NEWS

Genetics: Splicing gene alters expression of autism genes

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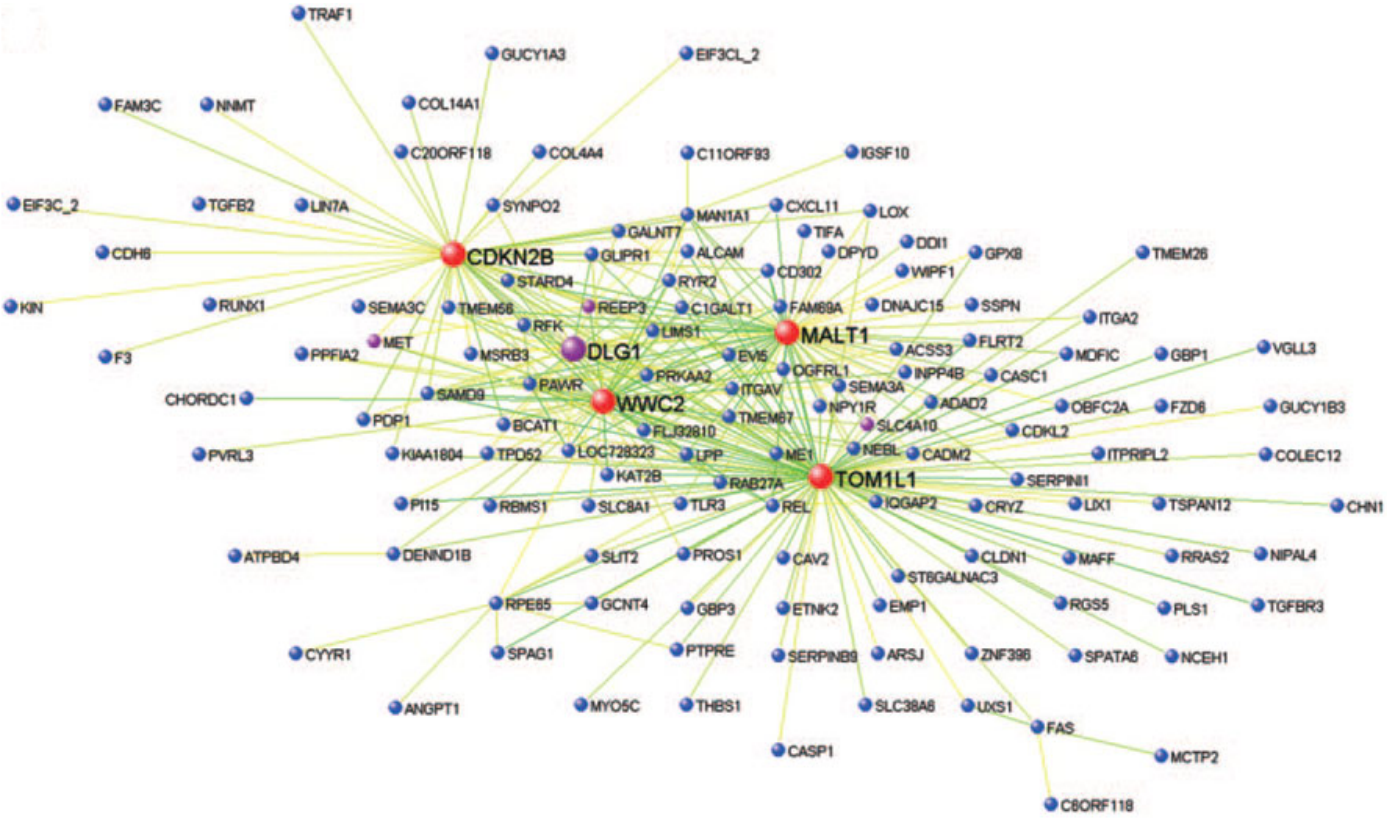

The autism-associated gene **RBFOX1** modifies the sequence of hundreds of genetic messages, a number of which affect the expression of other autism-linked genes, according to a study published 7 July in *Human Molecular Genetics*[1].

RBFOX1 is expressed specifically in neurons and is a splicing factor, piecing together different regions of the genetic messages that code for proteins. Through splicing, cells can generate

different proteins from the same gene.

Mutations in RBFOX1, also called A2BP1, have been linked to autism in a number of genetic studies, and RBFOX2 is expressed at **lower-than-typical levels** in postmortem brains from individuals with the disorder.

In the new study, researchers induced stem cells from fetal brains to develop into neurons. RBFOX1 expression increases as the cells become neurons, suggesting that it plays a role in neuronal development.

The researchers then knocked down levels of RBFOX1 by 60 to 70 percent, which mimics the loss of one gene copy, seen in some individuals with autism. This reduction alters almost 1,000 splicing events in 603 genes, the study found. About half of these are likely to be due to RBFOX2 activity directly, whereas the rest may be the result of altered levels of other splicing factors.

Lowering levels of RBFOX1 also changes the expression of 981 genes compared with controls. These genes are not alternatively spliced themselves, suggesting that RBFOX1 affects the splicing of proteins that in turn regulate gene expression.

The genes with different expression patterns, but not those that are alternatively spliced, include more autism-associated genes than would be expected based on chance alone, the study found. These include **GABRB3**, **NRXN1** and **MET**, as well as genes linked to other neurological disorders, such as schizophrenia.

The researchers also mapped the interactions between these genes and found two gene networks that each include a large number of autism-linked genes.

References:

1: Fogel B.L. *et al. Hum. Mol. Genet.* Epub ahead of print (2012) **PubMed**