

NEWS

# Proteins linked to top autism gene might aid early diagnosis

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26 FEBRUARY 2021

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Blood levels of proteins associated with the autism-linked gene PTEN could **influence the course of the condition**, according to a new study. Tests measuring these molecules could also help clinicians diagnose autism and other neurological conditions, and chart their trajectories, the researchers say.

“We might be able to make useful clinical predictions about outcomes that can help to tailor interventions earlier and to help patients and families plan for what is needed,” says lead investigator **Thomas Frazier**, professor of psychology at John Carroll University in University Heights, Ohio.

The **PTEN** gene encodes a protein that suppresses tumors and also influences the connections between neurons. Mutations in PTEN are linked not only to benign tumors and several types of cancer, but also to **autism and macrocephaly**, or an unusually large head.

Much remains unknown, however, about why PTEN mutations can affect people with and without autism differently. For example, PTEN mutations are often associated with impaired mental function in autistic people but not as often in non-autistic people, whose traits can vary widely.

In the new study, Frazier and his colleagues examined how the mutations affect blood levels of not just PTEN protein, but also the proteins it interacts with.

**Molecular links:**

The team assessed the blood levels of various proteins — as well as intelligence quotient (IQ) and other factors related to mental function — in 25 autistic and 16 non-autistic participants with PTEN mutations and macrocephaly, all about 9 years old on average. The researchers also examined 20 participants, about 14 years old on average, with autism, macrocephaly and no PTEN mutations.

PTEN protein levels reflected scores of mental function, the scientists found. For instance, although participants with PTEN mutations typically had the lowest levels of PTEN protein, those with high levels in all three groups tended to have lower IQs, working memory, language abilities and other measures of cognitive skills.

“That surprised me — I would have expected the lower the PTEN levels, the worse the IQ,” says **Huda Zoghbi**, professor of molecular and human genetics at Baylor College of Medicine in Houston, Texas, who was not involved in the study.

The participants with elevated PTEN levels might have abundant but abnormal versions of the protein, Frazier and his colleagues suggest.

“If they have higher levels of the protein, but it’s not a functional protein, that might be worse than lacking a copy of the gene for that protein,” Zoghbi says.

Higher levels of two PTEN-associated molecules — the protein kinase AKT and enzyme inhibitor p27 — also tracked with better mental function. Both proteins may help modify the effects of PTEN mutations, which could explain why PTEN mutations can have varied effects on behavior and cognitive skills, Frazier says. The findings appeared in January in *Molecular Autism*.

## Numbers game:

In addition, autistic children with PTEN mutations and macrocephaly had telltale blood levels of two other proteins: decreased MnSOD, which helps catalyze reactions in mitochondria, and increased P-S6, which helps regulate metabolism. Looking for that pattern might facilitate early diagnosis, the study suggests.

One limitation of the new work is that it included relatively few participants with PTEN mutations, Frazier cautions. He and his team plan to recruit more participants over time to help verify the findings and learn which proteins play important roles.

“Maybe that can help one decide what interventions might work better for one group than another,” Zoghbi says.

Further studies should also look at more proteins, says **Merlin Butler**, professor of psychiatry and pediatrics at the University of Kansas in Kansas City, who did not take part in this work.

“They need to characterize whether the PTEN mutations are very serious changes, where the protein is screwed up, or less severe ones where the protein was still functional,” Butler says. “But this is a good starting point.”