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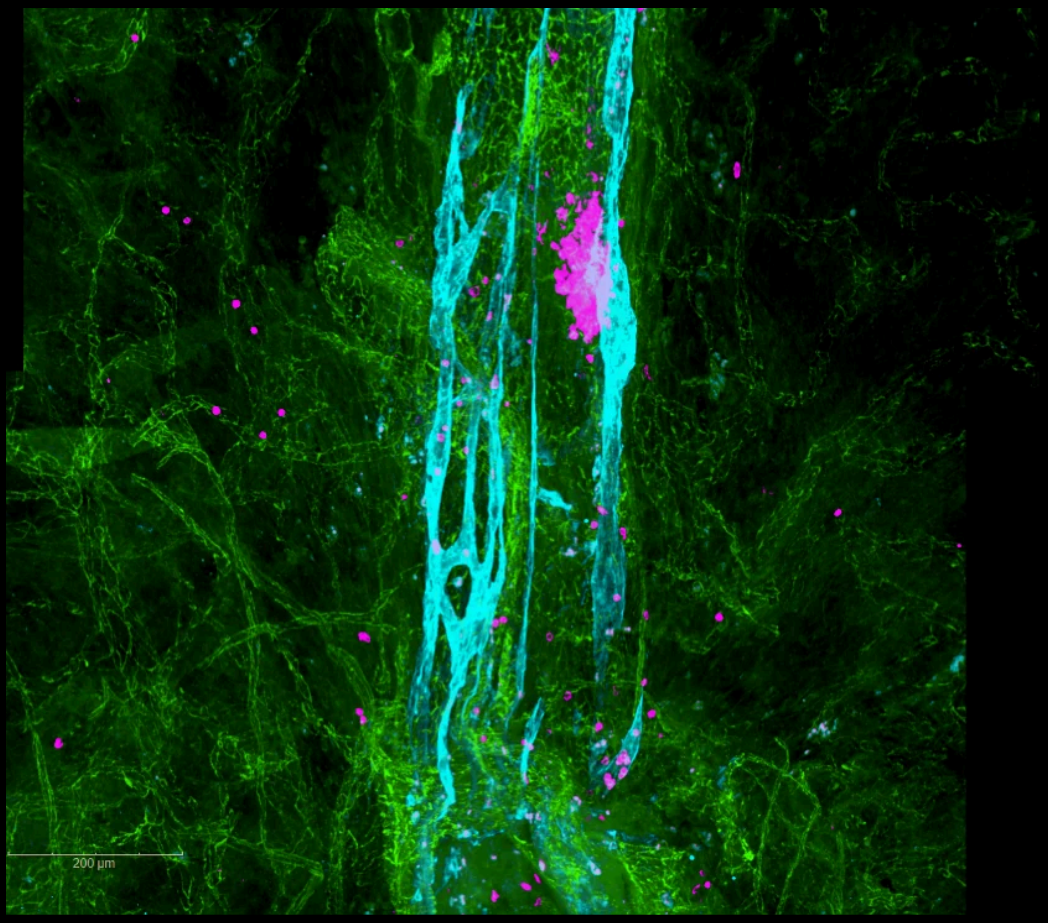
Okun Lab

Inside Our Research



The meninges, the protective tissue surrounding the brain, serves not only as a physical barrier, but also as an important site of immune activity and brain waste clearance. Blood vessels and lymphatic vessels within this tissue play complementary roles in immune defense: blood vessels transport immune cells and nutrients, while lymphatic vessels collect excess fluid and tissue waste, delivering it to lymph nodes where harmful pathogens can be identified and targeted.

In this image, we see a small aggregation of B cells (shown in purple) located within a large blood vessel (green) and in close proximity to a lymphatic vessel (cyan) in the meninges. Because the brain clears waste through meningeal lymphatic vessels such as these, the positioning of this B cell cluster suggests it may form in response

to signals originating from brain waste or inflammation, potentially triggering a localized immune response.

More research is needed to understand what exactly is being cleared from the brain that drives these immune cell clusters to form, and whether the molecules they release help protect the brain—or instead contribute to neurological damage.

Image credit: Amit Fruitman. Fluorescent imaging of immune cell aggregation near blood and lymphatic vessels in the meninges of a mouse brain. The Paul Feder Okun Laboratory for Alzheimer's Disease Research.

At the Brain's Borders: Hormones, Immunity, and Brain Health

The meninges, the protective tissue surrounding the brain, are increasingly recognized as an active site of communication between the brain and immune system. Beyond serving as a barrier, this tissue helps clear brain-derived waste and hosts specialized immune cells that monitor signals from the central nervous system. In our research, we are particularly interested in how small immune structures forming near blood and lymphatic vessels may contribute to brain health, aging, and disease.

One of our major questions is how sex hormones shape the communication between the immune system and the brain. Hormones such as estrogen, progesterone, and testosterone influence immune cells throughout the body, including B cells, T cells, and myeloid cells. They can change how strongly immune cells respond to tissue signals, how much inflammation they produce, and whether immune activity becomes protective or harmful. Because sex hormone levels change across life stages, including puberty, pregnancy, menopause, and aging,they may also therefore change how immune cells behave at brain borders.

These interactions may have important consequences for brain function. Immune cells and inflammatory molecules can influence memory, mood, learning, sleep, and vulnerability to neurodegenerative disease. The presence of B cells near meningeal lymphatic vessels raises the possibility that hormonal state may affect how brain waste is recognized, how immune responses are organized, and whether these responses support brain health or contribute to pathology.

Our lab is working to better understanding this link between sex hormones, immunity, and brain function may help explain why many neurological and autoimmune conditions differ between males and females, and why risk can change across the lifespan.

Highlights From The Field

What Happens When Weight-Loss Drugs Stop Working? The Rebound After GLP-1 Therapy

GLP-1 medications such as Ozempic and Wegovy have transformed the treatment of obesity and diabetes, helping many people lose weight and improve blood sugar control. But a new large-scale analysis suggests that what happens *after* stopping these medications deserves just as much attention.

Researchers reviewed data from nearly 3,800 participants across 18 clinical trials and found that many of the benefits of GLP-1 drugs begin to reverse after treatment ends. People often regained weight, blood sugar levels worsened, and some cardiovascular improvements such as lower blood pressure faded over time. The rebound was especially pronounced after longer periods without treatment and among users of certain longer-acting medications, including semaglutide (the active ingredient in Ozempic and Wegovy).

While these findings do not mean GLP-1 therapies are ineffective, they highlight an important message: obesity and diabetes may require long-term management strategies, rather than short-term fixes. The study emphasizes the need for gradual treatment transitions, lifestyle support, and continued medical follow-up to help maintain benefits after stopping therapy.

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