NEWS

Maternal asthma alters immune cells in fetal brain

BY **KATIE MOISSE**

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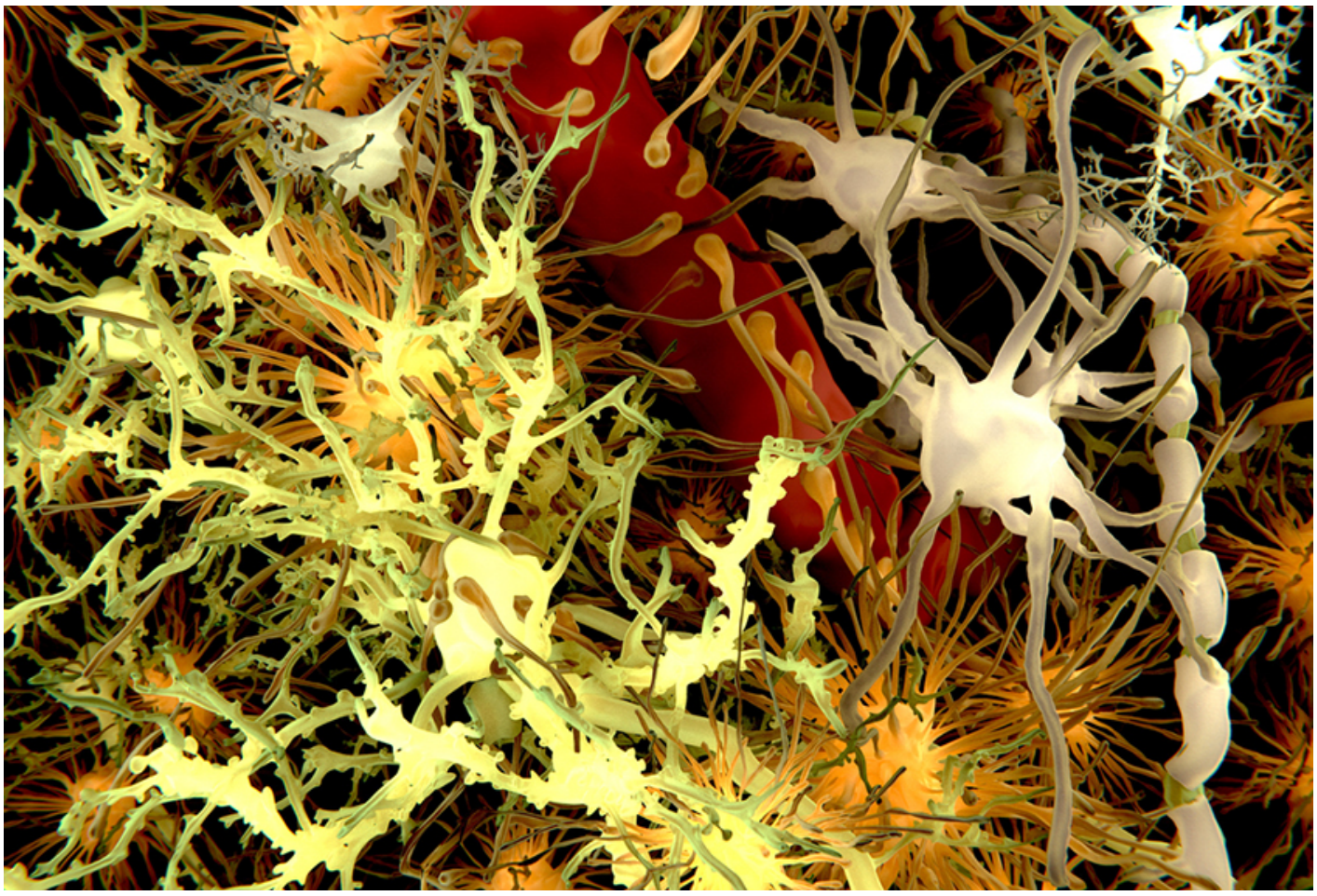

Mouse pups exposed to an immune response in the womb show autism-like behaviors and altered gene expression in brain cells called microglia.

Researchers presented the findings today at the **2017 Society for Neuroscience annual meeting** in Washington, D.C. The findings were also published today in *GLIA*[1].

Epidemiological studies suggest that women who have an **infection** or an **autoimmune condition** while pregnant are at an increased risk of having a child with autism. Mouse studies have shown that the mother's immune molecules can **disrupt fetal brain development** and lead to autism-like features, such as **repetitive behaviors** and social problems. Most of this work is based on mice treated with a chemical that mimics an infection.

In the new work, researchers injected female mice with a protein called ovalbumin. The mice become sensitive to the protein, such that subsequent aerosol exposures elicit an immune reaction reminiscent of allergic asthma in people.

Sensitized mice exposed to ovalbumin while pregnant have pups with behaviors similar to those seen in mouse models of maternal infection. "But the molecular mechanisms underlying these behaviors were not known," says Annie Vogel Ciernia, a postdoctoral researcher in **Janine LaSalle**'s lab at the University of California, Davis. "Our hypothesis was that there were changes in the immune systems of the developing mice."

She and her colleagues focused on microglia, the brain's resident immune cells. They isolated microglia from the brains of 35-day-old mice born to ovalbumin-sensitized mothers. They then examined the microglia for changes in gene expression and DNA methylation, a form of **epigenetic** modification that affects gene expression.

Uneven overlap:

Microglia from these mice show abnormal patterns of gene expression and methylation, the researchers found. Many of the genes that show abnormal methylation or an increase or decrease in expression are implicated in autism.

Affected genes include **PAX6**, **SYN1** and **PCDHA9**, which are mutated in some people with autism. Many of the genes are the same ones disrupted in mice exposed to infections in utero.

Surprisingly, there is little overlap between genes that show an increase or decrease in expression and those that are abnormally methylated. This suggests that the changes in DNA methylation are not driving the changes in gene expression.

The changes in methylation affect the inflammatory response, whereas those in gene expression influence how microglia sense and respond to the environment, Vogel Ciernia says.

The researchers plan to study the mice at different time points during development to see how patterns of microglial gene expression and methylation change.

“We think the methylation is more of a marker of past life experience — a leftover signature of the actual asthma induction during pregnancy,” Vogel Ciernia says. “Or it could be a sign that future immune responses will be misregulated. Or both.”

For more reports from the 2017 Society for Neuroscience annual meeting, please ***click here****.*

REFERENCES:

1. Vogel Ciernia A. *et al. GLIA* Epub ahead of print (2017) **Abstract**