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OU Assistant Professor of Cell Biology Lindsay Hayes

Unlocking the Link

OU RESEARCHERS ARE TRACING CONNECTIONS BETWEEN DEVELOPMENTAL DISORDERS AND INFLAMMATION DURING PREGNANCY.

By Chip Minty

THESE DAYS, NEARLY everyone knows a person who has autism. That's because one in 36 children in the United States has been diagnosed with the disorder. And, according to the Centers for Disease Control, that rate is up from 1 in 150 just two decades ago. The ratios are even higher for children diagnosed with learning disabilities, ADHD and other neurodevelopmental conditions.

Researchers don't yet know what is causing this increase, but alarm bells have been ringing across the biomedical community and a team of University of Oklahoma scientists joined the fray.

Lindsay Hayes, assistant professor of cell biology at the OU College of Medicine, says understanding the role of brain cells known as microglia could be key to the prevention of autism, ADHD, learning disabilities and other disorders.

"There are a number of harmful environmental exposures that can happen during pregnancy and change the trajectory of brain development," Hayes says.

She launched a new study this year that could open the door to a preventative treatment targeting the microglia, a specialized brain cell known for its hard work and hot temper.

Hayes joined with OU researchers Jed Friedman, director of the Harold Hamm Diabetes Center, and Karen Jonscher, associate professor of biochemistry and physiology at OU Health Sciences, to study pyrroloquinoline quinone, or PQQ. They say the natural compound—found in many fruits and vegetables—may have the ability to reduce general inflammation caused by viral infections or poor maternal diets, which could help prevent cellular anomalies in the early stages of fetal development.

Microglia cells are very good housekeepers, Hayes says. Within the brain, they eliminate dead brain cells and neurons that the brain no longer needs. Microglia prevent clutter, promote efficiency and strengthen connections. They also stop infection from damaging brain cells.

Microglia cells are part of the immune system, and—when they encounter inflammation—can become overly aggressive, leading to what Hayes calls neurodegeneration.

"There have been several papers showing problems originating from overzealous microglia," Hayes says, adding that their destructive potential is already being studied as a primary culprit in Alzheimer's disease and Huntington's disease.

By contrast, general inflammation during pregnancy appears to trigger a different transition, prompting microglia to decrease their immune reactivity and change the course of brain cell development in fetuses—contributing to autism and other neurodevelopmental disorders.

That harmful process is at the heart of research she began this summer through a half-million-dollar grant from the Burroughs Wellcome Fund.

"Microglia are one of the star players in age-related neurodegeneration, and I'm looking at the contrasting role they can have during fetal development," she says. "By modulating these cells, researchers hope to change the outcome of disease."

In a mouse study, Hayes is investigating the potential effects of inflammation from viral infections in pregnant mothers. She believes her study could show evidence that such issues can reprogram microglia, affecting fetal development.

Meanwhile, she is testing PQQ's effectiveness in reducing inflammatory responses and boosting cellular metabolism to calm provoked microglia cells.

Hayes says microglia have been a passion for much of her young career, starting when she was a Ph.D. student at Brown University and the National Institutes of Health. Her work in the area continued in postdoctoral training at Johns Hopkins University, and she began her current investigation just months after arriving at OU last December.

She says the collaboration with Friedman and Jonscher is at the foundation of her OU work because of their focus on unborn babies and PQQ's potential for preventing developmental disorders.

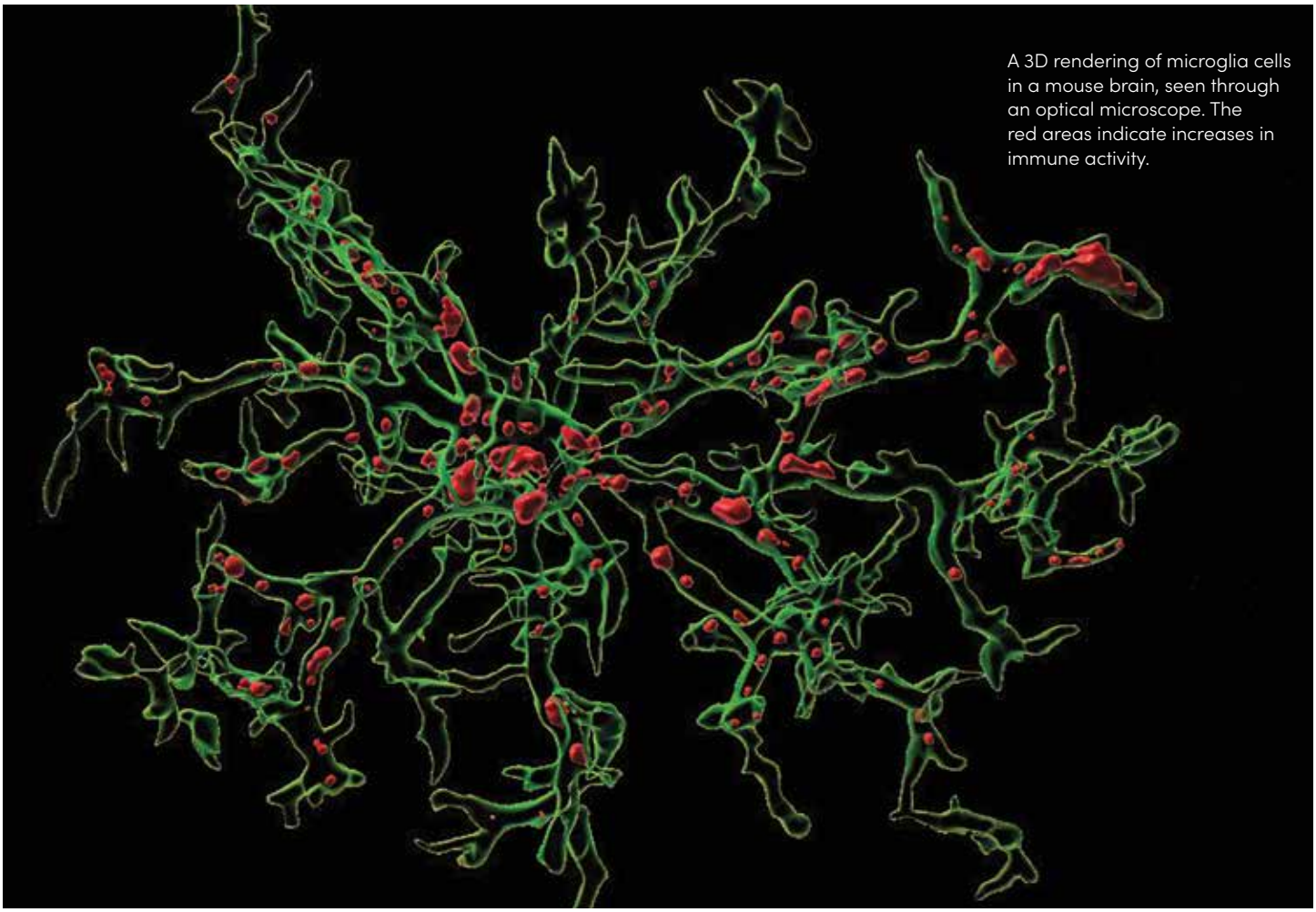
Friedman and Jonscher are conducting a second mouse study to determine the effects of the Western-style diet on pregnant mothers and their offspring. The researchers say that diet can cause inflammation, and there is evidence that obesity and diabetes can be passed from mother to child.

Hayes says pregnant mothers can reduce risks by getting the annual flu and COVID vaccines and eating a healthier, plant-based diet with whole foods. But many mothers hesitate to take such immune protection steps during pregnancy or struggle to turn away from prepackaged foods, red meat, sugar and other vestiges of the Western diet. So, Hayes, Friedman and Jonscher are investigating women taking PQQ as an alternate way of protecting fetuses against infectious or dietary inflammation.

PQQ is an emerging field of study, Hayes says. The compound is a potent antioxidant capable of reducing general inflammation with no known side effects. While PQQ has the potential to help unborn children overcome inflammatory stress from diet or infection, she notes that multiple other stressors also can afflict mothers and their babies during pregnancy.

"Through PQQ, we might be able to promote more resilient pregnancies and protect against many different types of environmental stressors, not just infection or the maternal Western-style diet," Hayes says. "We're excited about the potential."

Chip Minty is a Norman-based writer and the principal of Minty Communications, LLC.



A 3D rendering of microglia cells in a mouse brain, seen through an optical microscope. The red areas indicate increases in immune activity.