

NEWS

Molecular mechanisms: Master regulator altered in autism

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SP1, a protein that regulates the expression of several autism candidate genes, could increase risk of the disorder by simultaneously altering the expression of a number of the genes, according to a study published 24 October in *Biological Psychiatry*¹.

SP1 regulates the expression of numerous other genes and has been implicated in several neurological disorders, including schizophrenia². In the new study, researchers for the first time investigated SP1's role in autism by analyzing protein levels in postmortem brains from 8 individuals with autism and 13 controls.

SP1 levels are higher in autism brains compared with controls in the anterior cingulate gyrus, a brain region involved in emotion, learning and memory, the study found.

The researchers also looked at the expression levels of 15 autism candidate genes that have a potential binding site for SP1. Expression of **PTEN**, **MeCP2** and **ITGB3** — which is associated with **both blood serotonin levels** and autism — is elevated in the anterior cingulate gyrus of autism brains compared with that of controls, the study found. Expression of **reelin** is lower than in controls in the same region.

Levels of OXTR, the gene for the oxytocin receptor, are elevated in the motor cortex and the thalamus, which processes sensory information, and levels of **GABRB3** and HTR2A expression are dampened in the motor cortex, the study found.

To investigate whether SP1 is responsible for differences, the researchers looked at cultured neurons in which SP1 is inactivated either genetically or using chemical inhibitors. In either case, expression of five of the genes — GABRB3, ITGB3, OXTR, PTEN and reelin — is lower in these cells compared with controls, the study found.

SP1 levels are known to increase in response to several processes, including **inflammation of neurons or their support cells** and **oxidative stress**. Studies have also shown that **epigenetic effects**, which regulate gene expression without altering the DNA sequence³, can increase SP1 expression. All of these mechanisms are also associated with increased risk of autism, linking SP1 expression to the disorder, the researchers say.

References:

1: Thanseem I. et al. *Biol. Psychiatry* Epub ahead of print (2011) [PubMed](#)

2: Ben-Shachar D. and R. Karry *PLoS One* 2, e817 (2007) [PubMed](#)

3: Saffer J.D. et al. *Genes Dev.* 4, 659-666 (1990) [PubMed](#)