Eyes serve as immunological barrier in fight against brain pathogens, finds study

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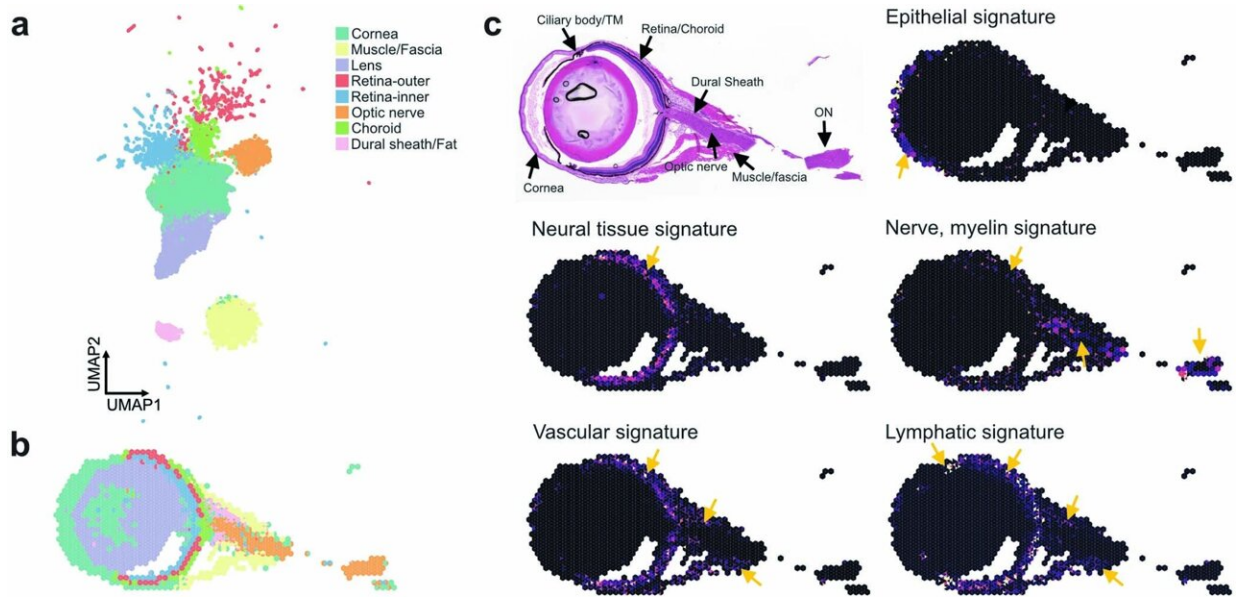

10x VISIUM Spatial sequencing of the mouse globe and optic nerve. Mouse eyes were processed using traditional FFPE-based histology preparation. Samples were processed using the 10x VISIUM platform and analyzed using Seurat. **a**, UMAP of different spatial sequencing blocks with categorization into overall tissue level structure. **b**, Projection of tissue-type clusters onto the globe and surrounding structures. **c**, Image of H&E staining and respective cell type gene signature projected onto spatial sequencing data (yellow arrows denote where the gene signature appears for given signature). Credit: *Nature* (2024). DOI: 10.1038/s41586-024-07130-8

The eyes have been called the window to the brain. It turns out they also serve as an immunological barrier that protects the organ from pathogens and even tumors, Yale researchers have found.

In a new study, researchers showed that vaccines injected into the eyes of mice can help disable the herpes virus, a major cause of brain encephalitis. To their surprise, the vaccine activates an immune response through lymphatic vessels along the optic nerve.

The results were published in the journal *Nature.*

"There is a shared immune response between the brain and the eye," said Eric Song, an associate research scientist and resident physician in Yale School of Medicine's Department of Immunobiology and corresponding author of the paper. "And the eyes provide easier access for drug therapies than the brain does."

Wanting to explore immunological interactions between the brain and eyes, the research team, which was led by Song, found that the eyes have two distinct lymphatic systems regulating immune responses in the front and rear of the eye.

After they vaccinated mice with inactivated herpes virus, the researchers found that lymphatic vessels in the optic nerve sheath at the rear of the eye protected mice not only from active herpes infections but from bacteria and even brain tumors.

Harnessing this new biology, Song's team is currently testing newly created drugs from his lab delivered through eye injections that may help combat macular edema or leaky blood vessels of the retina common in people with diabetes and glaucoma.

"These results reveal a shared lymphatic circuit able to mount a unified

immune response between the posterior eye and the brain, highlighting an understudied immunological feature of the eyes and opening up the potential for new therapeutic strategies in ocular and central nervous system diseases," the authors wrote.

Xiangyun Yin, an associate researcher in Yale's Department of Immunobiology; Sophia Zhang, an undergraduate student at Yale College; and Ju Hyun Lee, a doctoral student in the Department of Biomedical Engineering, are co-lead authors of the study.

More information: Eric Song, Compartmentalized ocular lymphatic system mediates eye–brain immunity, *Nature* (2024). DOI: 10.1038/s41586-024-07130-8.
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