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## **Normal role for schizophrenia risk gene identified**

### *DISC1 makes protein that helps new neurons integrate into our neural network*

How the gene that has been pegged as a major risk factor for schizophrenia and other mood disorders that affect millions of Americans contributes to these diseases remains unclear. However, the results of a new study by Hopkins researchers and their colleagues, appearing in *Cell* this week, provide a big clue by showing what this gene does in normal adult brains.

It turns out that this gene, called *disc1*, makes a protein that serves as a sort of musical conductor for newly made nerve cells in the adult brain, guiding them to their proper locations at the appropriate tempo so they can seamlessly integrate into our complex and intertwined nervous system. If the DISC1 protein doesn't operate properly, the new nerves go hyper.

DISC1 plays a broader role in the development of adult nerves than we anticipated," says Hongjun Song, Ph.D., an associate professor at Hopkins Institute for Cell Engineering. Some previous studies hinted that DISC1 is important for nerve migration and extension, but our study in mice suggests it is critical for more than that and may highlight why DISC1 is associated with multiple psychiatric disorders."

Almost every part of the nerve integration process speeds up, adds fellow author Guo-li Ming, M.D., Ph.D., also an associate professor at ICE. The new nerves migrate and branch out faster than normal, form connections with neighbors more rapidly, and are even more sensitive to electrical stimulation.

While it may not be obvious why high-speed integration would be detrimental, Song notes that because of the complexity of the brain, timing is critical to ensure that new nerves are prepared to plug into the neural network.

Ming, Song and their collaborators at the National Institutes of Health and UC Davis tracked the abnormal movements of the hyperactive nerve cells by injecting a specially designed virus into

a part of a mouse brain known as the hippocampus -a region important for learning and memory and therefore quite relevant to psychiatric disorders. The virus would only infect newly born cells and would both knock down the expression of the disc1 gene and make the nerves glow under a microscope.

Combined with other recent Hopkins research that successfully engineered mouse models that have abnormal DISC1 and can effectively reproduce schizophrenia symptoms such as anxiety, hyperactivity, apathy and altered senses, these current findings teasing out the normal role of this protein may help unravel the causes for this complex disease

Song and Ming add that their studies in the hippocampus - one of the few places where new nerves are made in the adult brain - might answer why symptoms typically first appear in adults despite the genetic basis of many psychiatric illnesses. They plan on continuing their mouse work to try and find those answers.

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On the Web:

<http://www.hopkins-ice.org/neuro/int/song.html>

<http://www.cell.org>

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