NEWS

Mutations in tuberous sclerosis gene may be rife in autism

BY **ANN GRISWOLD**

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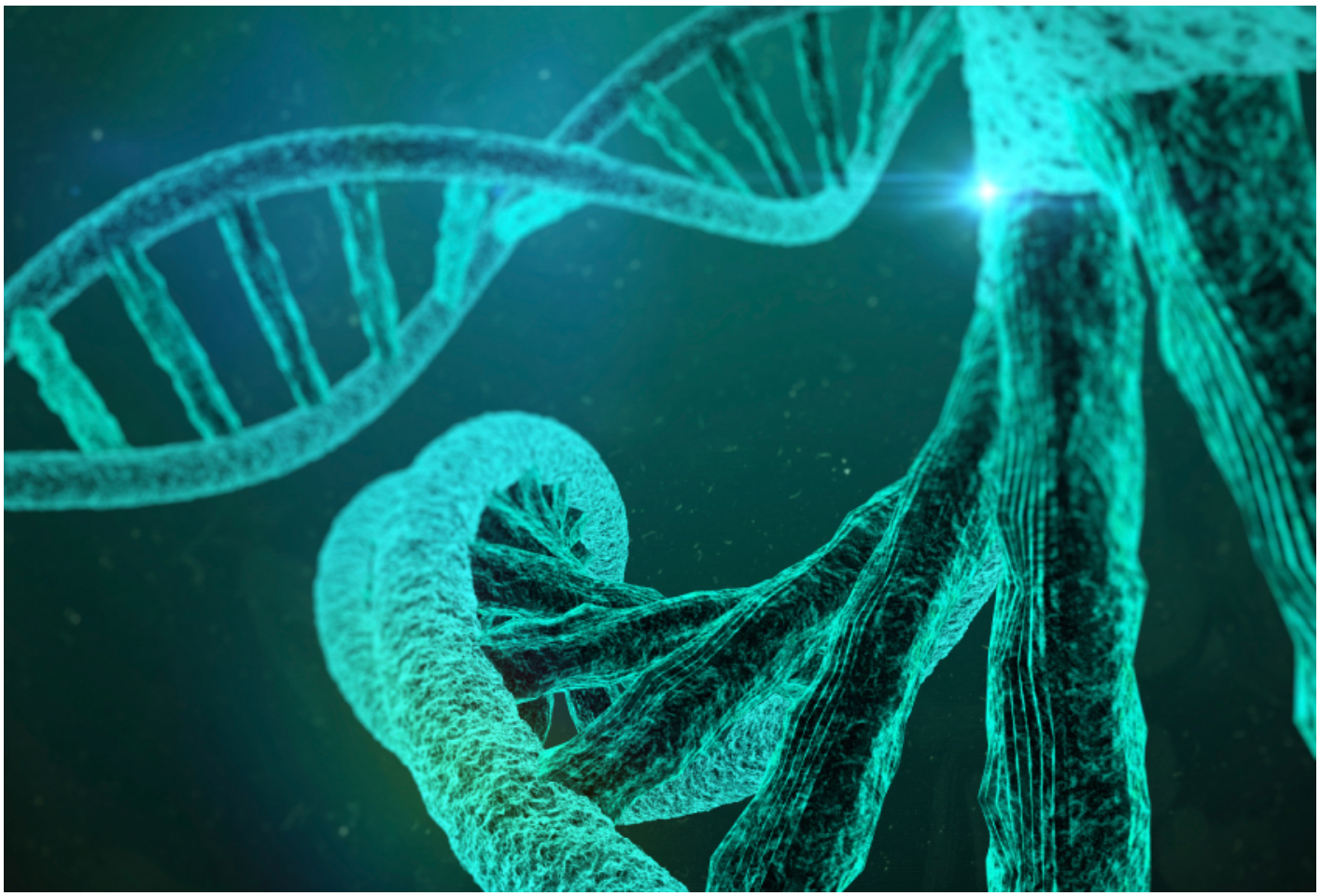

Mutations in TSC2, a gene typically associated with a syndrome called tuberous sclerosis, are found in many children with autism, suggests a genetic analysis presented yesterday at the **2016 International Meeting for Autism Research** in Baltimore.

The findings support the theory that **autism results from multiple 'hits'** to the genome.

Tuberous sclerosis is characterized by benign tumors and skin growths called macules. Autism symptoms show up in about **half of all people with tuberous sclerosis**, perhaps due to **abnormal wiring of neurons** in the brain. Tuberous sclerosis is thought to result from mutations in either of two genes: TSC1 or TSC2.

The new analysis finds that mutations in TSC2 can also be silent, as far as symptoms of the syndrome go: Researchers found the missense mutations in 18 of 87 people with autism, none of whom have any of the characteristic traits of tuberous sclerosis.

"They had no macules, no seizure history," says senior researcher **Louisa Kalsner**, assistant professor of pediatrics and neurology at the University of Connecticut School of Medicine in Farmington, who presented the results. "We were surprised."

The researchers stumbled across the finding while searching for genetic variants that could account for signs of autism in children with no known cause of the condition. They performed genetic testing on blood samples from 87 children with autism.

Combined risk:

To see whether silent TSC2 mutations are equally prevalent in the general population, the researchers scanned data from 53,599 people in the Exome Aggregation Consortium database. They found the mutation in 10 percent of the individuals.

The researchers looked more closely at the children with autism, comparing the 18 children who have the mutation with the 69 who do not.

Children with TSC2 mutations were diagnosed about 10 months earlier than those without a mutation, suggesting the TSC2 mutations increase the severity of autism features. But in her small sample, Kalsner says, the groups show no differences in autism severity or cognitive skills. The researchers also found that 6 of the 18 children with TSC2 mutations are girls, compared with 12 of 69 children who don't have the mutation.

TSC2 variants may combine with other genetic variants to increase the risk of autism. "We don't think TSC is the sole cause of autism in these kids, but there's a significant chance that it increases their risk," Kalsner says.

The results are preliminary. Comparing DNA samples from the children and their parents, for example, could reveal whether the mutations are spontaneous or inherited.

Still, "the findings are intriguing," says **Mustafa Sahin**, associate professor of neurology at

Children's Hospital Boston, who was not involved in the work. "The key is to replicate the findings in an independent and larger set of samples."

For more reports from the 2016 International Meeting for Autism Research, please ***click here****.*