

Scientists identify gene that may indicate predisposition to schizophrenia

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In a new study from *The American Journal of Human Genetics*, a research team lead by Xinzhi Zhao and Ruqi Tang (Shanghai Jiao Tong University) present evidence that genetic variation may indicate predisposition to schizophrenia. Specifically, their findings identify the *chitinase 3-like 1* gene as a potential schizophrenia-susceptibility gene and suggest that the genes involved in biological response to adverse conditions are likely linked to schizophrenia.

Analyzing two separate cohorts of Chinese patients with schizophrenia, the researchers observed a positive association between schizophrenia and genetic variations in the promoter region of the *chitinase 3-like 1* (*CHI3L1*) gene, an association that was significant in both population-based and family-based investigations.

The *CHI3L1* gene acts as a survival factor in response to adverse environments, countering various types of physiological stress, such as inflammation, nutrient deprivation, and oxygen deficiency, all of which may induce high expression of *CHI3L1*. The gene is located on chromosome 1q32.1, a region that has been previously shown to have a weak correlation to schizophrenia.

A number of environmental factors, including prenatal exposure to disease, have been reported as risk factors of schizophrenia. However, the researchers argue that sensitivity to environmental stressors varies widely among individuals, and "at least part of this variation may be genetic in origin and/or involve gene-environment factors," they write.

Genetic variations that change the expression of *CHI3L1* can influence key processes dependent on *CHI3L1* levels, knocking out portions of the AKT-mediated signal pathway. The AKT-mediated signal pathway has been shown to be impaired in patients with schizophrenia, and antipsychotic medication may induce AKT activation, to compensate for the impairment.

Additionally, activation of the inflammatory response has been observed in those with schizophrenia and other affective disorders.

"In conclusion, our findings identify *CHI3L1* as a potential schizophrenia-susceptibility gene," write the authors. "Our results . . . support the proposal that genes involved in biological response to adverse environmental conditions play roles in the predisposition to schizophrenia."

Citation: Xinzhi Zhao, Ruqi Tang, et al., "Functional Variants in the Promoter Region of Chitinase 3-Like 1 (*CHI3L1*) and Susceptibility to Schizophrenia." *The American Journal of Human Genetics*, 2007;80:12-00018.

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