# Genetic variants associated with major depressive disorder have been identified

July 16 2015, by Bob Yirka

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(Medical Xpress)—A very large team of researchers made up mostly of members in China and calling itself the CONVERGE consortium, has identified two genetic variants that appear to be associated with major depressive disorder (MDD). In their paper published in the journal *Nature*, the team explains how they conducted their research, the results they found, and what their findings might mean for treating people with

the disorder. Patrick Sullivan, with the University of North Carolina offers a News & Views piece on the work done by the team in the same journal issue.

MDD is a uniquely difficult problem—patients report mostly similar symptoms, such as feelings of sadness, lack of emotions all together and lethargy, but science has not been able to find its cause, much less find a cure. One area of study has been genetics, as scientists wonder if perhaps some people are more susceptible due to DNA passed down from their parents. Unfortunately, despite several studies, no genetic link has been found—until now. In this new effort, the team reports that they have found two genetic variants that appear to be tied to people with the most severe form of MDD.

Because of failures in other genetic studies, the researchers with this new effort chose to go a different route; first they started by selecting China as the place, because of the large population and because MDD is not often diagnosed there, which they figured meant, those that due get such a diagnosis are likely severe cases. Next, they restricted study cases to just women of Han Chinese ancestry. They also chose to use low-convergence whole genome sequencing.

The team identified two regions in the genome which appeared to be associated with MDD. The first one was near the SIRT1 gene, the other was in an intron region of the LHPP gene. The first region is possibly the most intriguing Sullivan notes, due to its closeness to the SIRT1 gene—it suggests a possible connection with mitochondria, the part of cells involved in energy production. If that turns out to be the case, this discovery could lead to treatments dedicated to reinvigorating cells at their energy centers.

The discovery by the team is truly groundbreaking, though they suggest that a lot more work still needs to be done with MDD in general to truly

understand its cause and then to come up with a better way to treat it.

**More information:** "Sparse whole-genome sequencing identifies two loci for major depressive disorder." *Nature* (2015) DOI: 10.1038/nature14659


## Abstract

Major depressive disorder (MDD), one of the most frequently encountered forms of mental illness and a leading cause of disability worldwide1, poses a major challenge to genetic analysis. To date, no robustly replicated genetic loci have been identified2, despite analysis of more than 9,000 cases3. Here, using low-coverage whole-genome sequencing of 5,303 Chinese women with recurrent MDD selected to reduce phenotypic heterogeneity, and 5,337 controls screened to exclude MDD, we identified, and subsequently replicated in an independent sample, two loci contributing to risk of MDD on chromosome 10: one near the SIRT1 gene ($P = 2.53 \times 10^{-10}$), the other in an intron of the LHPP gene ($P = 6.45 \times 10^{-12}$). Analysis of 4,509 cases with a severe subtype of MDD, melancholia, yielded an increased genetic signal at the SIRT1 locus. We attribute our success to the recruitment of relatively homogeneous cases with severe illness.


Press release


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