

## Blood-based epigenetic research may hold clues to autism biology, study suggests

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Using data from blood and brain tissue, a team led by researchers at Johns Hopkins Bloomberg School of Public Health found that they could gain insights into mechanisms that might help explain autism by analyzing the interplay between genes and chemical tags that control whether genes are used to make a protein, called epigenetic marks.

The findings, to be published Oct. 24 in *Nature Communications*, could

ultimately help lead to new ways of treating and preventing the disorder.

Researchers have long known that chemical modifications, a collection of "marks" on DNA known as the epigenome, play a key role in how cells operate by guiding differences between various [tissue](#) types in a given individual's body, despite the fact that they all carry the same genetic code.

"The reason a brain cell is different from a heart cell is because of the epigenome, which affects which parts of a cell's DNA are read," says study lead M. Daniele Fallin, PhD, chair of the Bloomberg School's Department of Mental Health and director of the School's Wendy Klag Center for Autism and Developmental Disabilities. "Think of it like an encyclopedia with a bunch of tabs. Cells don't need to read the entire encyclopedia; they jump to the tabs they need to get things done."

The current work shows that changes in the genetic code of a particular gene can control [epigenetic marks](#) at different genes, implying that a gene's genetic code can affect whether other genes are turned on and off, which makes it important to understand the function of all genes involved, not just the one with the so-called misspelling. "Our findings suggest that looking only at genes with misspellings related to [autism](#) might be too narrow a focus," says Fallin. "Instead of looking solely at the genes directly implicated in autism through their genetic code changes, we really should be also studying the functions of the other genes implicated by these changes in genetic code through epigenetic connections. "

Autism spectrum disorder (ASD) is a neurodevelopmental condition characterized by deficits in socialization, verbal and nonverbal communication, and repetitive behaviors. Since the 1960s, the prevalence rates have skyrocketed, with one in 68 U.S. children now being diagnosed with ASD, according to the Centers for Disease Control

and Prevention.

While a few rare gene variants can explain a fraction of ASD cases, Fallin and other researchers suspected that the epigenome could add significantly more to understanding this disease. However, researchers have been skeptical of blood-based epigenetic studies for one main reason: While the genome is the same in any cell from the same individual, the epigenome necessarily changes from tissue to tissue. And although brain tissue—the tissue most affected by ASD—might yield the most useful epigenetic data, it can't be sampled from living individuals. The findings show the promise of collecting epigenetic data in blood.

To investigate this question, Fallin and her colleagues started by surveying four different tissue types—blood and cord blood from their own collections, as well as lung and fetal brain tissue from public collections—to find small variations in the genetic code of each sample that appear to be responsible for DNA methylation state, a type of epigenetic modification, in that particular tissue.

The researchers examined millions of these genetic code variations, known as single nucleotide polymorphisms (SNPs) and found thousands that control DNA methylation in some or all tissue types. They then matched up these SNPs with those already known to be associated with autism and saw that more autism-associated genes act to control DNA methylation than would be expected by chance. This was true in both blood and fetal brain tissue.

When the researchers looked at the role of genes that were methylated by genes with code differences related to ASD, including additional genes beyond those with direct [code](#) changes, they found that the majority were involved in biological pathways that were important in immune function. The finding wasn't surprising, Fallin explains—numerous studies have identified abnormal gene expression of

immune genes in autism samples and environmental experiences such as prenatal infection or prenatal exposure to pollutants that can ramp up immune responses are risk factors for ASD. However, none of the [genetic code](#) mutations directly identified in autism had pointed to these pathways. It is only when considering which other genes they may regulate that this biology is revealed.

More study on these biological pathways, she says, could lead to specific [genes](#) or proteins that could be modifiable with pharmaceuticals or other interventions, possibly offering new ways to prevent or treat ASD.

"We made our findings here by comparing brain data to blood data," she says, "but the vast majority we could have learned from blood."

**More information:** Shan V. Andrews et al. Cross-tissue integration of genetic and epigenetic data offers insight into autism spectrum disorder, *Nature Communications* (2017). [DOI: 10.1038/s41467-017-00868-y](https://doi.org/10.1038/s41467-017-00868-y)

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