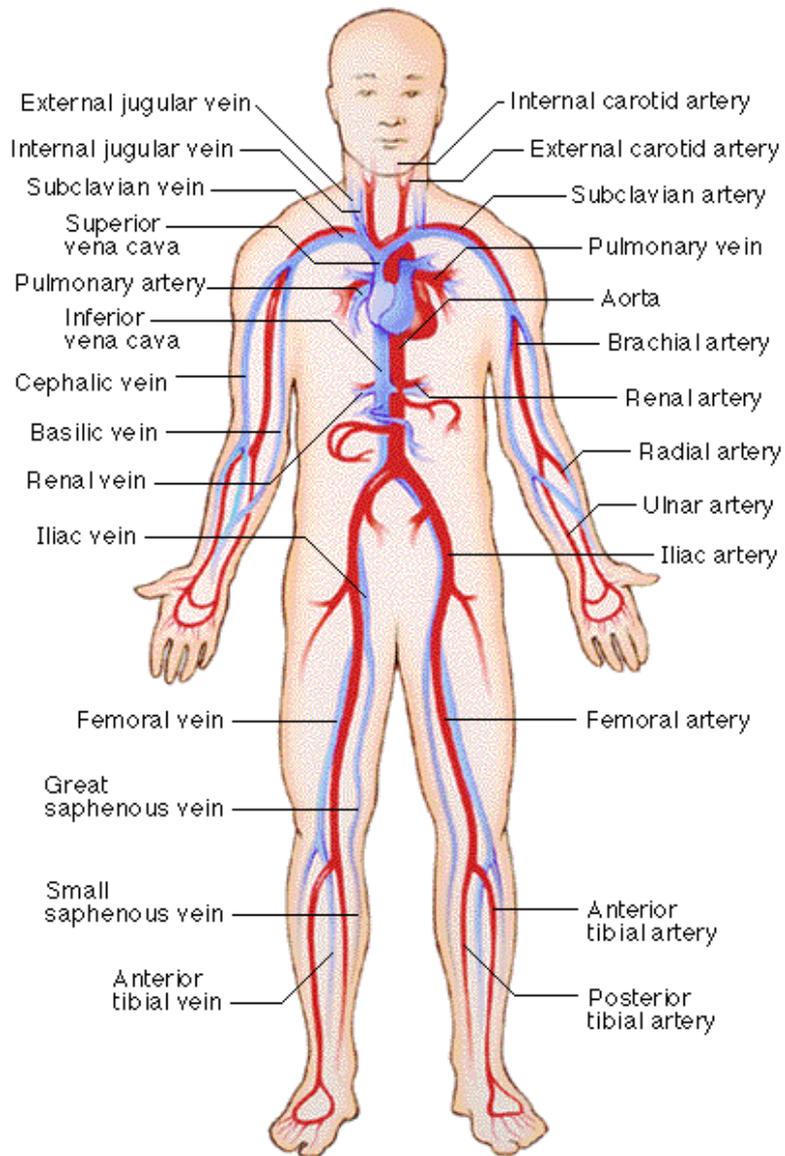
A fluorescence microscopy image of brain tissue. The image shows a network of cells and fibers. The cells are stained green, and the fibers are stained orange. The overall appearance is a complex, interconnected network of green and orange structures.

**Vascular and serum
biomarkers of
BBB dysfunction in
neuroinflammatory disease**

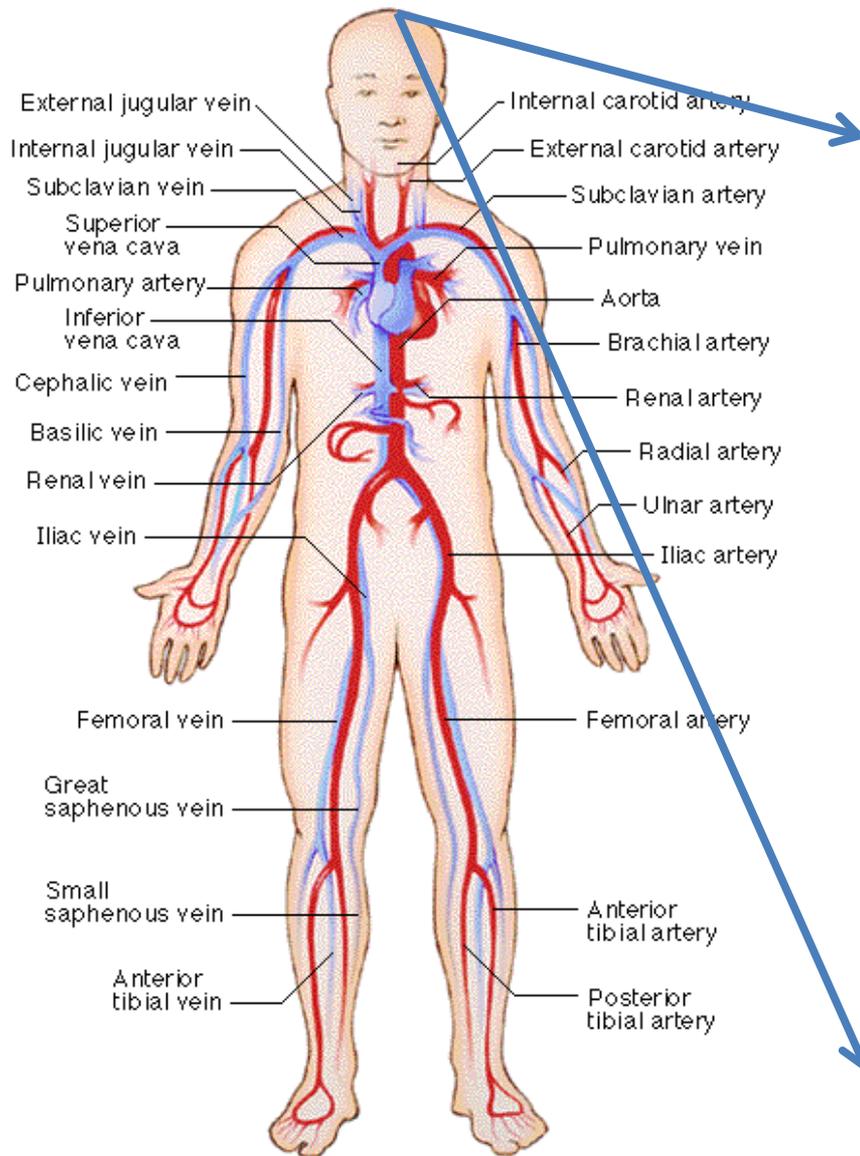
Richard Daneman

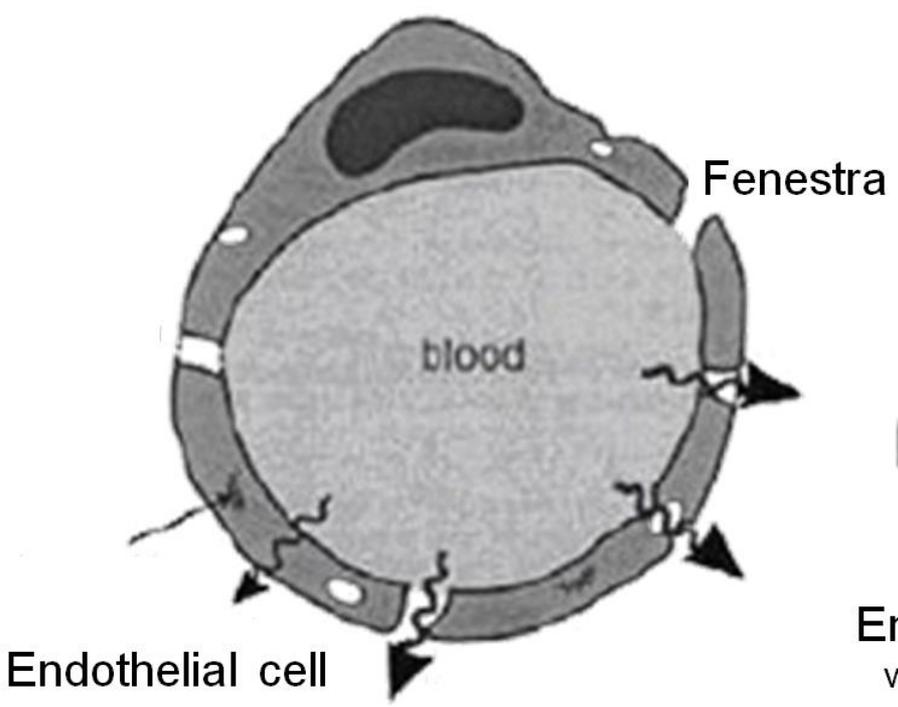
**University of California, San Diego
Departments of Neuroscience and Pharmacology**

Vascular Network

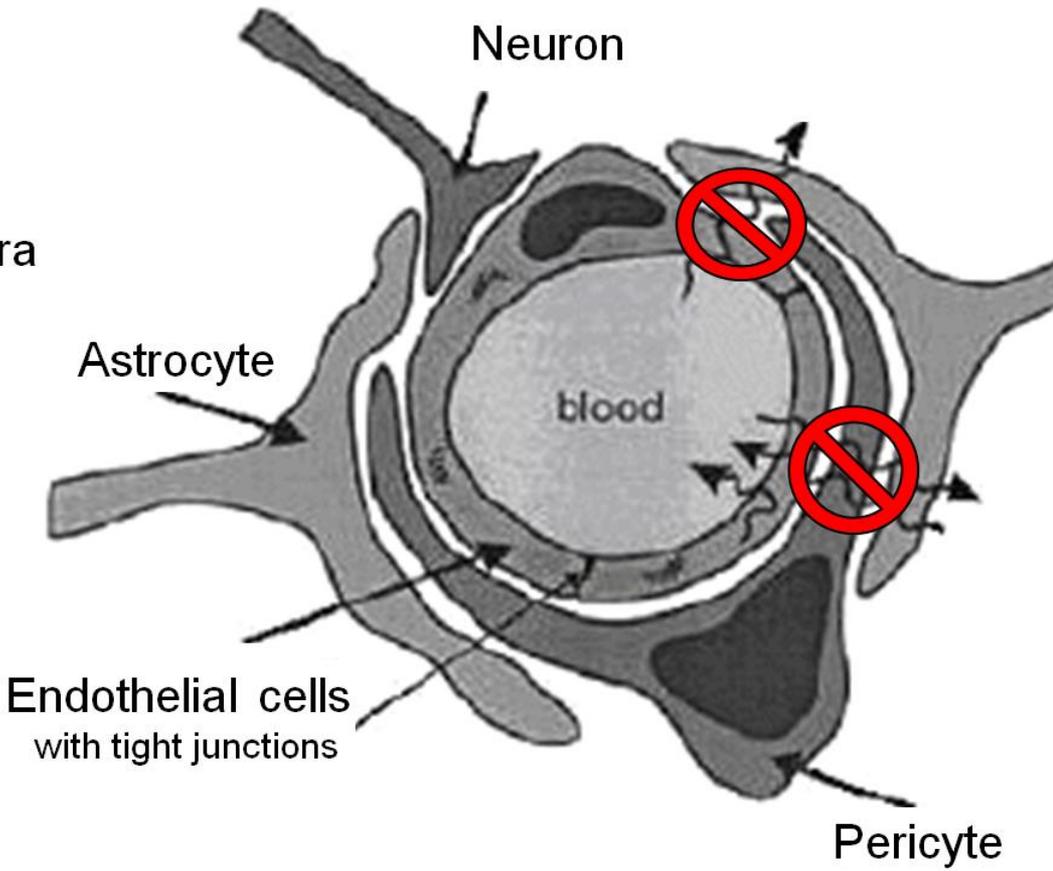


Vascular Network





Peripheral Capillary



CNS Capillary

Evan's Blue

Skin

Intestine

Kidney

Liver

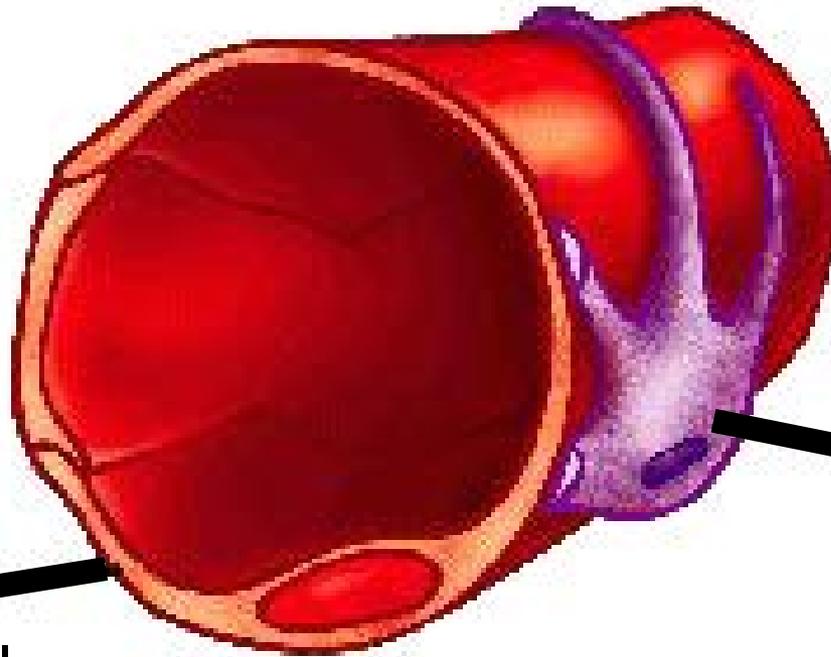
Brain



- Stroke
- Brain Traumas
- Epilepsy
- Multiple Sclerosis
- Other Neurological Diseases



Cell Biology of Capillaries

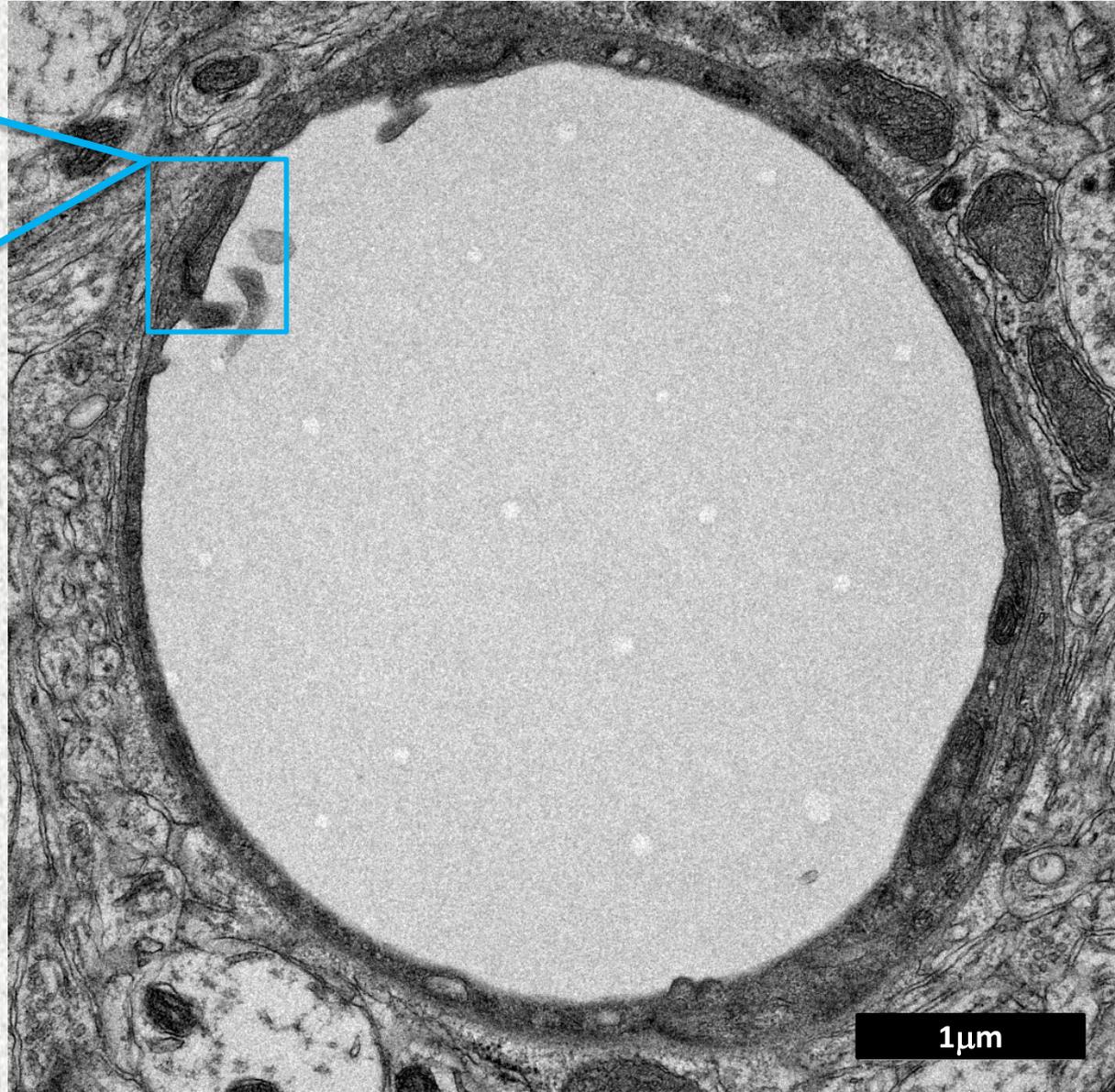
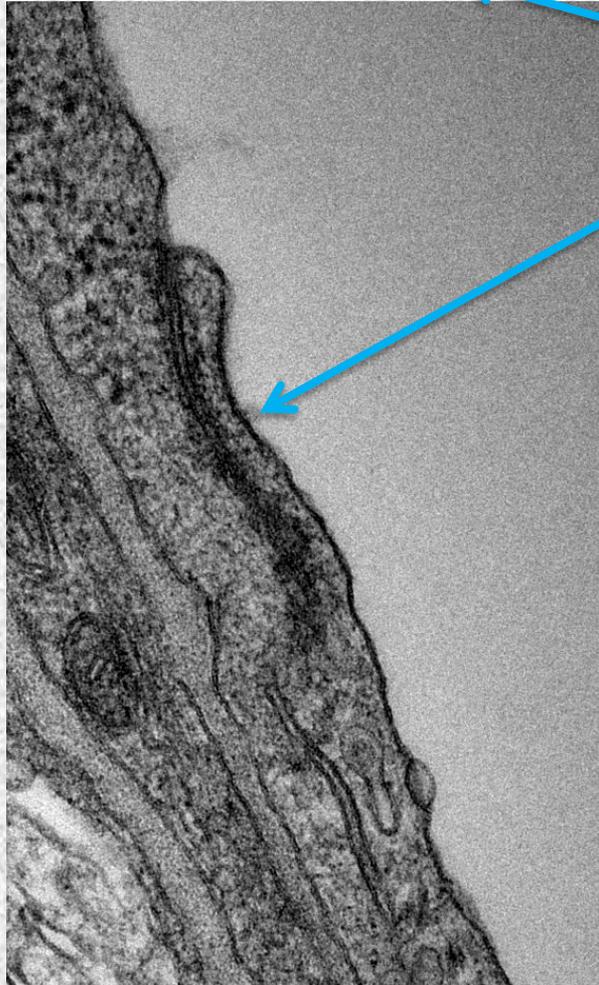


Endothelial cell

Pericyte

Properties of the BBB

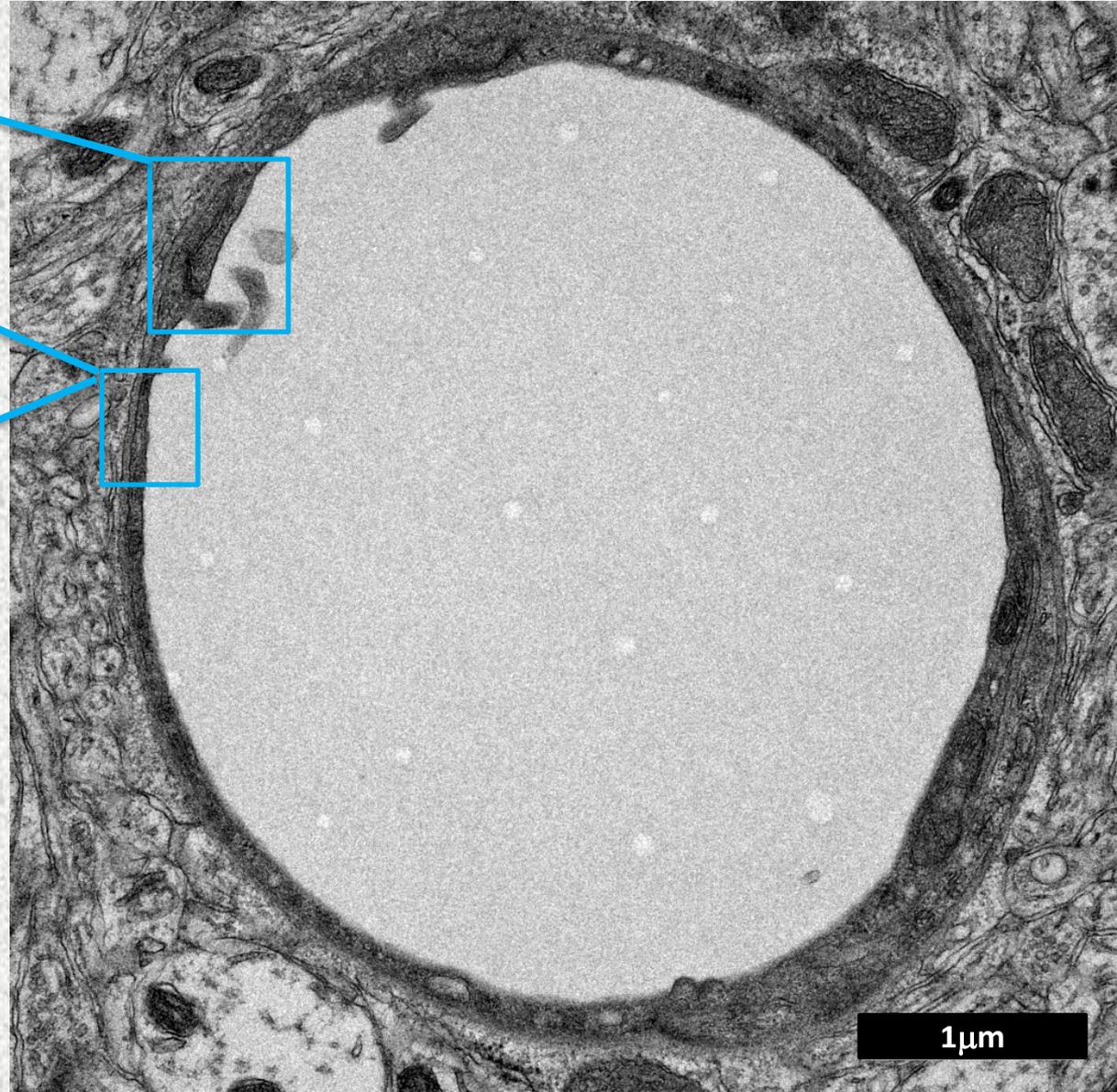
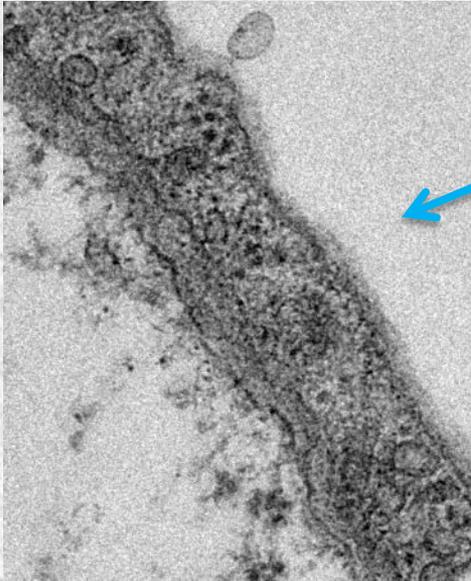
1. Tight junctions



Properties of the BBB

1. Tight junctions

2. Low rates of transcytosis



1 μm

Properties of the BBB

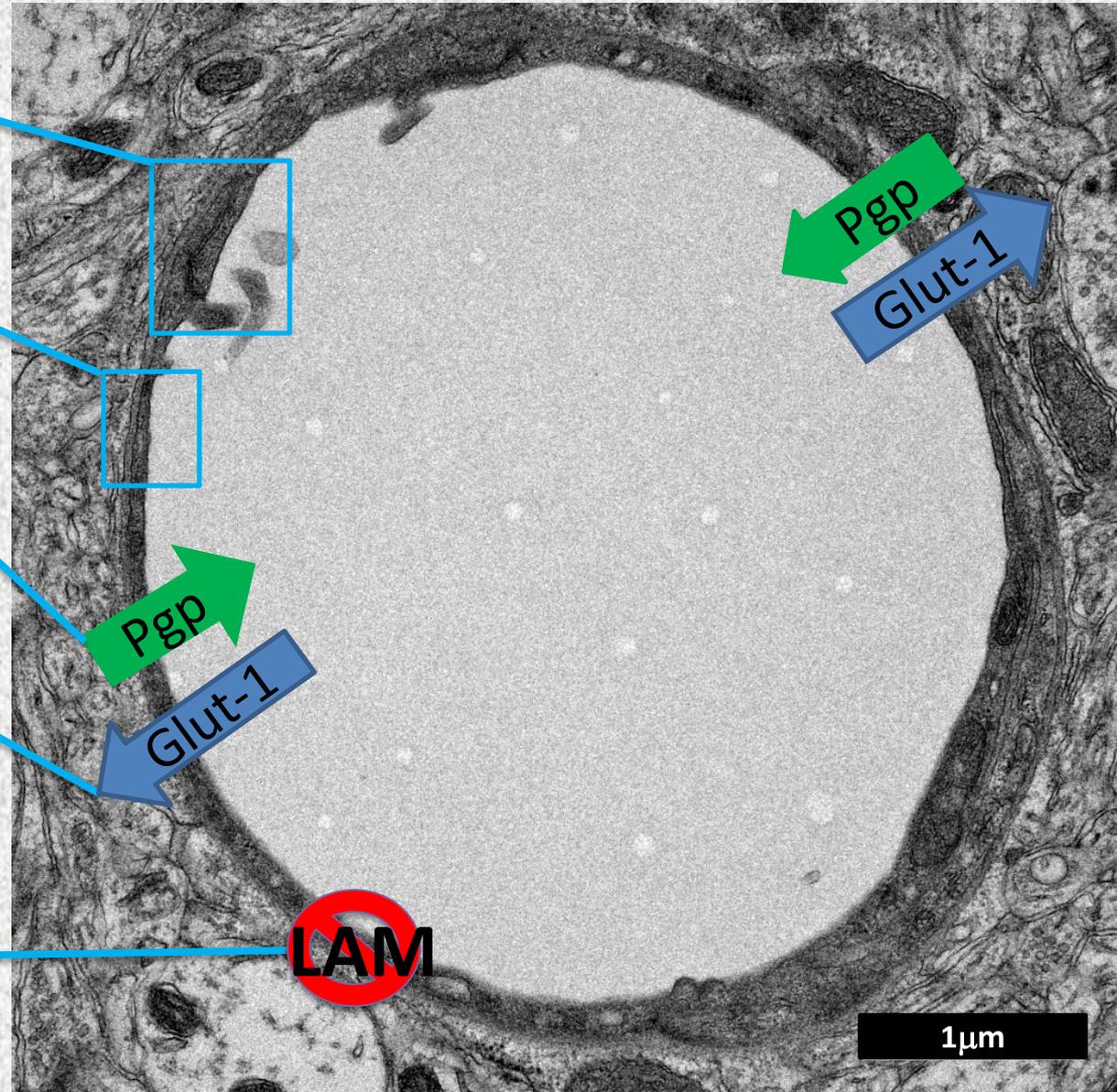
1. Tight junctions

2. Low rates of transcytosis

3. Express extrusion pumps

4. Express selective transporters for specific metabolites

5. Low expression of leukocyte adhesion molecules



1 μm

I) Can we identify vascular biomarkers of BBB dysfunction?

II) Can we identify serum biomarkers of BBB dysfunction?

1) Can we identify vascular biomarkers of BBB dysfunction?



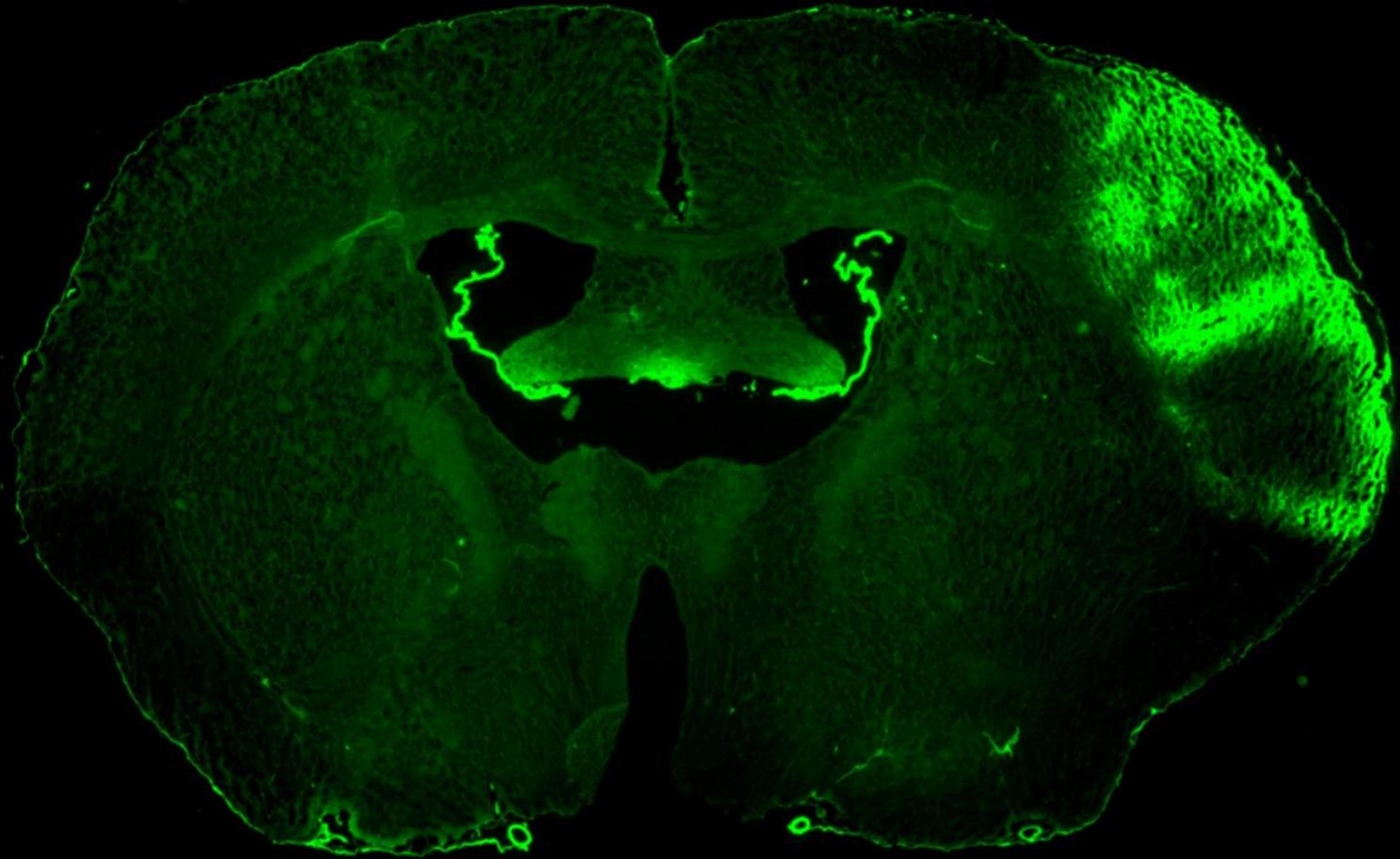
Allison Soung

Identification of global BBB gene expression changes during disease

<u>Disease</u>	<u>Trigger</u>	<u>Mouse Model</u>
Stroke	hypoxia/ischemia	MCAO -Hashimoto Lab
Multiple Sclerosis	inflammation	EAE -Zamvil Lab
Brain Injury	trauma	TBI -Noble Lab
Epilepsy	neural activity	Kainic Acid

BBB dysfunction is observed in each model

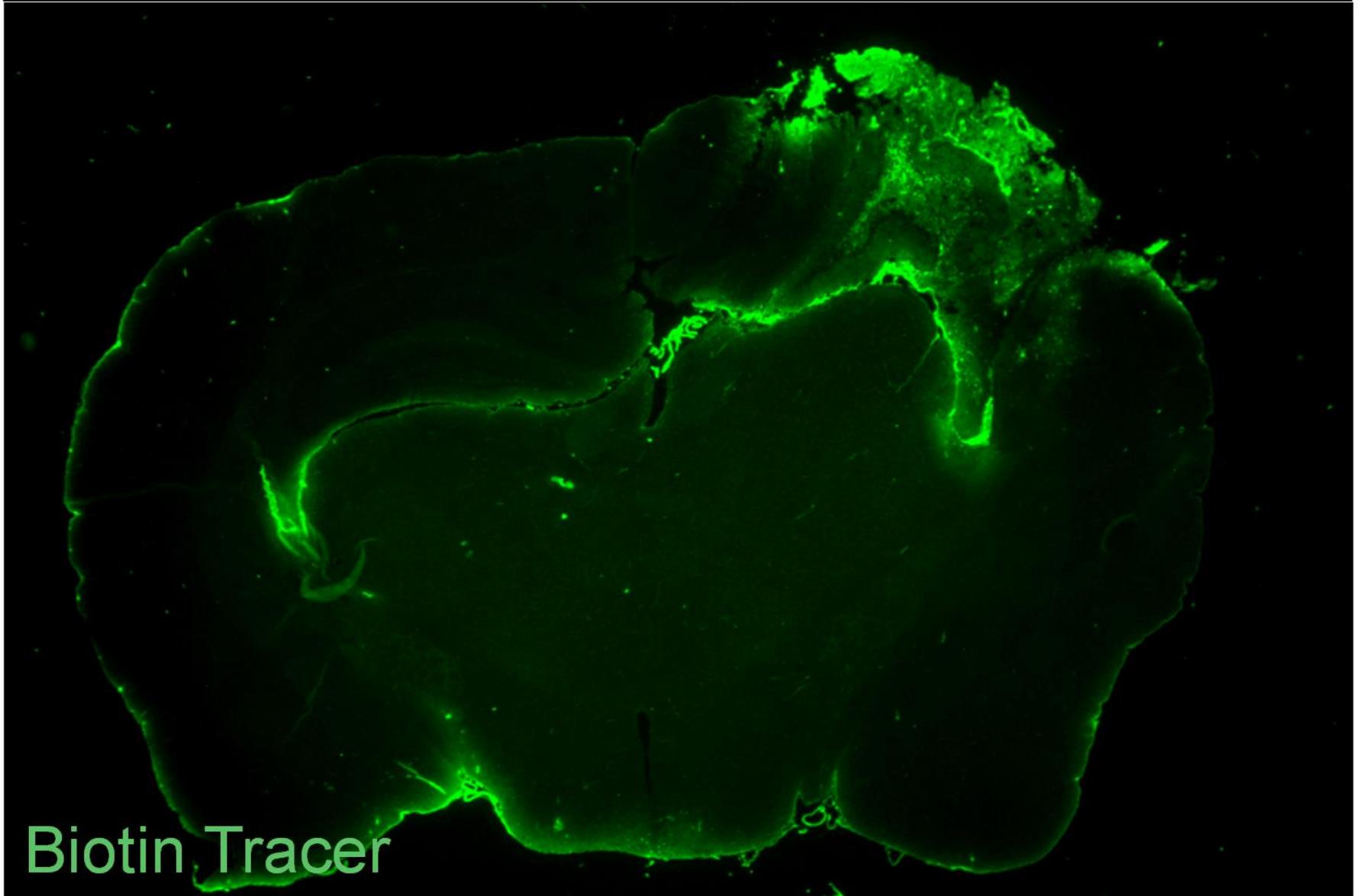
Stroke (MCAO)



Biotin Tracer

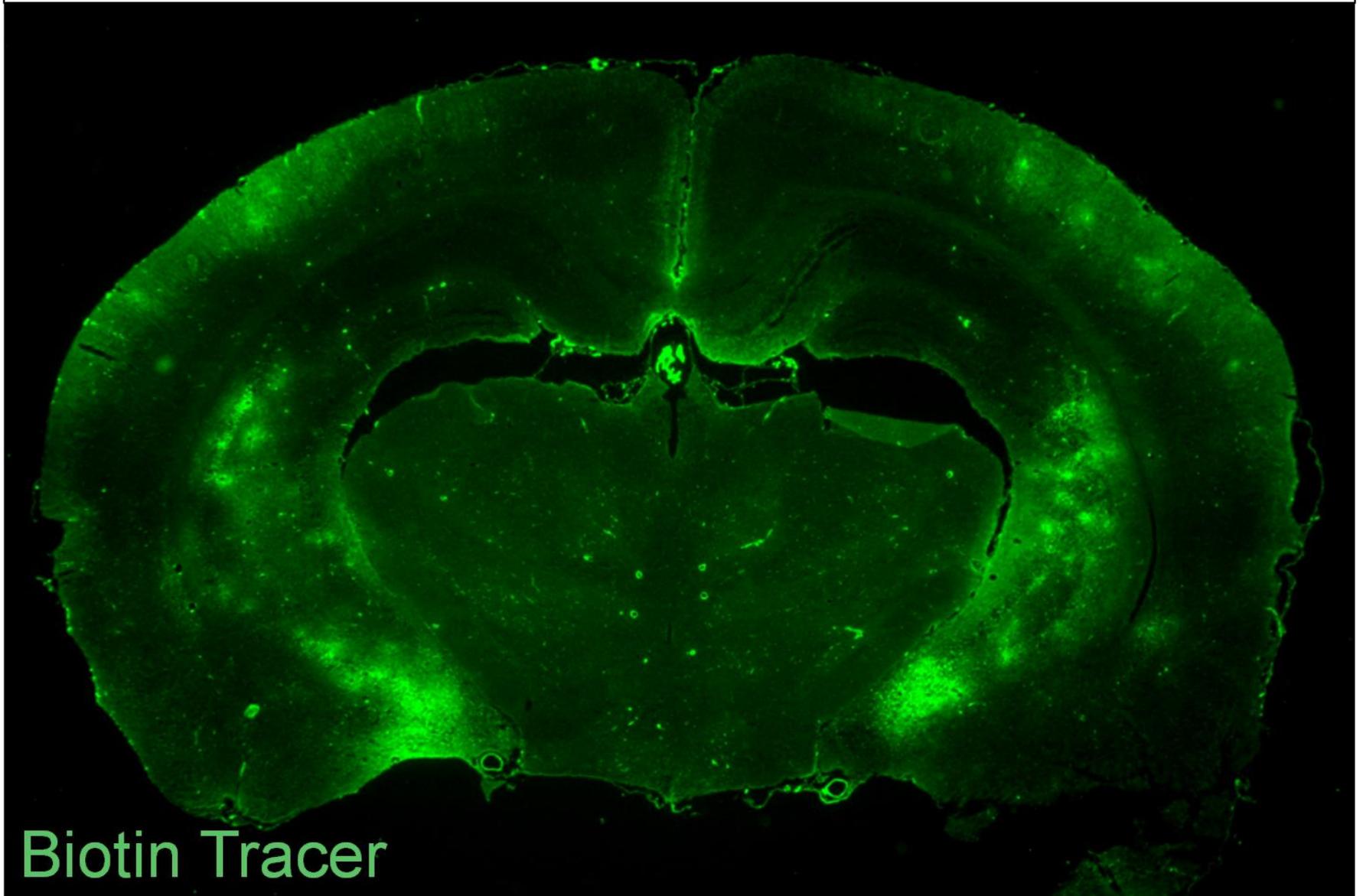
BBB dysfunction is observed in each model

TBI



BBB dysfunction is observed in each model

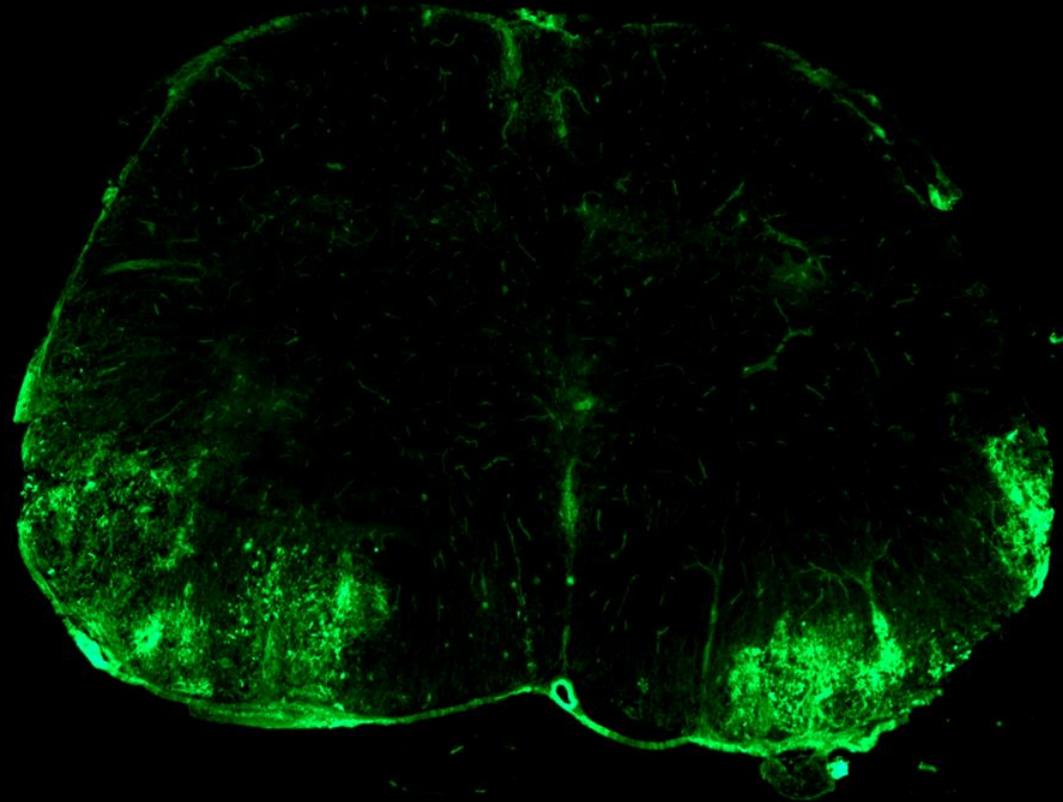
Epilepsy (Kainic Acid)



Biotin Tracer

BBB dysfunction is observed in each model

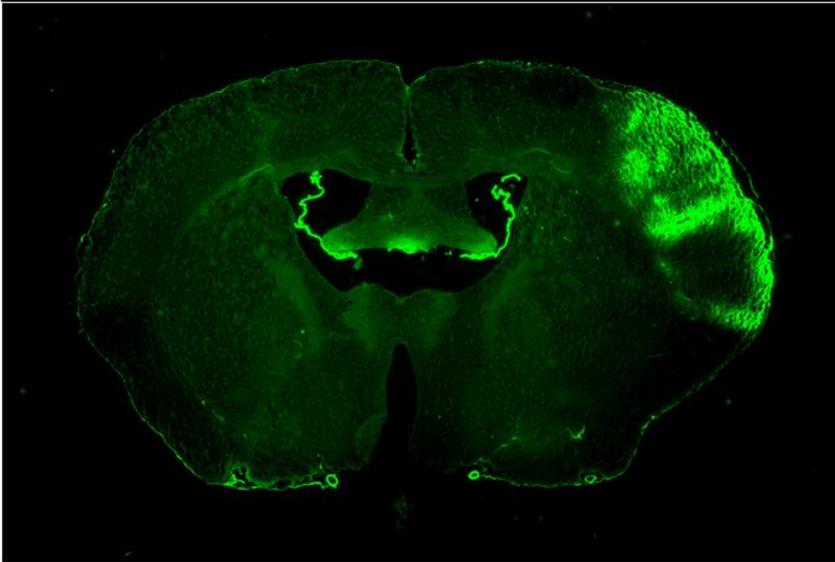
Multiple Sclerosis (EAE-spinal cord)



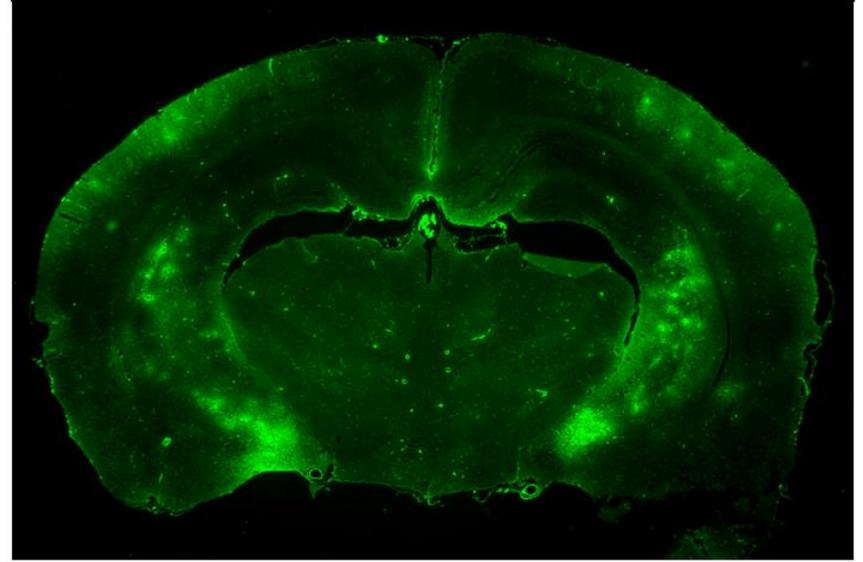
Biotin Tracer

BBB dysfunction is observed in each model

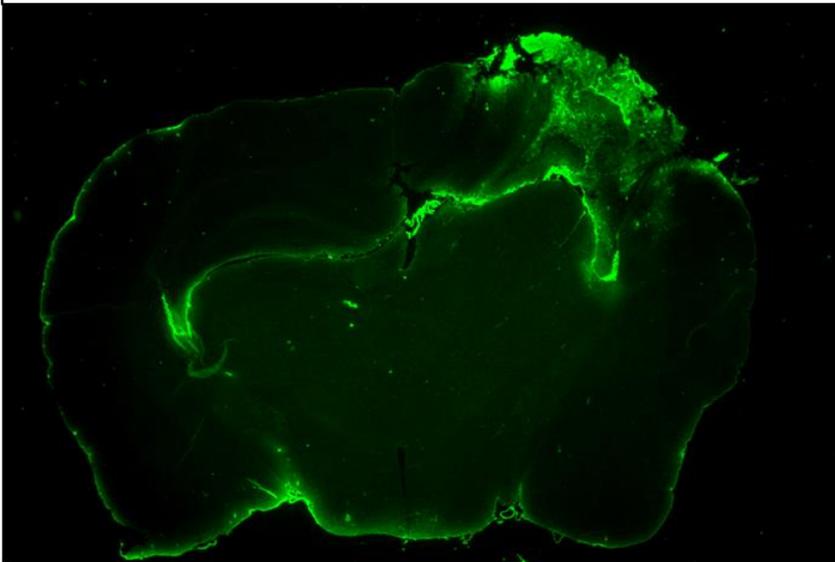
Stroke (MCAO)



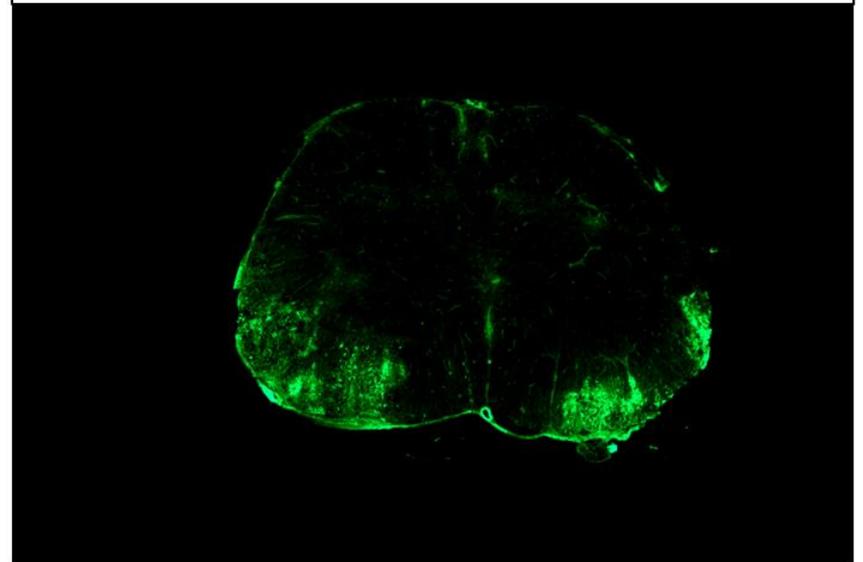
Epilepsy (Kainic Acid)



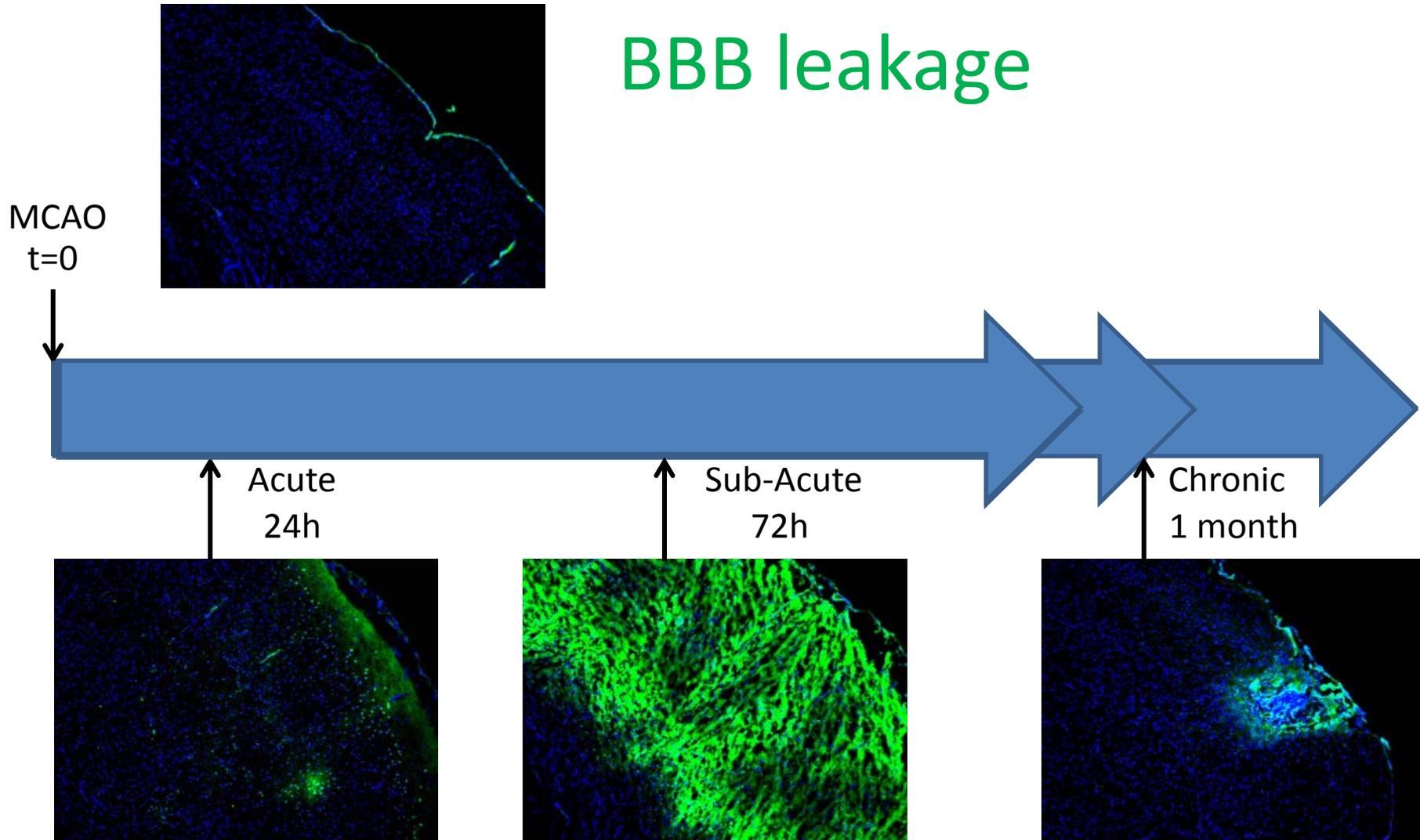
TBI



Multiple Sclerosis (EAE-spinal cord)

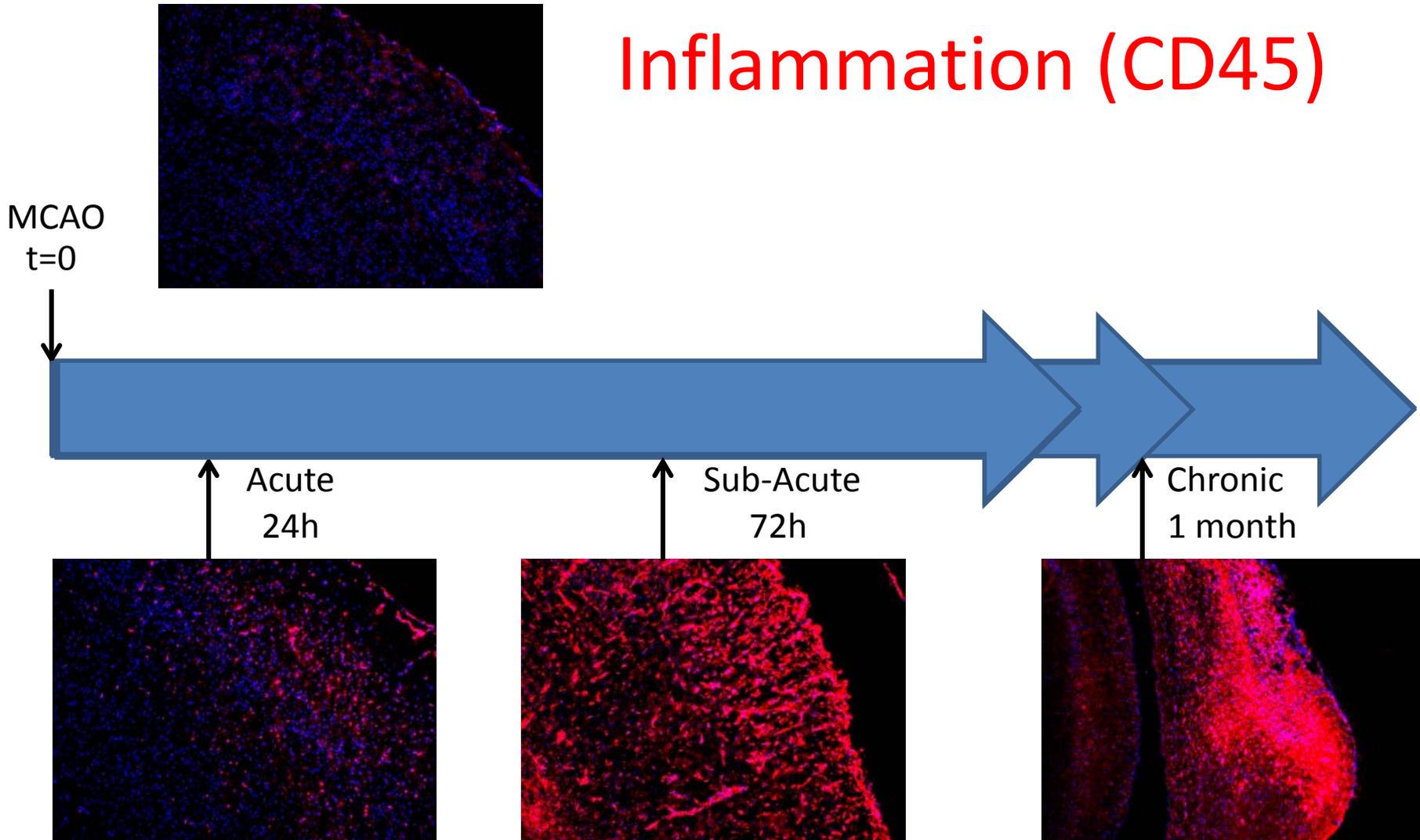


Time course for BBB RNAseq: eg Stroke



Time course for BBB RNAseq: eg Stroke

Inflammation (CD45)





Allison Soung

Identification of global BBB gene expression changes during disease

<u>Disease</u>	<u>Trigger</u>	<u>Mouse Model</u>
Stroke	hypoxia/ischemia	MCAO
Multiple Sclerosis	inflammation	EAE
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Epilepsy	neural activity	Kainic Acid