NEWS

Some autism genes may be especially vulnerable to mutations

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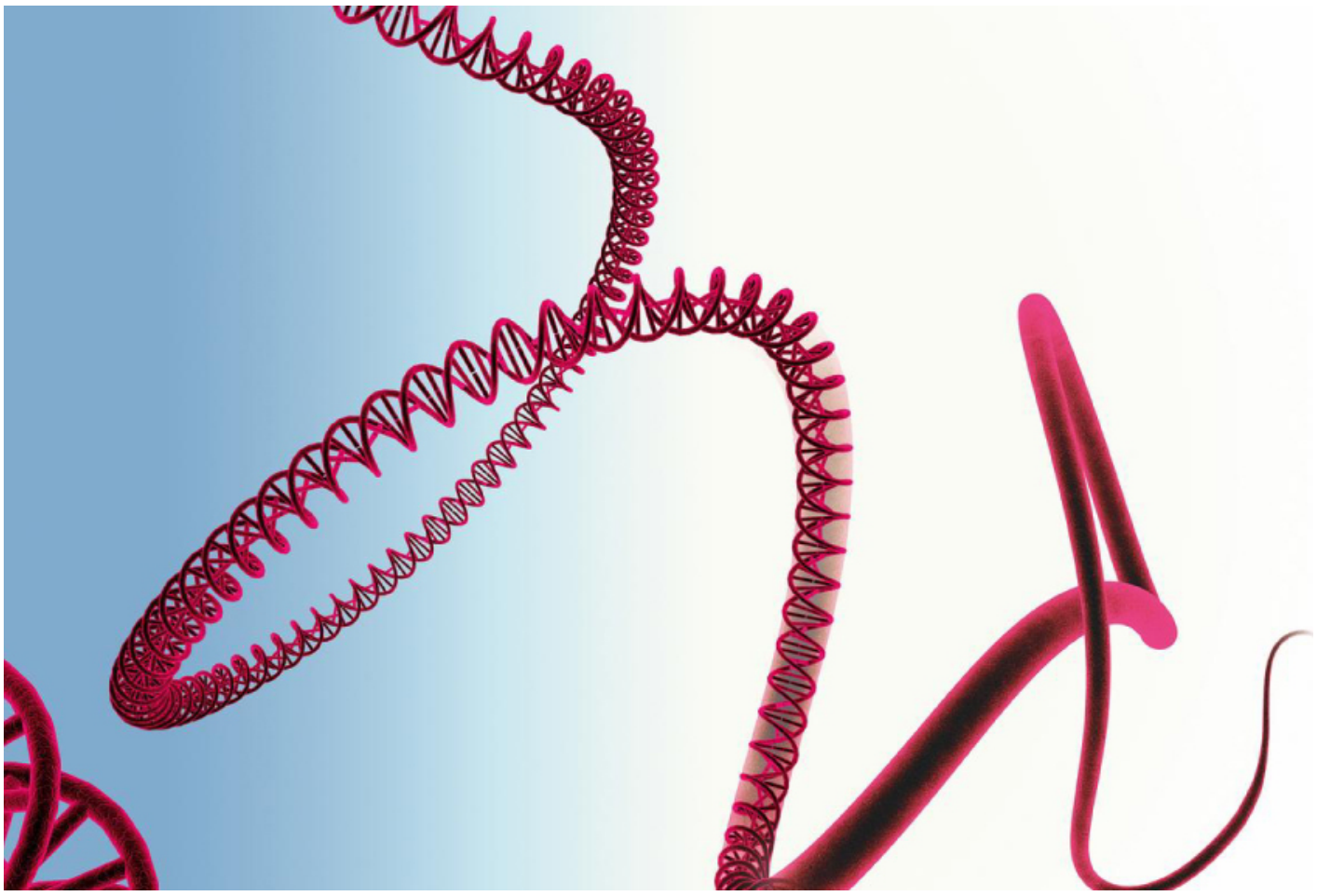

A small number of autism genes are located in fragile regions of the genome — those prone to breaking when cells copy DNA.

Researchers presented the unpublished findings yesterday at the **2018 Society for Neuroscience annual meeting** in San Diego, California.

“We think this [vulnerability] is contributing to the development of some neurological diseases,” says **Meiyan Wang**, a graduate student in **Fred Gage**’s lab at the Salk Institute for Biological Studies in La Jolla, California, who presented the findings.

Wang and her colleagues studied stem-cell precursors to neurons. To identify fragile regions of the genome, they created a ‘bait’ break at a precise location using the gene-editing tool CRISPR. They then treated the cells with an antibiotic that stalls the cellular machinery for copying DNA and renders the genome susceptible to breaks.

As cells repair the damage, they sometimes join the bait break to regions with breaks induced by the antibiotic. The researchers sequenced pieces of DNA attached to the bait region to identify sites where the genome had broken.

Delicate DNA:

The breaks tend to cluster in 37 regions that range in length from about 100,000 to more than 2 million bases.

All but one of these regions overlap partially or entirely with genes. The affected genes are enriched for those that play roles in nervous-system development and at **synapses**, the junctions between neurons. They also tend to be unusually long; long genes are **implicated in autism**.

Of the 37 regions, 18 include at least parts of genes linked to autism, such as **CTNND2**, **RBFOX1** and **AUTS2**. The neural precursor cells actively make RNA from genes in all but two of the regions. RNA production at these sites may make them **especially vulnerable to breaks**.

“These breaks were enriched in genes that are implicated in neurodevelopment,” Wang says.

Wang and her colleagues repeated the analyses using skin cells and precursors of glia, support cells for neurons. They found that most of the fragile regions in the neuron precursors are not fragile in either glia precursors or skin cells.

The researchers are exploring whether breaks in fragile regions give rise to mosaic mutations — those that occur in only some cells — in the brain. They also plan to examine whether neural precursors made from skin cells of autistic people are prone to breaks in long genes associated with autism.

*For more reports from the 2018 Society for Neuroscience annual meeting, please **click here**.*