NEWS

Results of 16p11.2 study show promise for autism biomarker

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Come together: Abnormalities in a signaling pathway link deletion of the 16p11.2 chromosomal region to a set of rare and little-know

The level of activity of a cellular signaling pathway correlates with the degree of social and cognitive impairments in children with an autism-linked genetic abnormality, according to unpublished research presented Sunday at the **2013 Society for Neuroscience annual meeting** in San Diego.

“This is a test case in a defined genetic disorder to develop biomarkers,” says **Elliott Sherr**, professor of neurology at the University of California, San Francisco, who presented the work.

Biomarkers are objective biological measurements — such as the level of a certain chemical in the blood — that would enable scientists to reliably identify individuals with autism or predict how these individuals will fare over the long term.

Researchers have **struggled to identify biomarkers for autism**, aiming for earlier diagnosis of the disorder, or to pinpoint subgroups that are most likely to benefit from specific therapies.

In the new study, Sherr and his colleagues collected blood from children who carry a deletion of the chromosomal region **16p11.2**. They measured the levels of proteins involved in a signaling cascade known as the MAPK/ERK pathway in these blood cells.

The work is part of the Simons Variation in Individuals Project, an effort to comprehensively study a large number of individuals with deletion or duplication of the 16p11.2 region. (The project is funded by SFARI.org's parent organization.)

The 16p11.2 region contains two genes that are involved in the MAP/ERK pathway: **MAPK3** (also known as ERK1) and MVP, thought to be a master regulator of this pathway. Individuals who carry a deletion of this region have only one copy of these genes, rather than the usual two.

The researchers found that, as expected, the blood cells of individuals with 16p11.2 deletion contain lower levels of MAPK3 than do those of controls.

However, activity of the MAPK/ERK signaling pathway overall is higher in children who carry the deletion than in the controls.

To test MVP's role in this phenomenon, the researchers manipulated the gene in laboratory experiments. They showed that temporarily silencing MVP in skin cells taken from controls increases the activity of the MAPK/ERK pathway.

Overactivity of this pathway is also implicated in **a set of rare disorders called RASopathies**. Like 16p11.2 deletion, RASopathies are characterized by intellectual disability, an enlarged head and an increased risk for autism.

Finally, the researchers looked at the relationship between blood MVP levels, intelligence quotient (IQ) and score on the Social Responsiveness Scale, a test measuring autism-related behaviors. Among children with 16p11.2 deletion, those with low levels of MVP also have low IQs and more severe autism symptoms, they found.

"This might be a critical pathway influencing behavior and outcomes in these kids," Sherr says.

The researchers plan to expand these studies to try to identify biomarkers — related to the MAPK/ERK pathway or other signaling pathways — in the broader autism population.

*For more reports from the 2013 Society for Neuroscience annual meeting, please **click here**.*