish Schizophrenia Genomics Consortium & the Wellcome Trust Case Control Consortium 2 ([doi: 10.1016/j.biopsych.2012.05.035](https://doi.org/10.1016/j.biopsych.2012.05.035)). The article appears in *Biological*

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