NEWS

# Little-known gene tied to autism, developmental delay

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Rare mutations in a gene called BAZ2B are associated with various conditions of brain development, including autism, according to a new study[1]. The gene is highly active in prenatal brains, and its activity tracks with that of other genes linked to autism.

“This particular gene is quite important for the genes that need to turn on when your brain’s developing,” says lead investigator **Daryl Scott**, associate professor of molecular and human genetics at Baylor College of Medicine in Houston, Texas. When it does not work properly, it may cause developmental delay, intellectual disability and autism, he says.

BAZ2B helps regulate the activity of other genes. It codes for a protein that is involved in opening up **chromatin**, the tightly wound package of DNA and proteins inside a cell’s nucleus. This rearrangement makes genes accessible, allowing them to be transcribed, or ‘turned on.’

Scientists have previously linked other **genes involved in chromatin** regulation to autism. And they have found BAZ2B mutations in people with developmental conditions[2]. The new study cements the link between BAZ2B and brain development and provides a more complete picture of the consequences of mutations in the gene.

“It is collecting all of the different disparate mutation data into one report, so it has got great utility from that point of view,” says **James Sutcliffe**, associate professor of molecular physiology and biophysics at Vanderbilt University in Nashville, Tennessee, who was not involved in the research.

## Autism association:

The research team began by analyzing data from **BrainSpan**, an atlas of **gene expression data** for various ages. They found that BAZ2B is expressed at higher levels in the brain in utero than after birth, suggesting the gene is involved in fetal brain development.

“That means that it might be an important gene for brain development,” Scott says, and “may make a difference in how the brain is put together.”

BAZ2B’s expression in the fetal brain closely matches that of hundreds of other genes linked to autism and related conditions. The results were published in January in *Human Mutation.*

The finding raises the possibility that BAZ2B could be involved in moderating the expression of other autism genes. “Future studies may provide us with insight into what genes BAZ2B is turning on,” Scott says.

The researchers also analyzed sequencing data from nearly 11,000 people with autism, intellectual disability or other developmental conditions. They found five people with de novo, or spontaneous, mutations in BAZ2B. This frequency is higher than would be expected in a group of this size.

## Case studies:

The team used two clinical databases to identify seven other people with BAZ2B mutations that might inactivate or dial down one copy of the gene.

Most people have two copies of the gene, but in those who have one of these mutations, “there is only one that we think is really working full on,” Scott says. All seven people have some combination of autism, intellectual disability and developmental delay.

However, it is still unclear which cellular processes go awry and which genes may be affected when BAZ2B is mutated, says **Kenneth Kosik,** professor of neuroscience at the University of California, Santa Barbara, who was not involved in the research. “It doesn’t really get at the mechanism yet, and that’s of course going to be very important,” he says. “What are the cell biological implications of these genetic variants that they found in BAZ2B?”

Researchers have not yet determined how these mutations increase the odds of autism. “We would have to see many, many more kids and get a better feel for the type of spectrum that's out there,” Scott says. “But this is a first step.”

**REFERENCES:**

1. Scott T.M. *et al. Hum. Mutat.* Epub ahead of print (2020) **PubMed**
2. McRae J.F. *et al. Nature* **542**, 433-438 (2017) **PubMed**