A 3D illustration of brain tissue and neural pathways. The brain is shown in shades of purple and blue, with a network of white and yellow neural fibers extending from it. The background is a dark blue gradient.

Can we rejuvenate the brain?

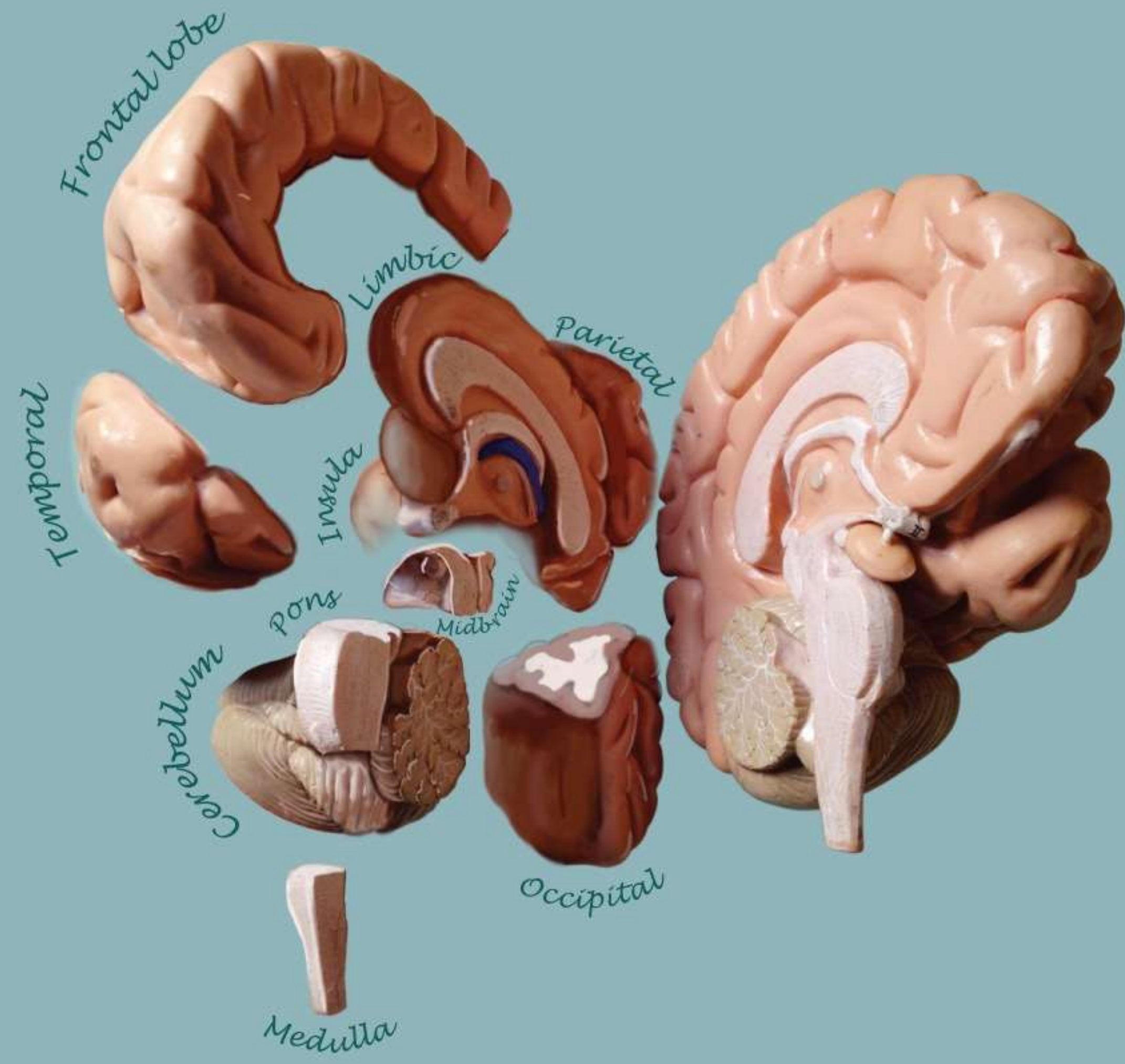
Jonathan Kipnis

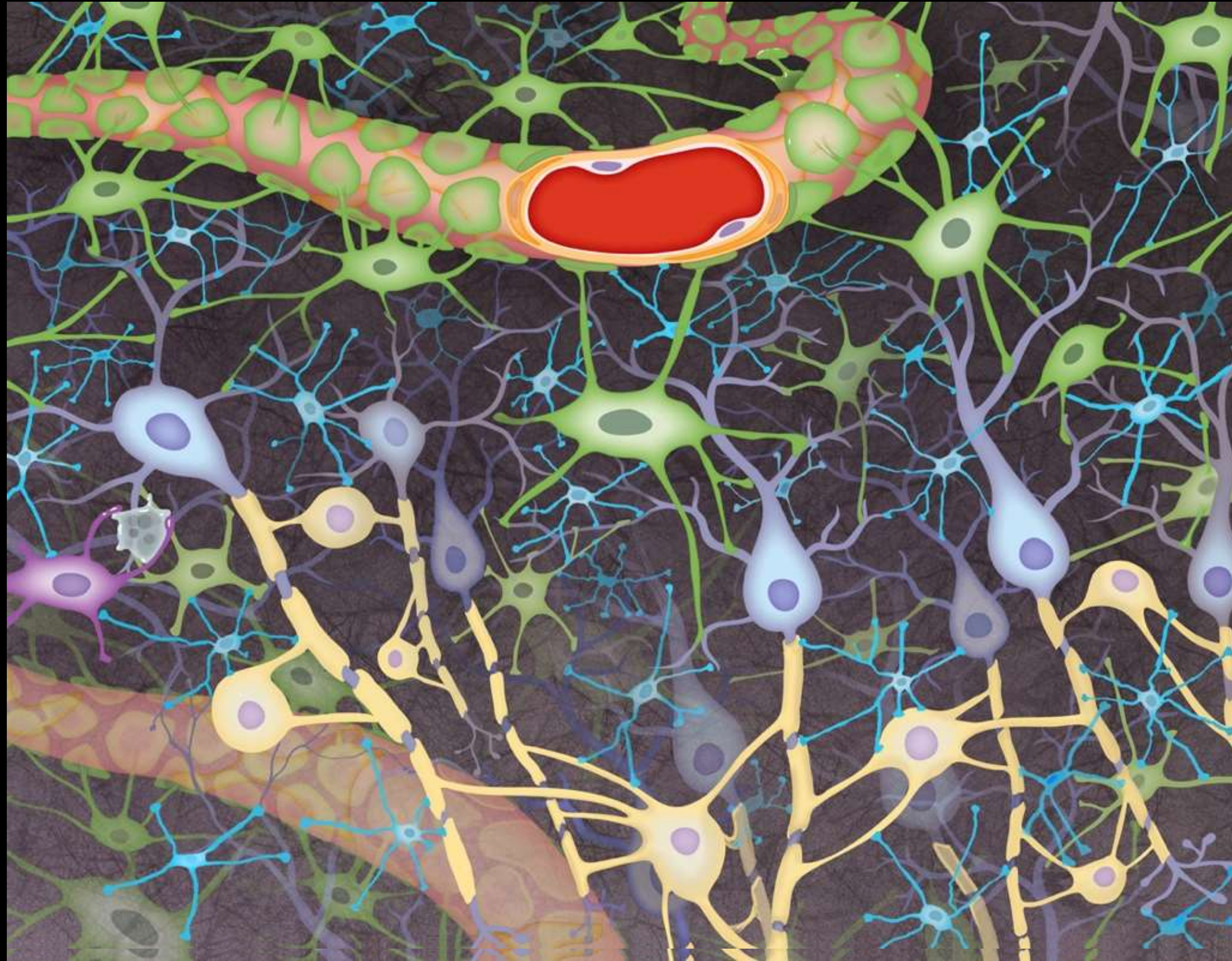
Washington University in St. Louis, School of Medicine
Department of Pathology & Immunology and
Brain Immunology and Glia (BIG) Center

What is unique about neurological disorders?

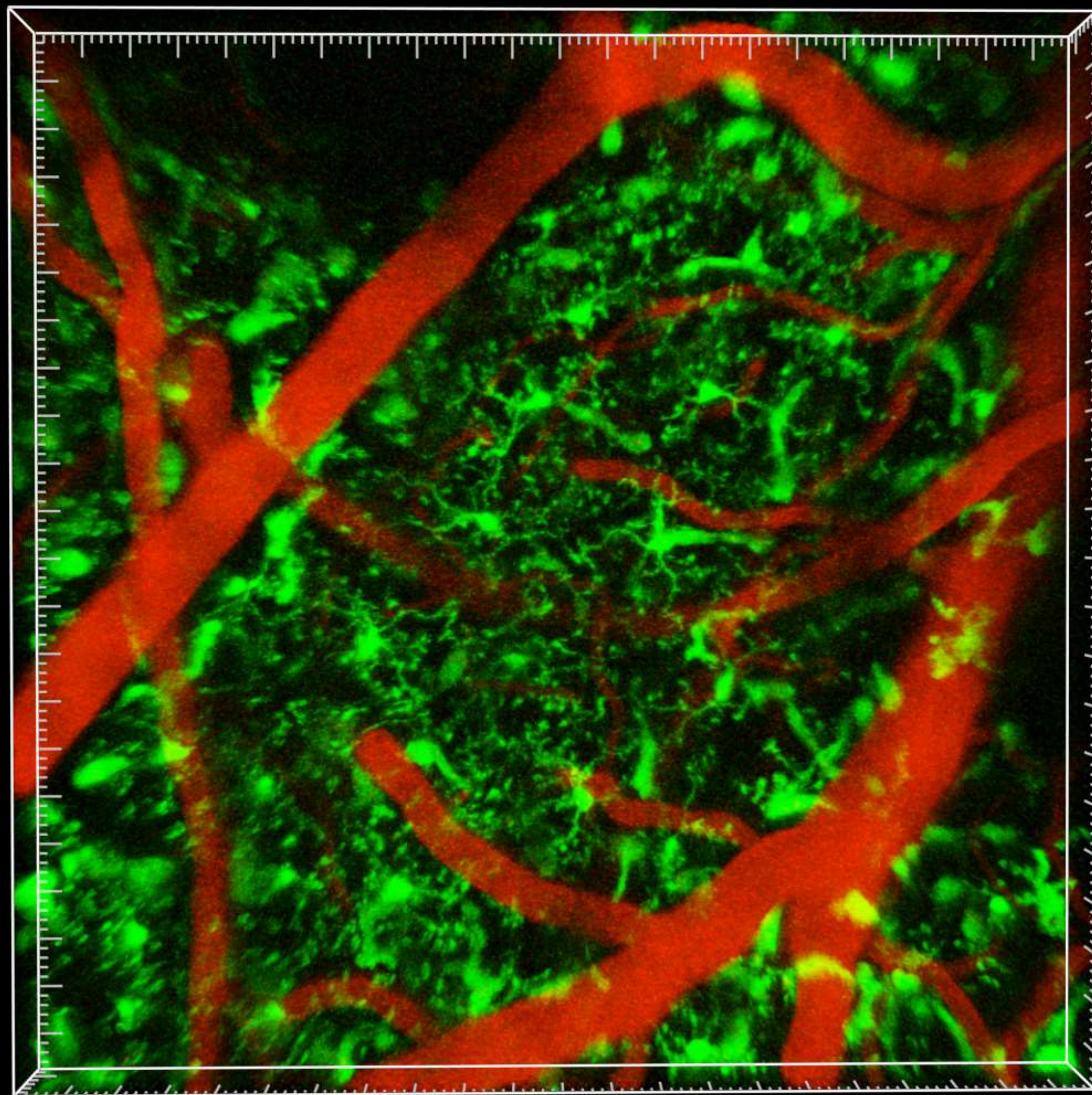
Most have no efficient therapy





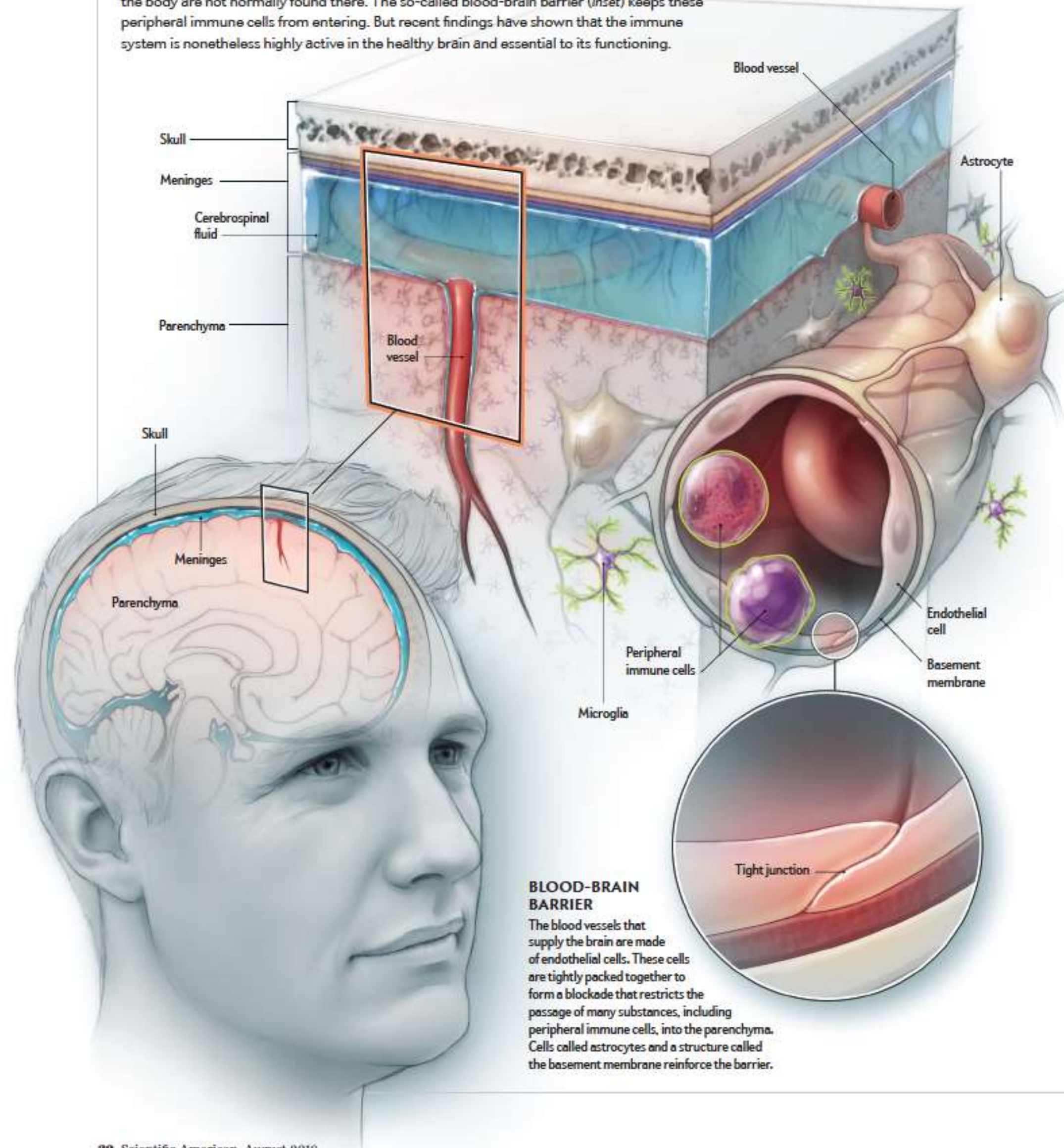


50 μm



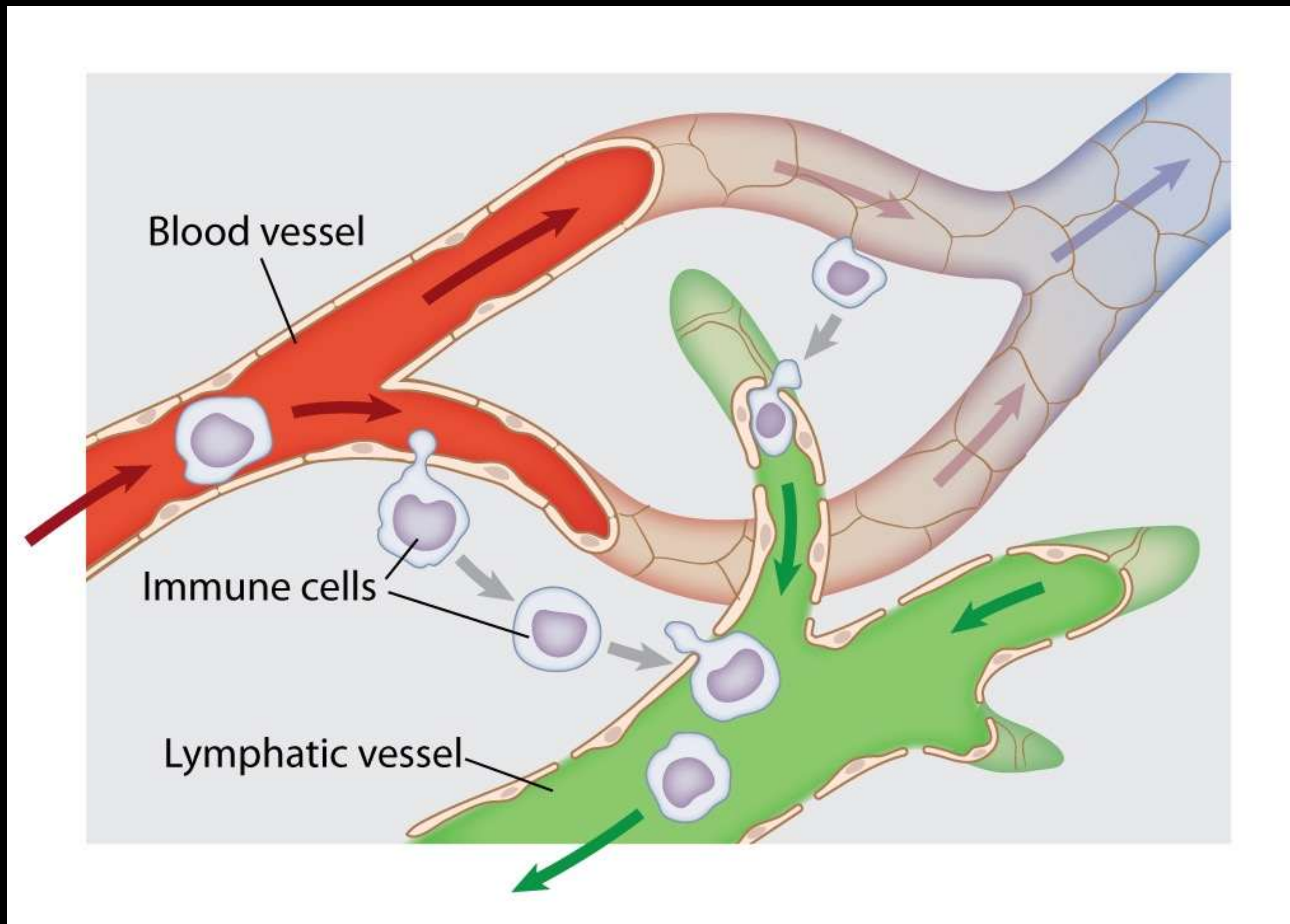
The Brain-Immune Connection

The healthy brain was long thought to be off-limits to the immune system. Although the brain harbors native immune cells known as microglia, immune cells that originate elsewhere in the body are not normally found there. The so-called blood-brain barrier (inset) keeps these peripheral immune cells from entering. But recent findings have shown that the immune system is nonetheless highly active in the healthy brain and essential to its functioning.



BLOOD-BRAIN BARRIER
The blood vessels that supply the brain are made of endothelial cells. These cells are tightly packed together to form a blockade that restricts the passage of many substances, including peripheral immune cells, into the parenchyma. Cells called astrocytes and a structure called the basement membrane reinforce the barrier.

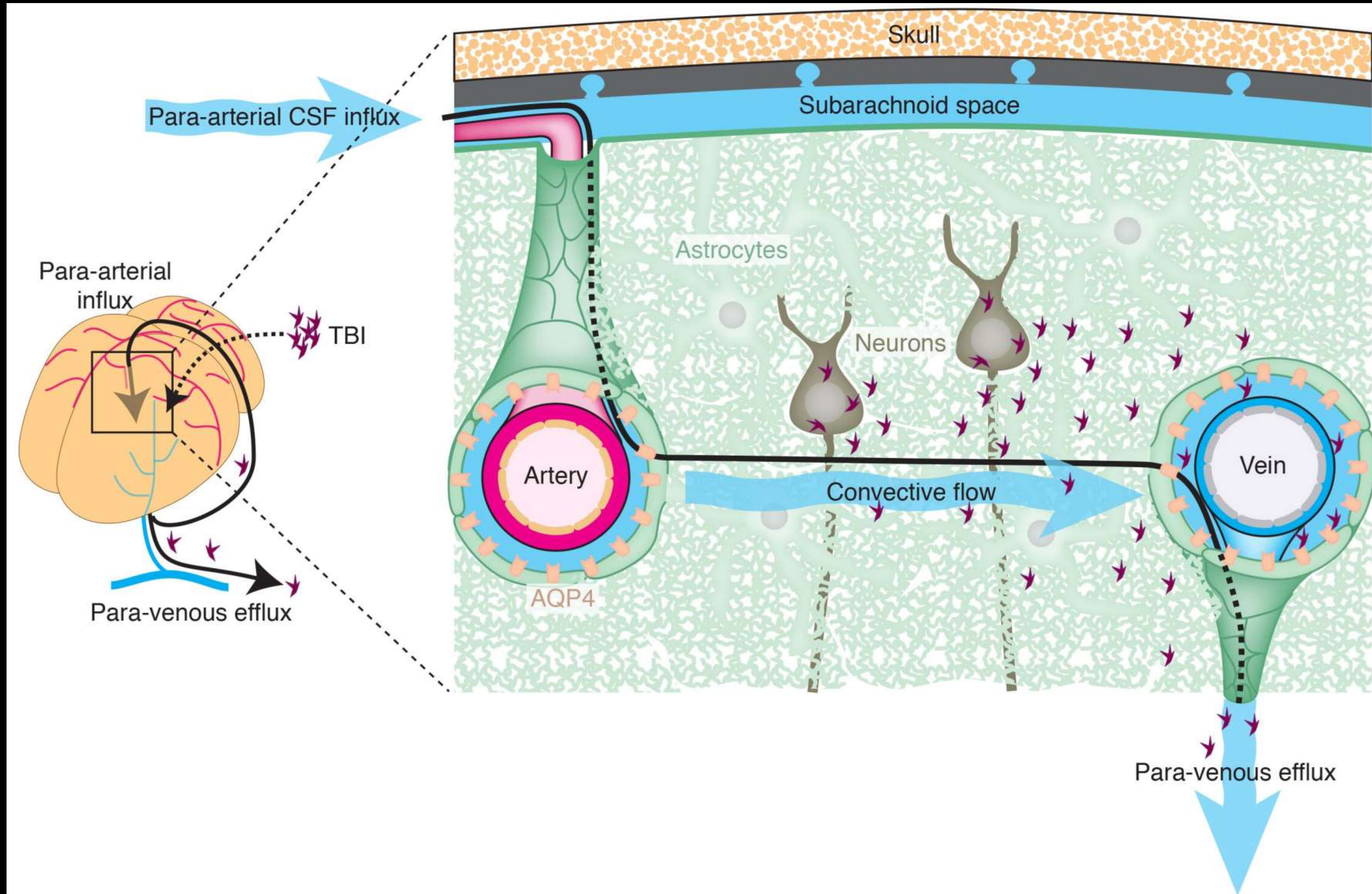
Blood and lymphatic vasculature





<http://electronicstoece.blogspot.com/2012/05/brain-draingood-or-bad.html>

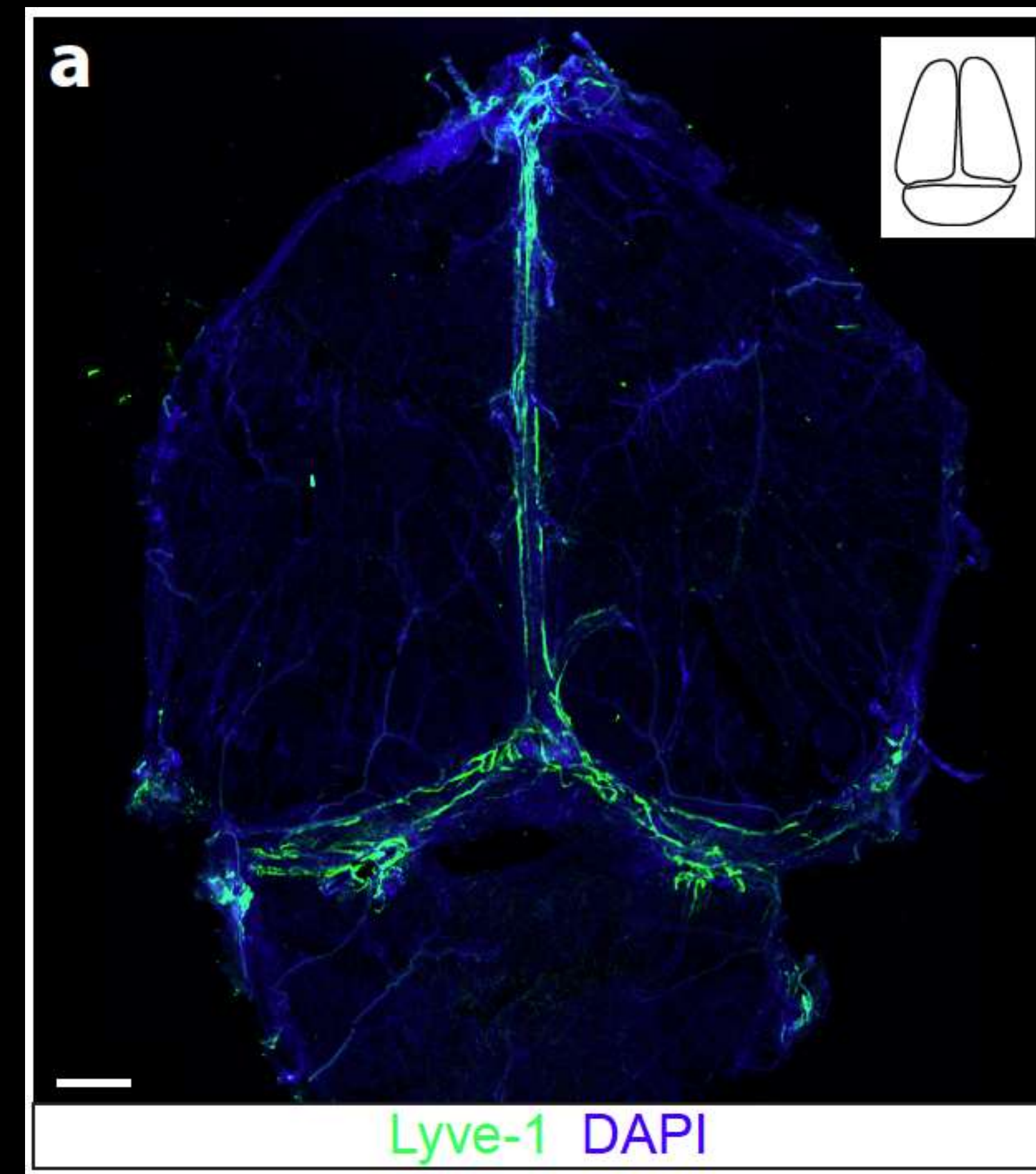
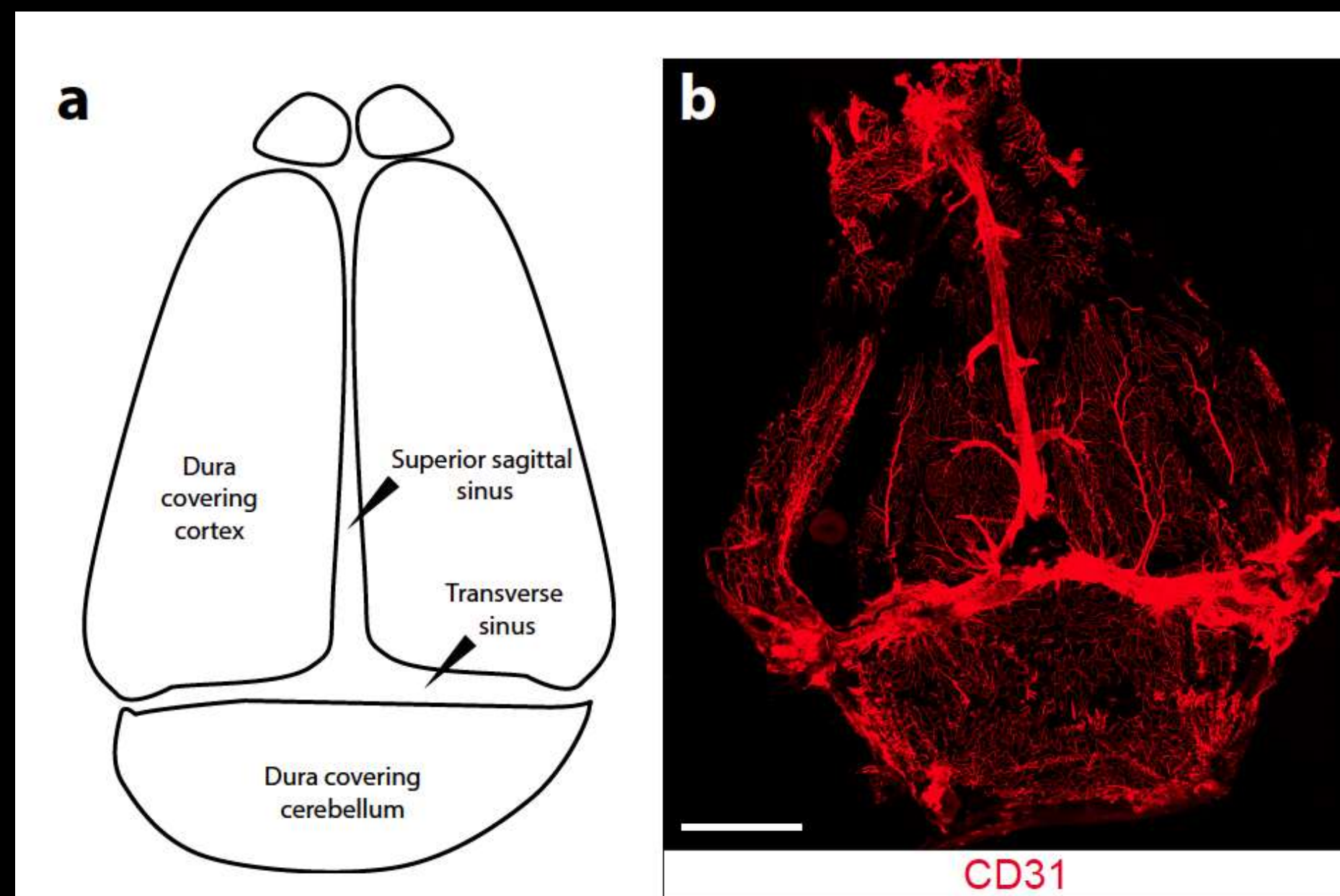
Glymphatic system

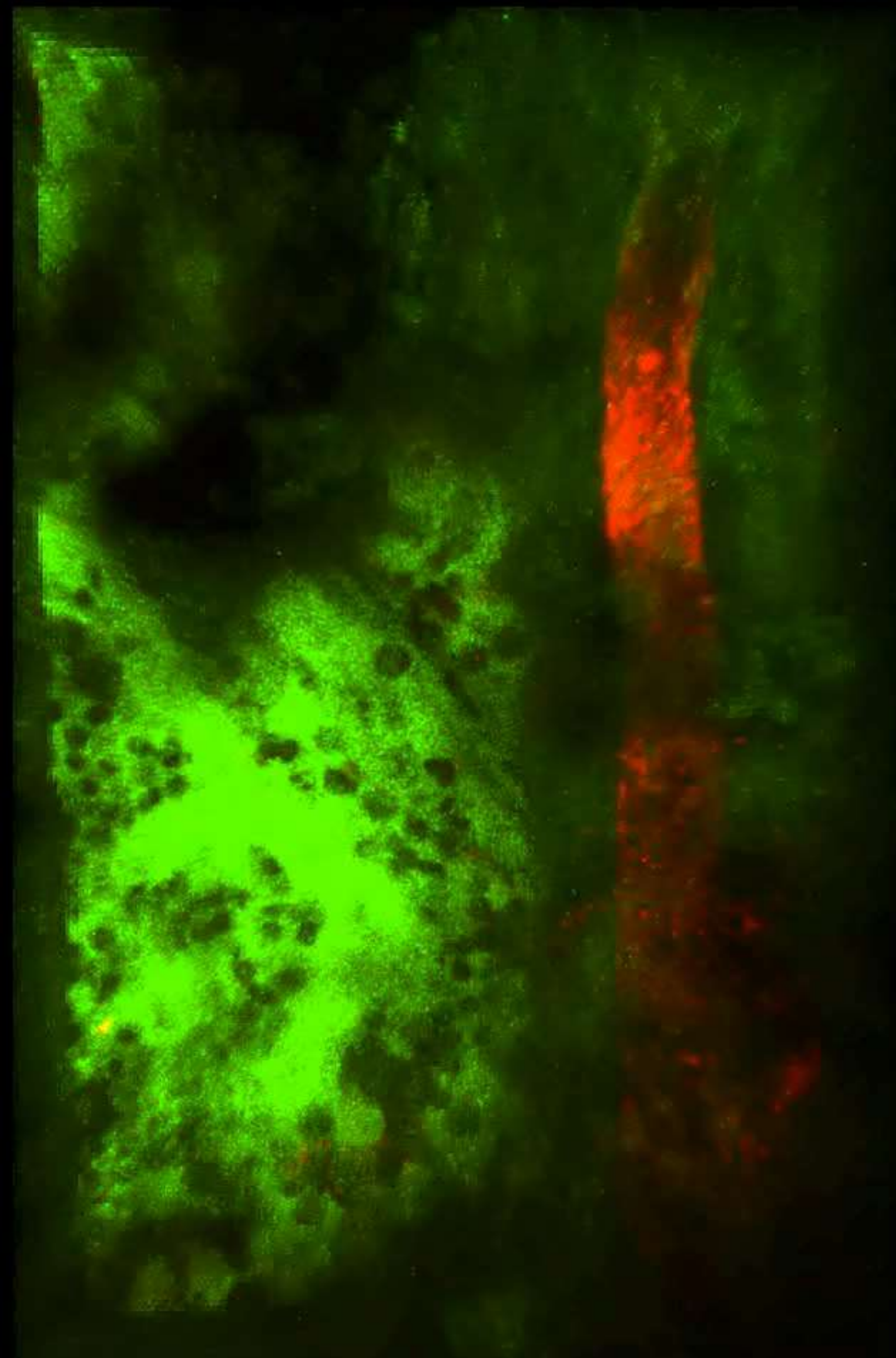


Whole mount meninge



Antoine Louveau





20 μm

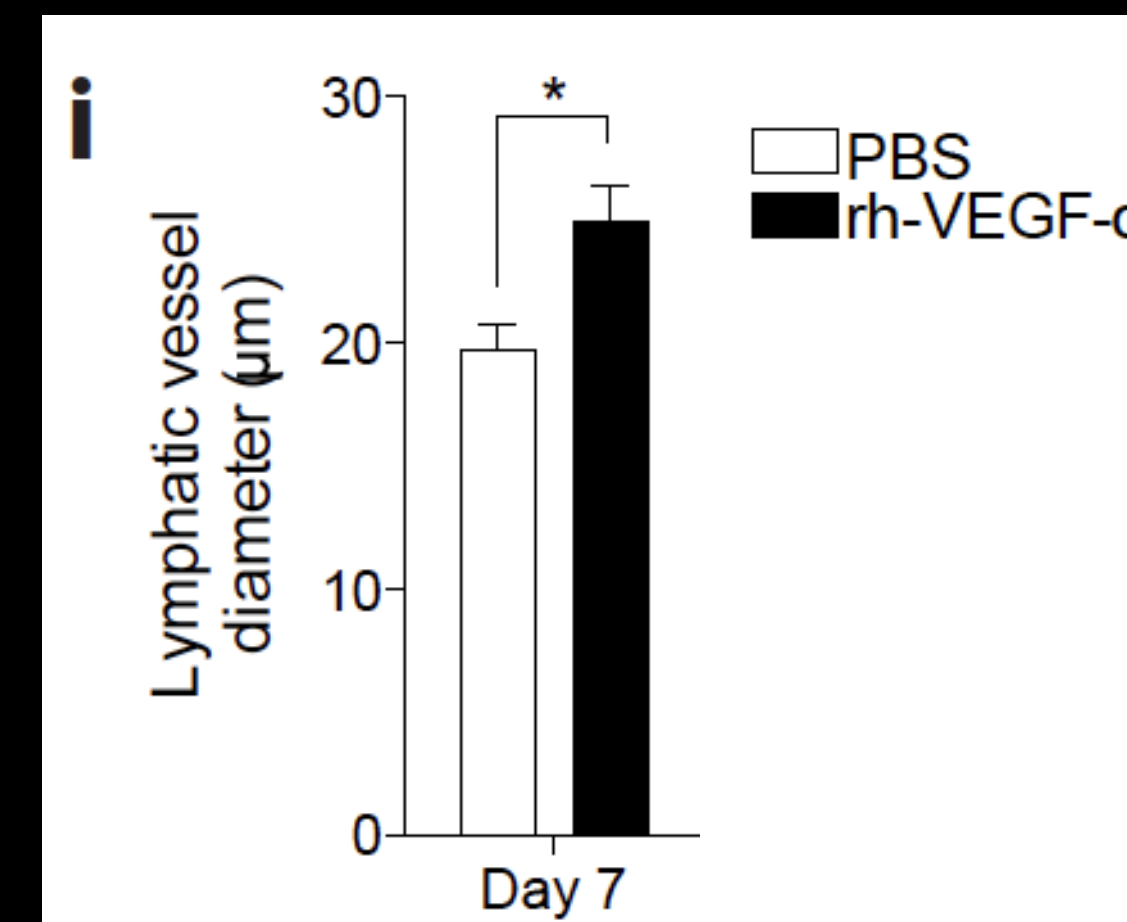
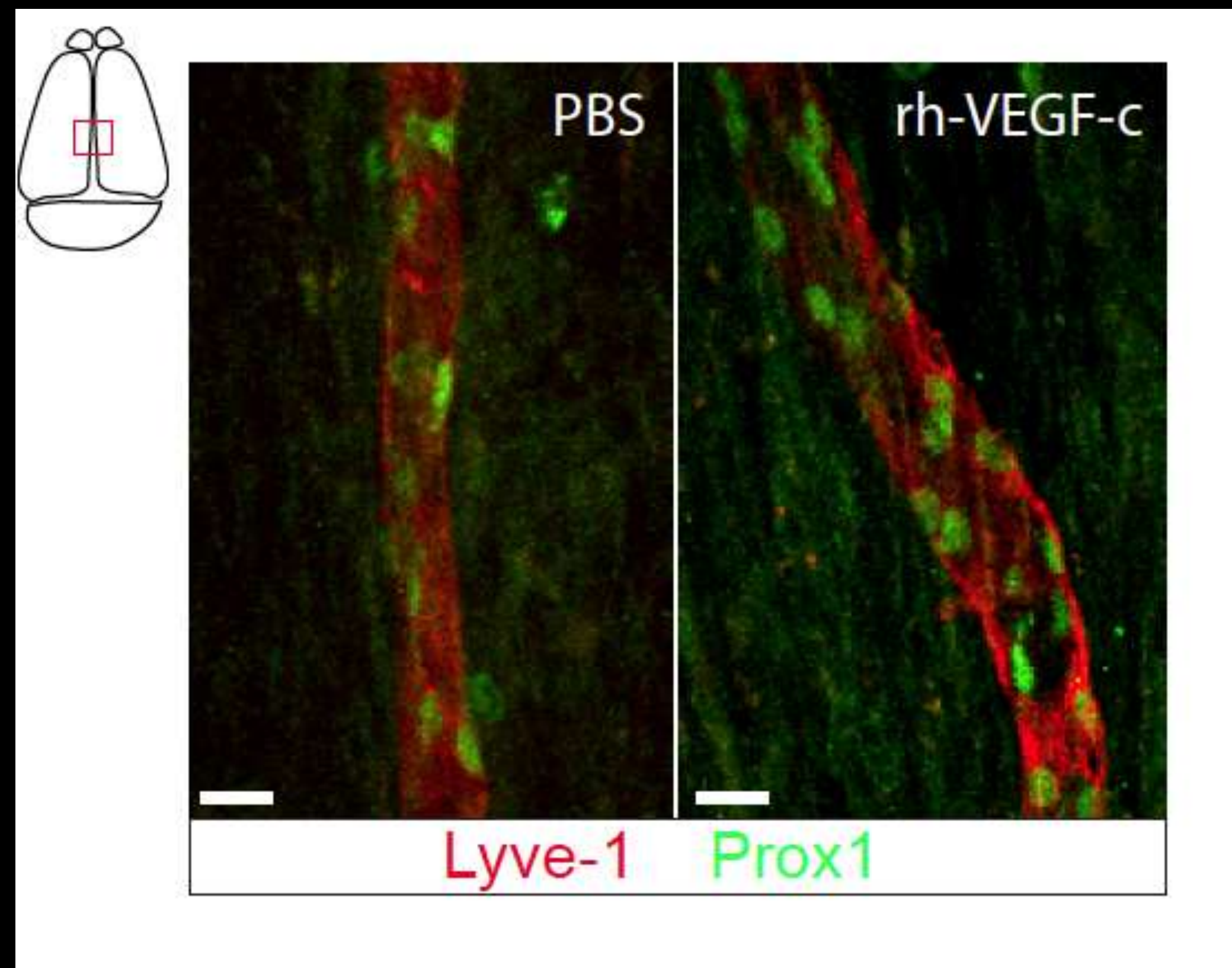


0.00 sec

100 μm



Brain-draining lymphatic vessels could be enhanced by VEGF-c



Human and nonhuman primate meninges harbor lymphatic vessels that can be visualized noninvasively by MRI

Martina Absinta^{1†}, Seung-Kwon Ha^{1†}, Govind Nair¹, Pascal Sati¹,
Nicholas J Luciano¹, Maryknoll Palisoc², Antoine Louveau³, Kareem A Zaghloul⁴,
Stefania Pittaluga², Jonathan Kipnis³, Daniel S Reich^{1*}

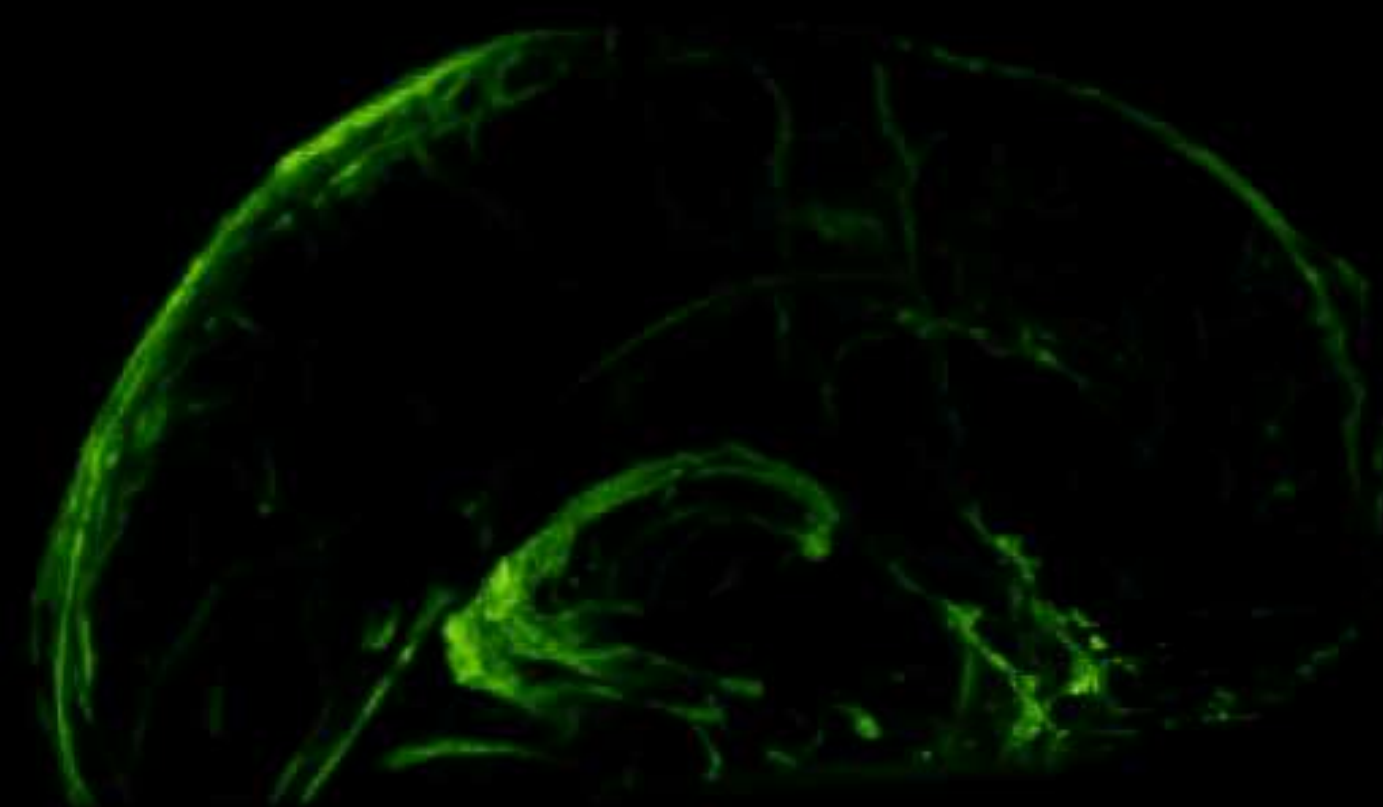
WL: 120 WW: 241

S

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Brain's missing 'pipes' are found

Vessels, tied to immune system, may hold clues to a range of diseases

BY AMY ELLIS NUTT

"Throw out the textbooks" and "missing link" are words rarely heard anymore in science, but that's what researchers around the world are saying about the discovery of microscopic lymphatic vessels in the brain.

First women

Two soldiers' feat marks breakthrough for female service members

BY DAN LAMOTHE

Two female soldiers will graduate from the Army's Ranger School on Friday, becoming the first women to complete what is considered one of the military's most difficult courses to develop leaders, a senior official said.

The accomplishment is a major breakthrough for the armed services, as each of the military's branches has been required to integrate women as infantry soldiers. But even before the graduation, the military's top leaders were already celebrating the breakthrough.

LATEST MAGAZINE VIDEOS

HEALTH NEUROSCIENCE

Game-Changing Discovery Links the Brain and the Immune System

Alissa Greenberg @alissaleewrites | June 3, 2015

New research could affect how we approach everything from Alzheimer's to autism

Researchers at the University of Virginia have made a dazzling discovery. **COSMOS**



Meningeal lymphatic vessels

From Wikipedia, the free encyclopedia

The **meningeal lymphatic vessels** (or **meningeal lymphatics**) are a recently discovered network of **sinuses** and **meningeal arteries** of the mammalian central nervous system (CNS). As a part of the lymphatic system, they drain **immune cells**, small molecules, and excess fluid from the CNS and into the deep cervical lymph nodes.

While it was initially believed that both the brain and meninges were devoid of lymphatic vessels, the discovery was made by Jonathan Kipnis at the University of Virginia and the other by Aleksanteri Aspelund and his colleagues at the University of Copenhagen and Danish neuroscientist Maiken Nedergaard in identifying the pathway connecting the glymphatic system to the lymphatic system.

Currently, the role that the meningeal lymphatics play in neurological disease is yet to be explored, but it is thought that they may be involved in autoimmune and inflammatory diseases of the CNS due to their role in connecting the immune system to the brain.

Contents [hide]

1 Background

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NATURE REVIEWS NEUROLOGY | RESEARCH HIGHLIGHT

Uncovering the secrets of the 'brain drain'—the CNS lymphatic system is finally revealed

Heather Wood

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June 15, 2015

Lymphatic Vessels Discovered in Central Nervous System

By Ashley P.

At a Glance

- Scientists discovered that the brains of mice contain functional lymphatic vessels that can carry fluid and immune cells from cerebrospinal fluid.
- Further work will explore whether problems in this system might play a role in neurological disorders such as Alzheimer's disease, meningitis, and multiple sclerosis.



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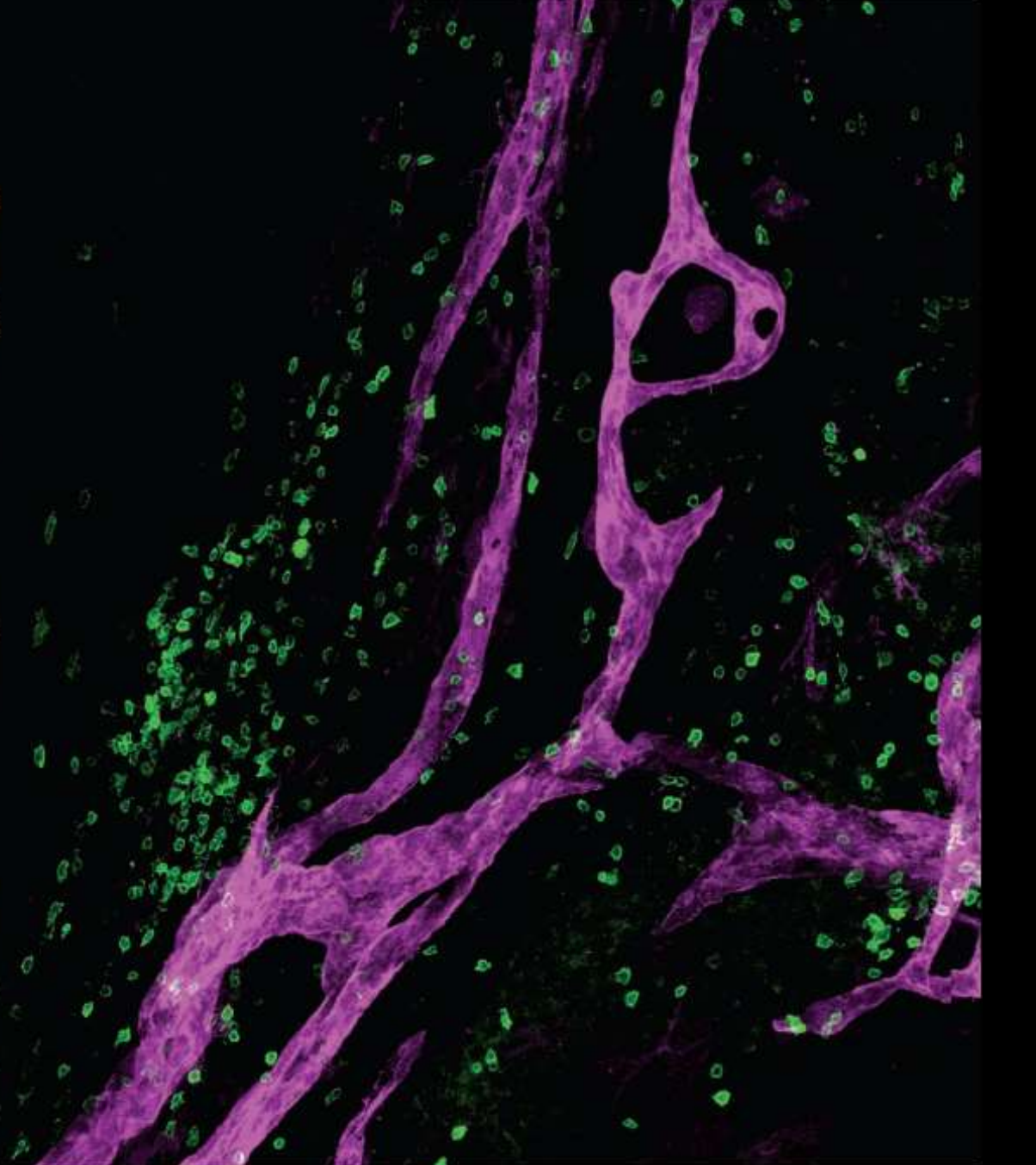
2015 BREAKTHROUGH OF THE YEAR | RUNNERS-UP

Lymphatic vessels: The brain's well-hidden secret

To anatomists who thought they had the body's systems mapped out, this summer's discovery was like sighting a new continent. An unexpected finding revealed that the lymphatic system—a web of vessels that helps clear waste and transport immune cells in the body—extends into the brain instead of stopping in the neck as most scientists had assumed.

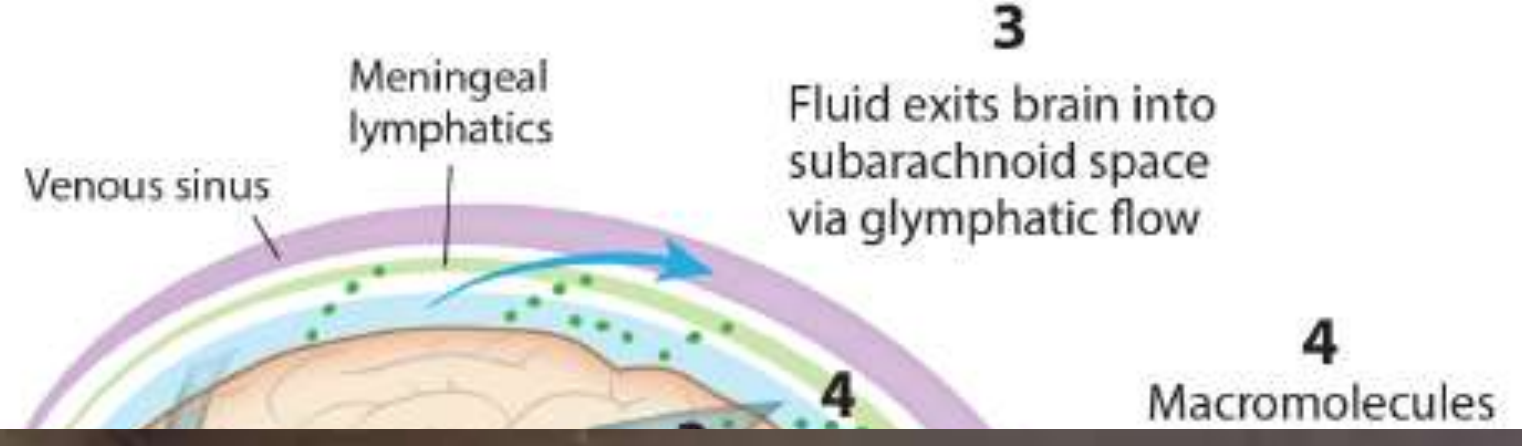
More than 2 centuries ago, an Italian physician, Paolo Mascagni, proposed that the brain has the same lymphatic plumbing as the rest of the body. His claim was largely ignored, but this year, researchers exploring the role of immune cells in the brains of mice spotted a suspiciously well-organized set of T cells in an outer layer of the brain. Nearby vessels seemed to be guiding the cells, and biomarkers showed that the mystery tubes were extensions of the mouse's lymphatic system. Since then, tissue evidence has suggested that human brains harbor similar vessels.

Tucked away in the meninges, the outermost layer covering the brain, the well-hidden vessels may offer insights into how the immune system and brain interact. Scientists had thought that brains had their own, self-contained immune defenses, sealed off from the rest of the body. The discovery—or rediscovery—of a physical link could open new avenues for exploring neurodegenerative and neuroinflammatory diseases like Alzheimer's, multiple sclerosis, and meningitis. But researchers say that for now, their top priority is fathoming the basic structure and function of the newly discovered network. —Hanae Armitage



Hidden vessels benefit brain and immune system

...ng could be overturned by discover...
...poor health and brain disorders such...



Brain borders and AD

Vol. 120, No. 3, 1984
May 16, 1984

BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATION
Pages 885-89

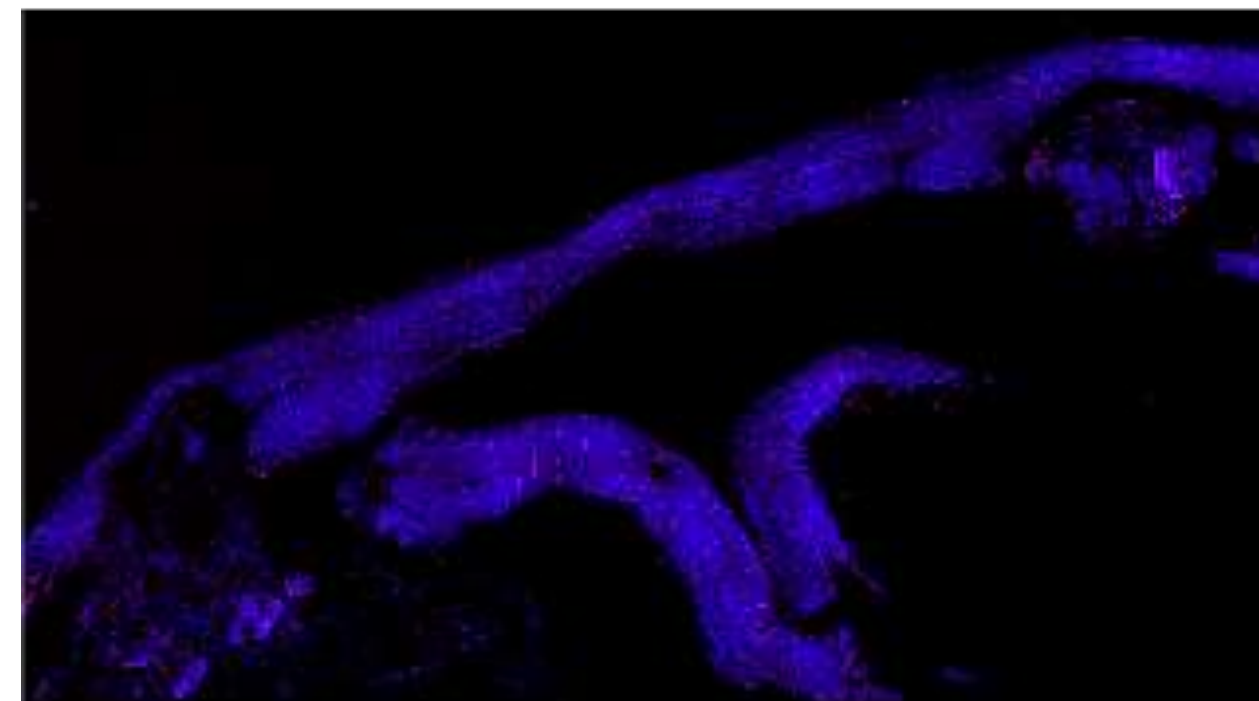
ALZHEIMER'S DISEASE: INITIAL REPORT OF THE PURIFICATION
AND CHARACTERIZATION OF A NOVEL CEREBROVASCULAR AMYLOID

George G. GLENNER, M.D. and Caine W. W.

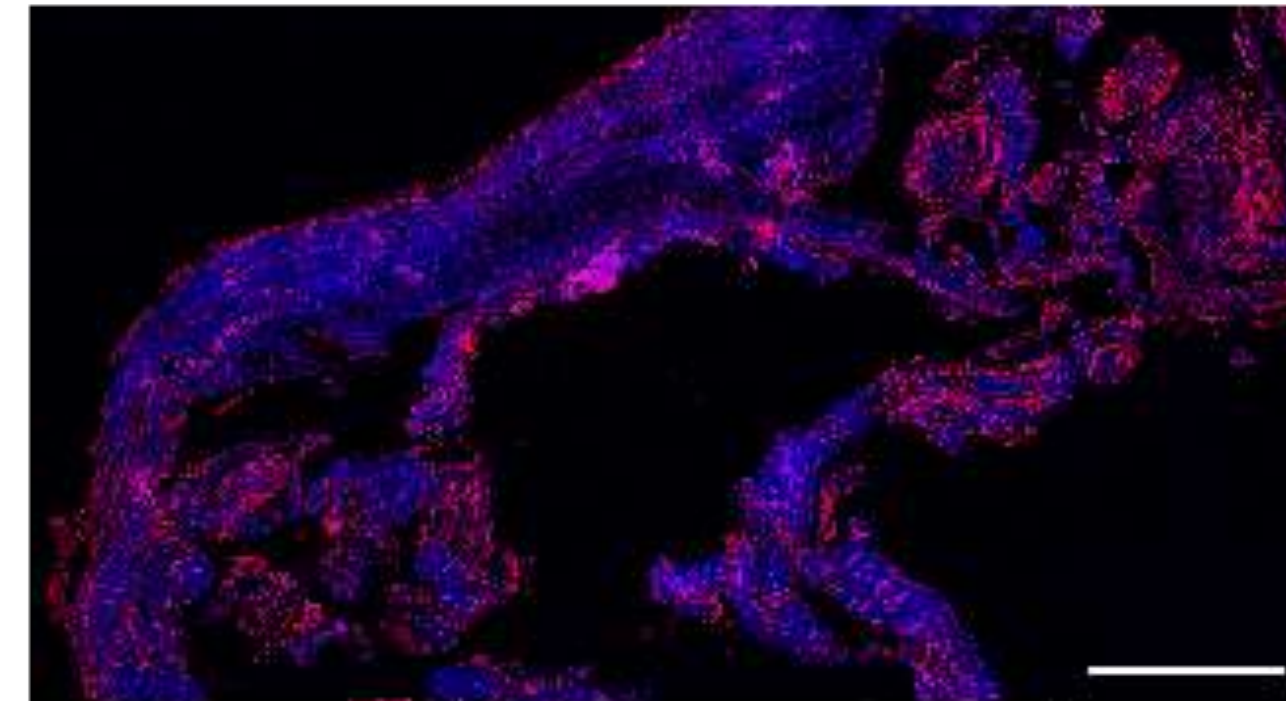
University of California, San Diego (M-012), La Jolla, California

Received April 2, 1984

Non-AD superior sagittal sinus

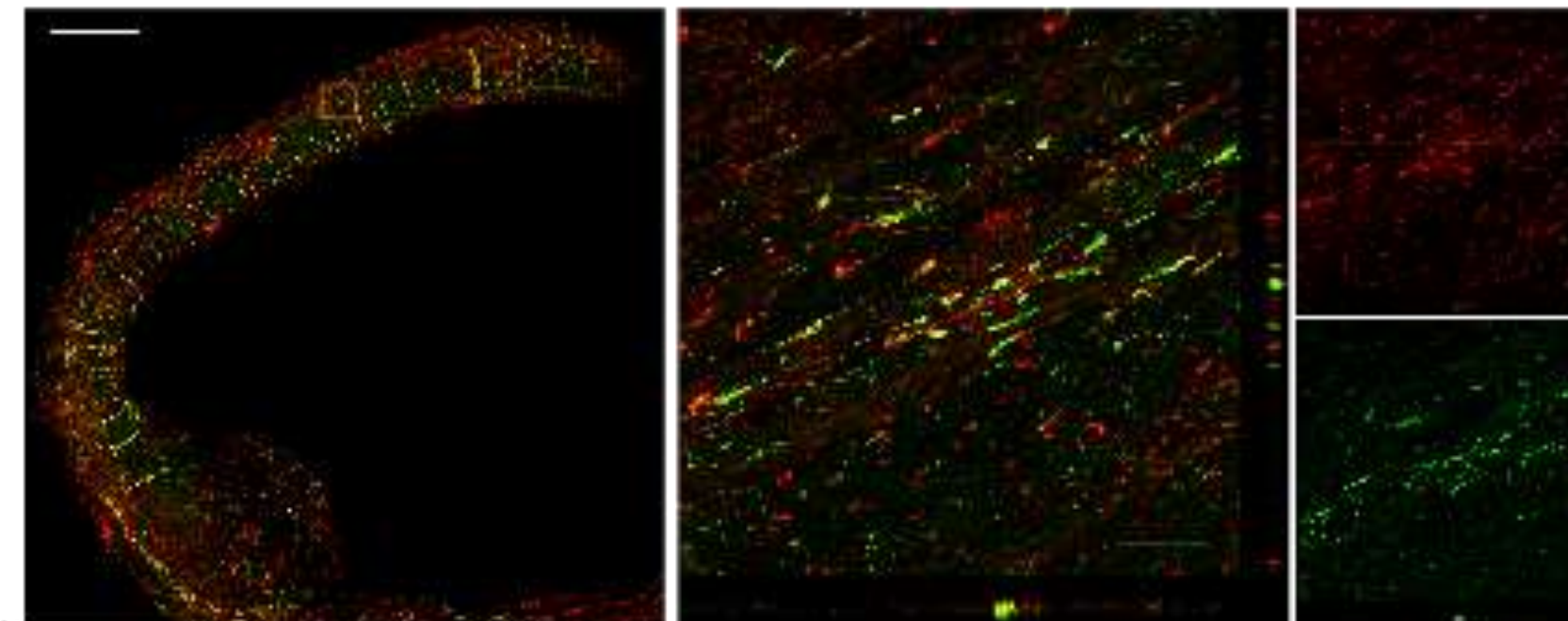


AD superior sagittal sinus



DAPI Aβ

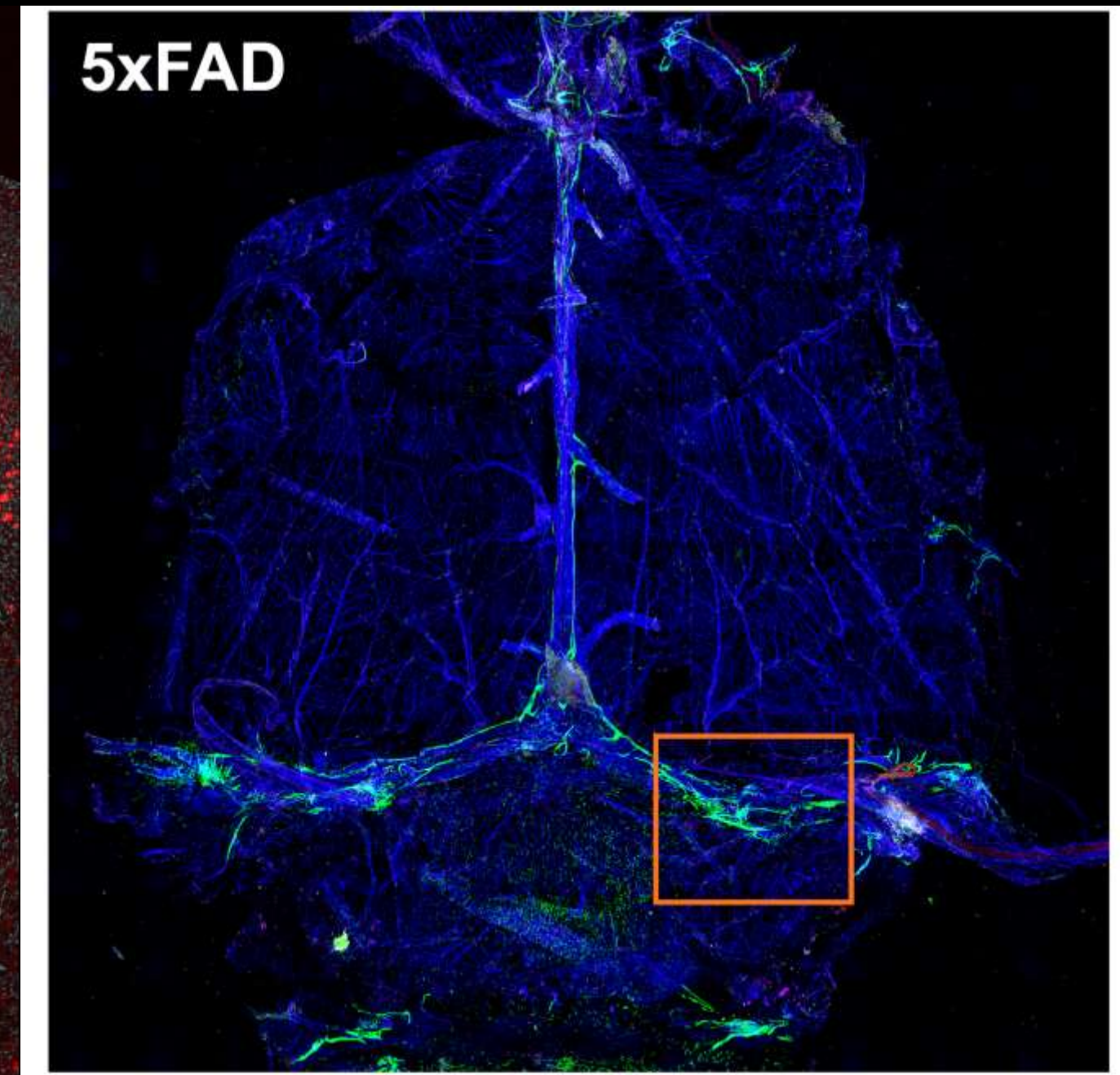
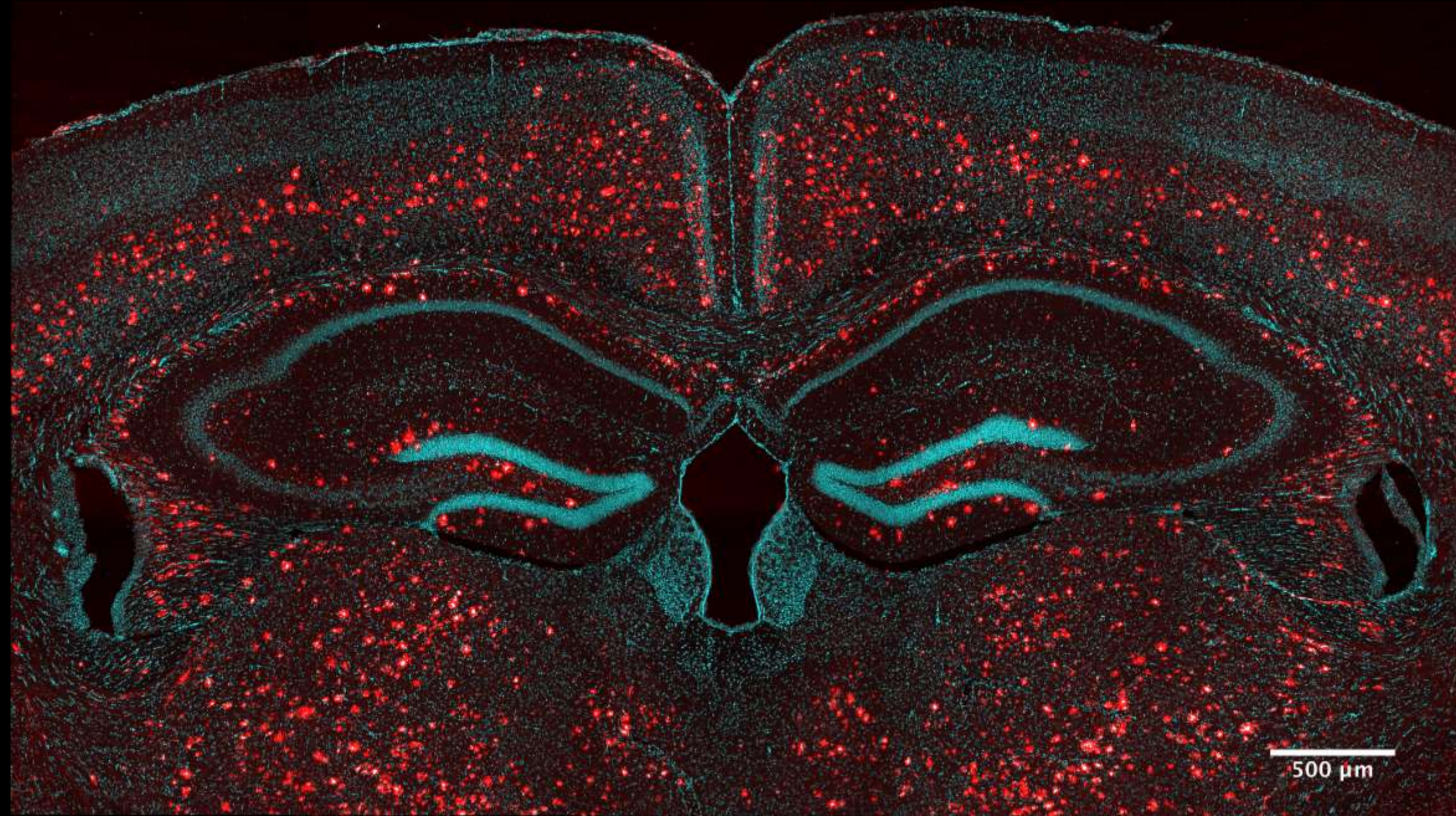
AD dura mater



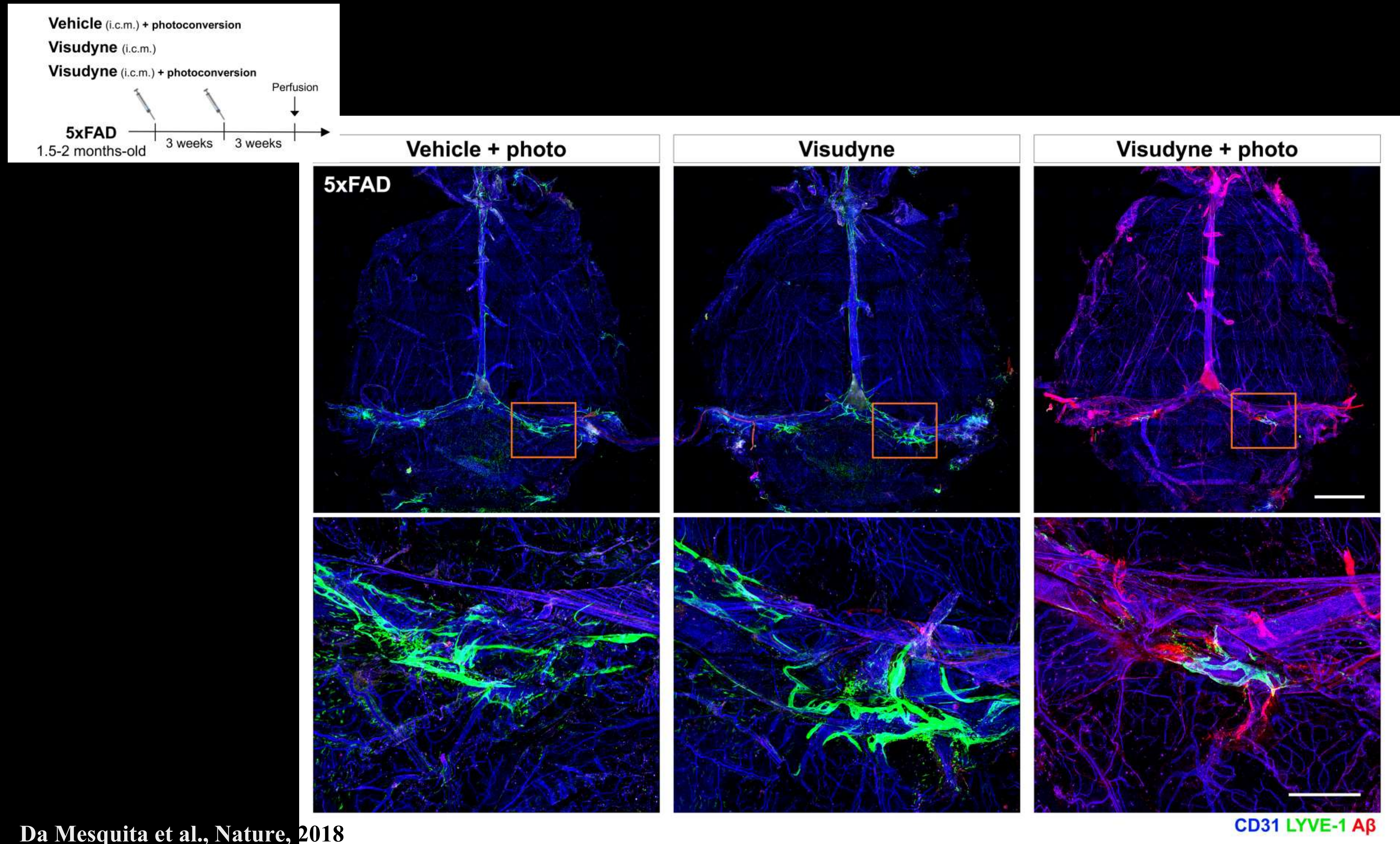
IBA1 Aβ

n=8-9 samples per group

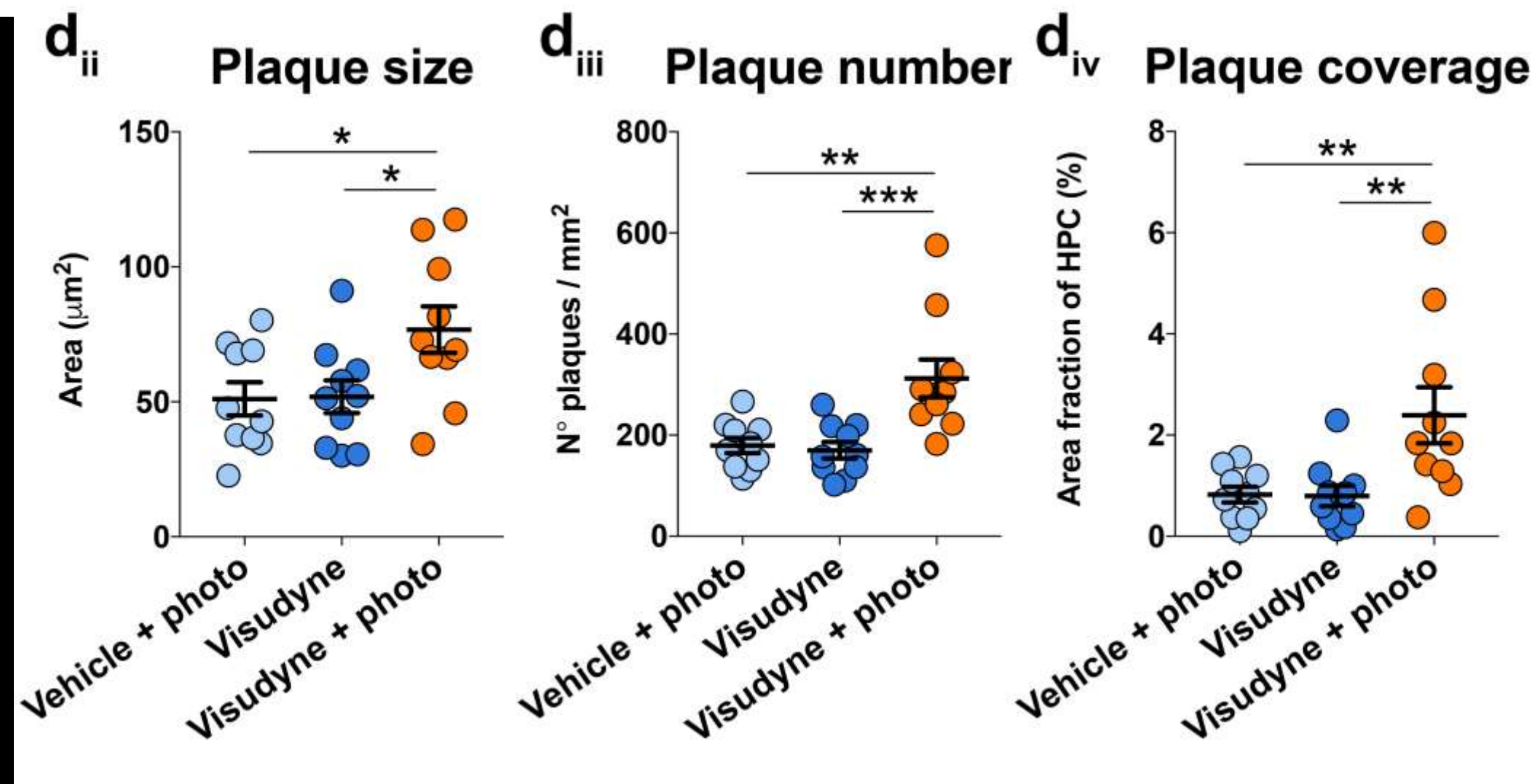
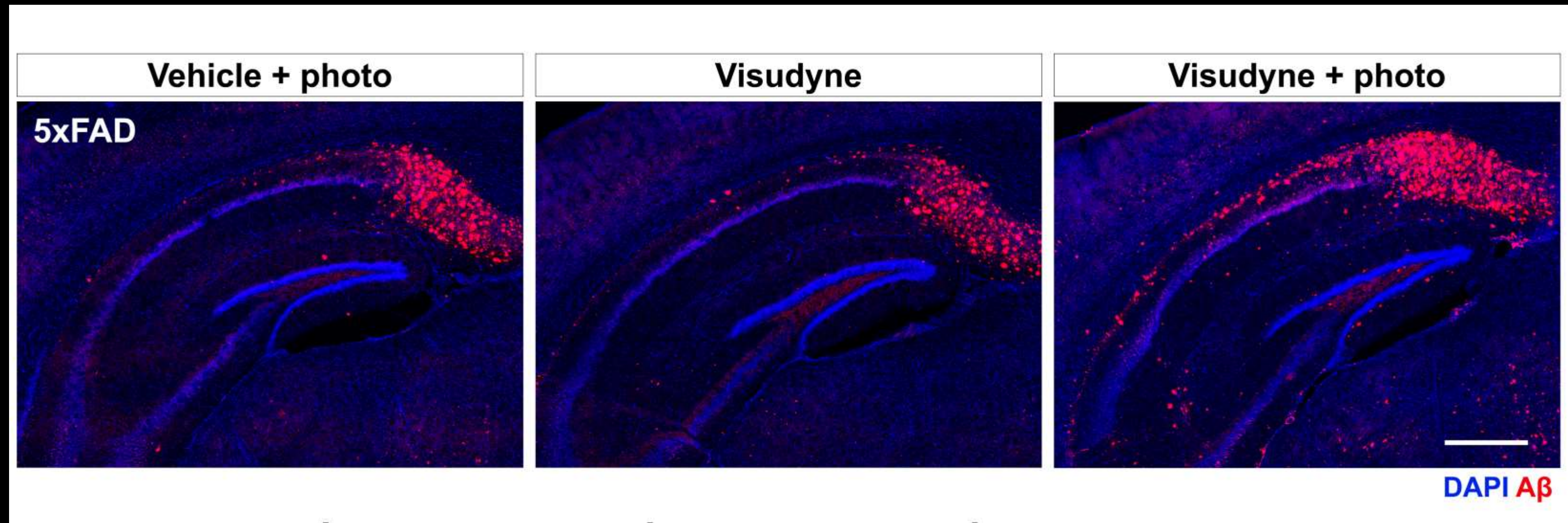
Are there meningeal plaques in AD mice?



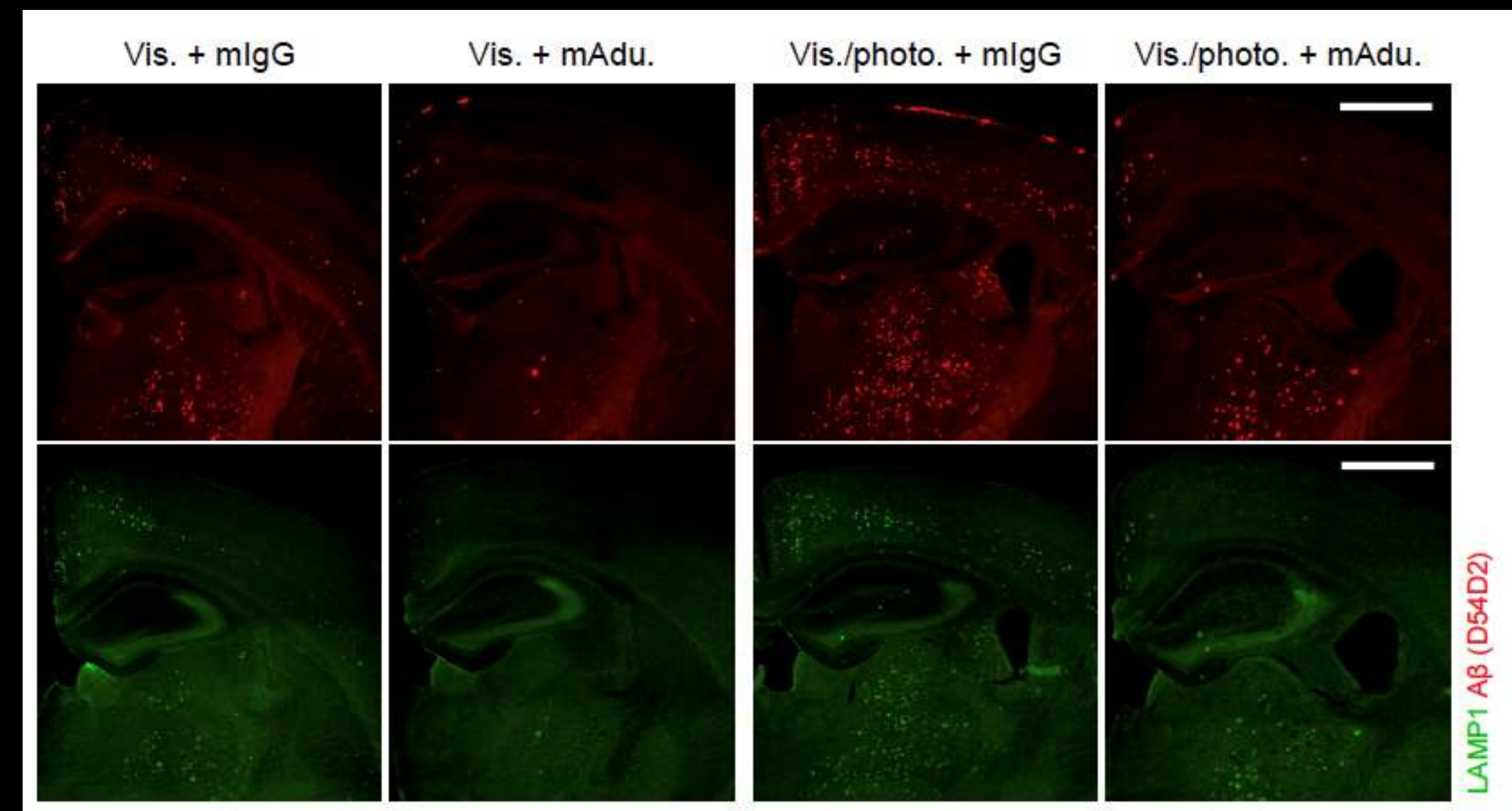
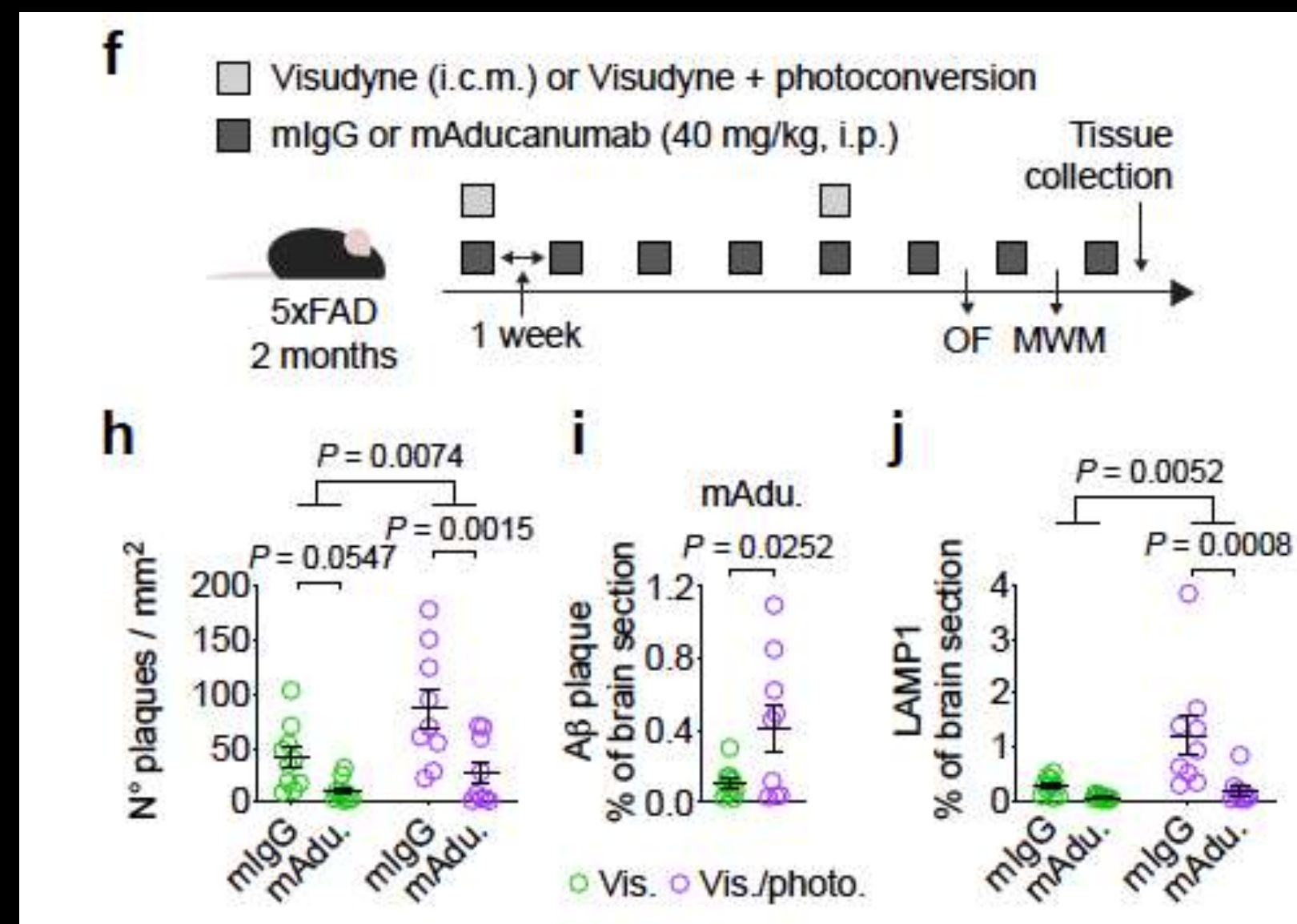
Acceleration of meningeal amyloid beta pathology and inflammation after lymphatic ablation in 5XFAD mice



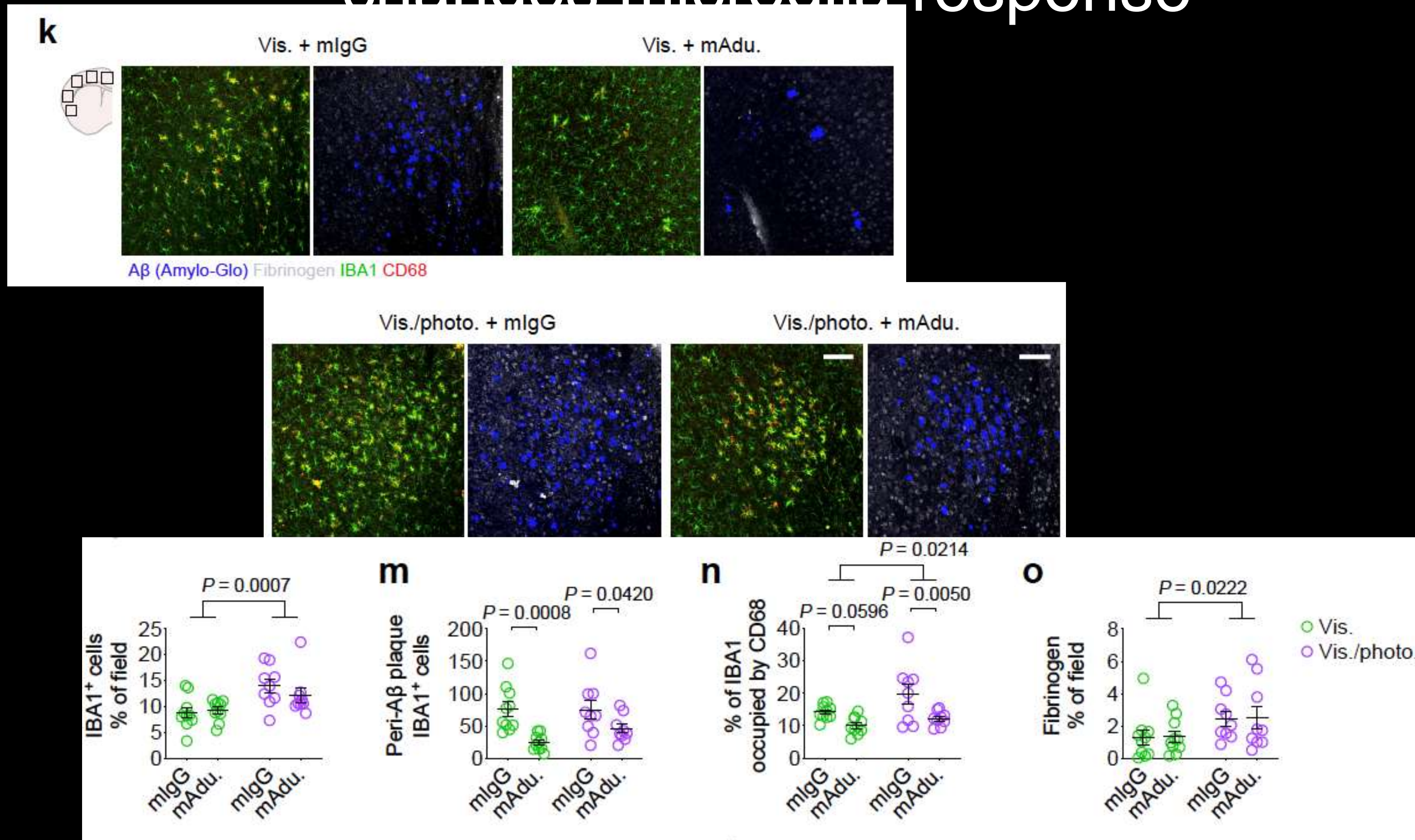
Acceleration of parenchymal amyloid beta pathology and inflammation after lymphatic ablation in 5XFAD mice



Ablation of meningeal lymphatics in AD mice alters the outcome of anti-amyloid immunotherapy

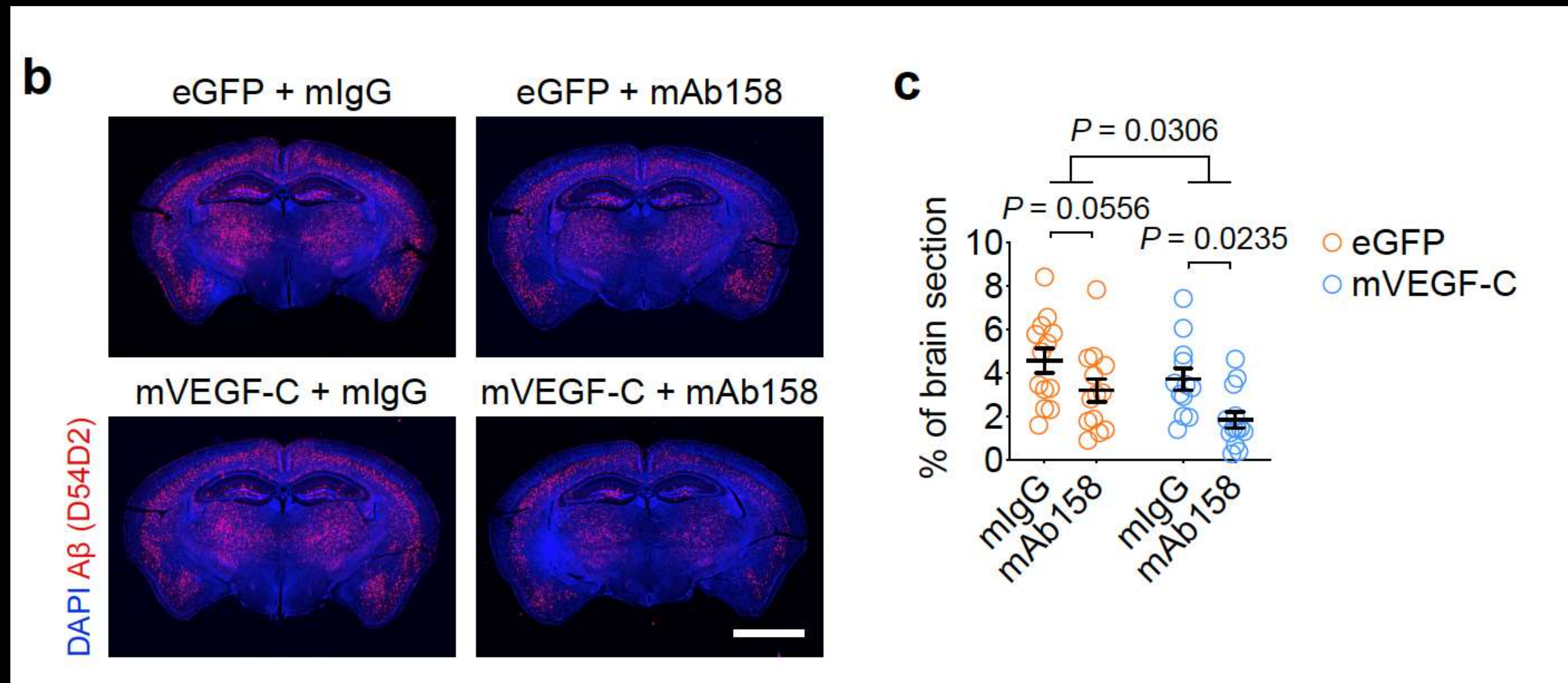
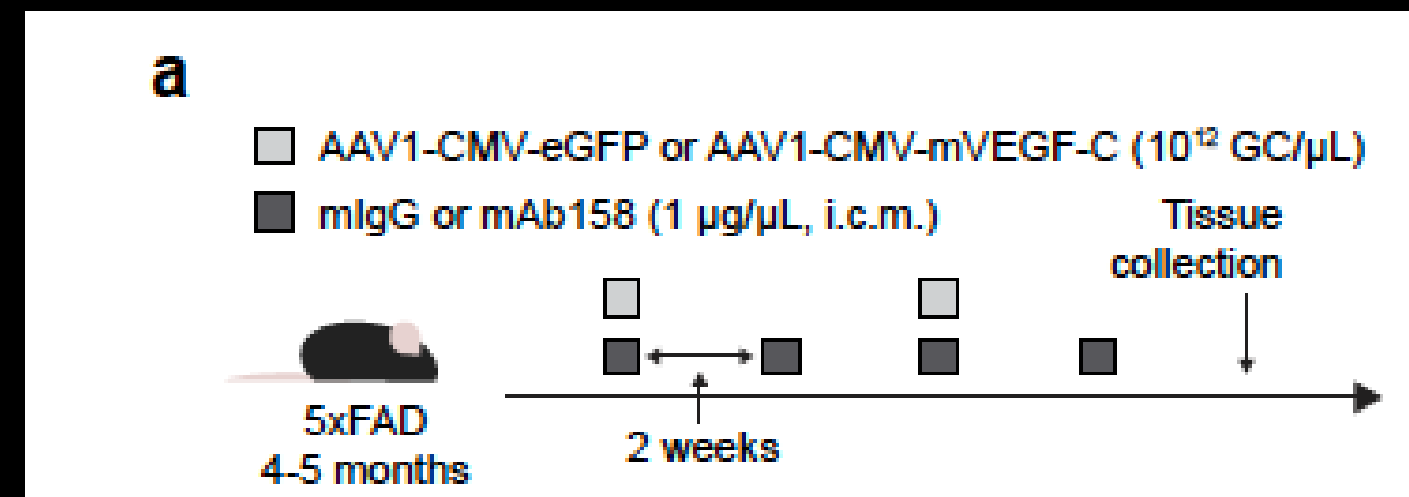


Ablation of meningeal lymphatics in AD mice changes microglia response

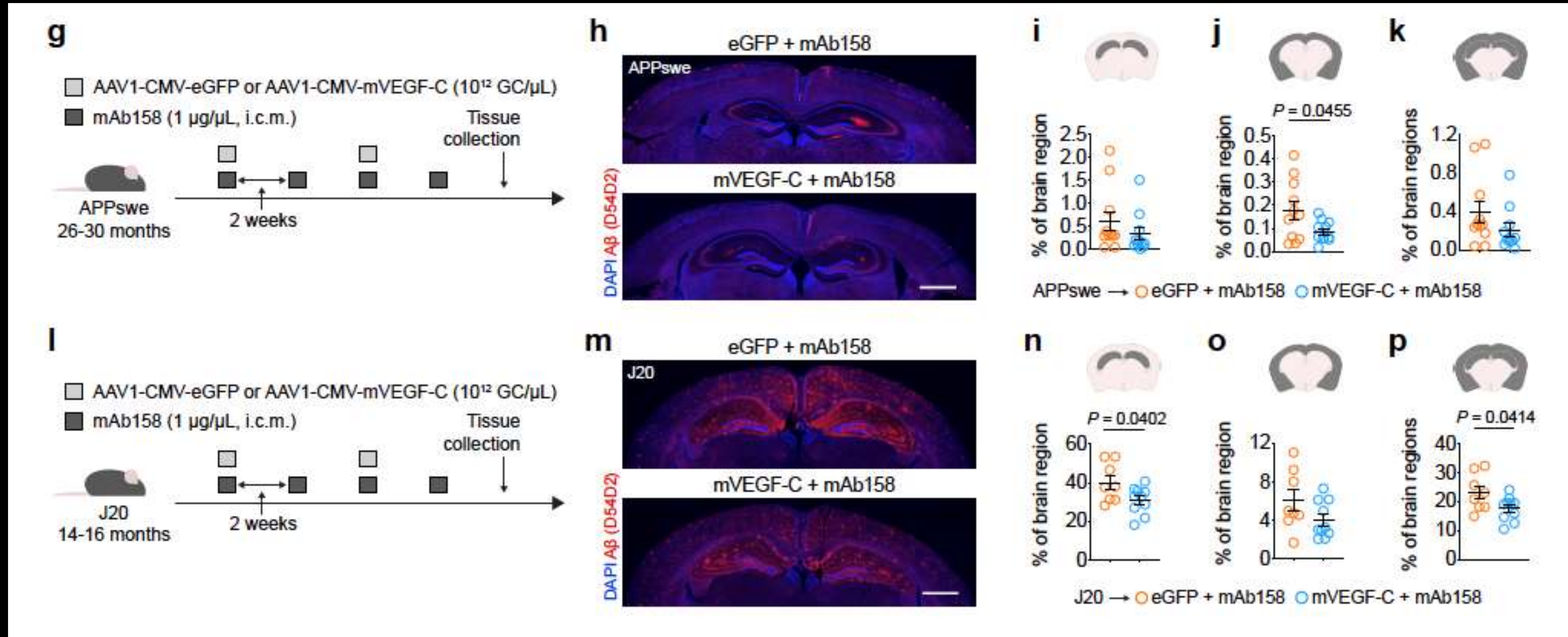


Would combination therapy (lymphatic enhancement+immunotherapy) show a synergistic effect?

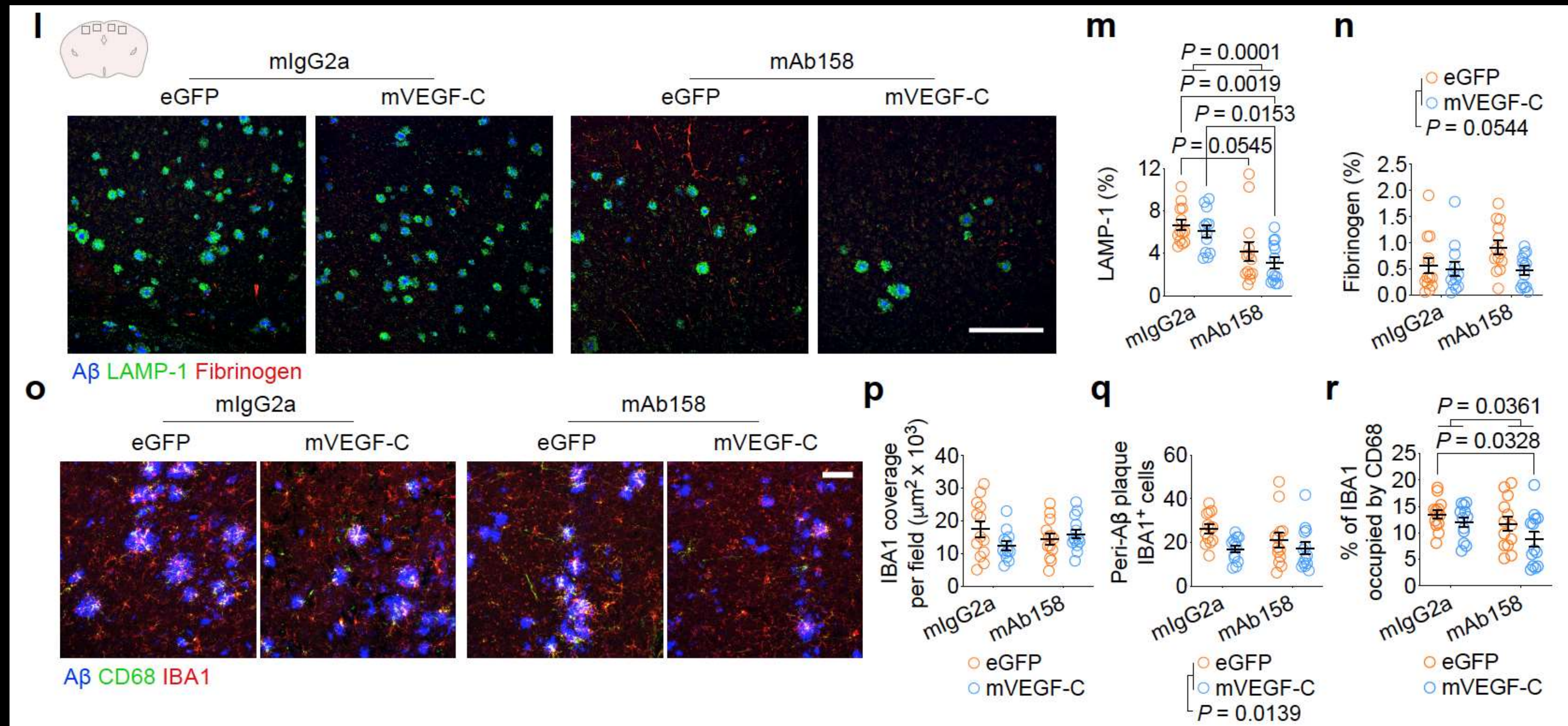
Enhancement of meningeal lymphatics function via VEGFc improves anti-myeloid immunotherapy in 5XFAD mice



Enhancement of meningeal lymphatics function via VEGFc improves anti-myeloid immunotherapy in old APPswe and J20 mice



Enhancement of meningeal lymphatics function via VEGFc improves anti-myeloid immunotherapy beyond plaque clearance



Can we rejuvenate the
brain?



Kipnis lab:

Leon Smyth
Antoine Drieu
Wenqing Gao
Steffen Storck
Iverchao Xu
Li-Feng Jiang-Xie
Kyungdeok Kim
James Walsh
Gustavo Davanzo
Zach Papadopoulos
Jang Hyun Park
Jenolyn Alexander
Andrea Salvador
Andrea Cugurra
Min Woo (Mitch) Kim
Jose Matzzitelli Perez
Siling Du
Igor Smirnov
Jasmin Herz
Taitea Dykstra
Dee Xu
Lucky Gu
Susan Blackburn
Zichen Tian
Keshni Bhasiin
Abena Apaw
Liz Griffin
Sean Brophy
Tracy Duckett



Collaborators

Washington University in St. Louis

Marco Colonna
David Holtzman
Gwen Randolph
Krikor Dikranian
Song Hu

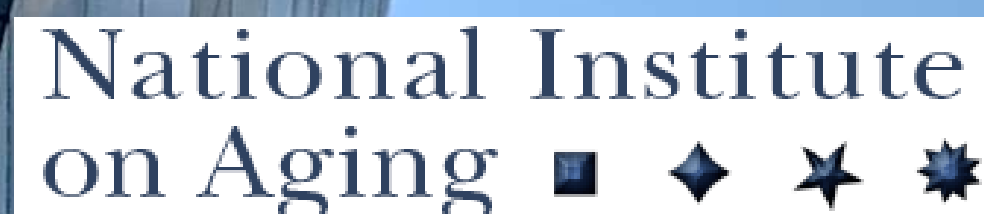
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