Repairing a leaky blood-brain barrier in epilepsy

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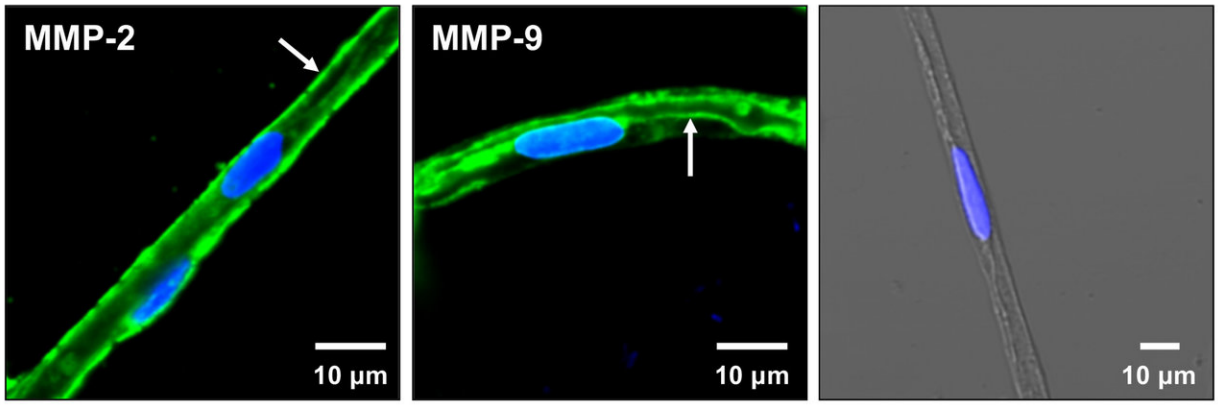

The representative immunostaining for MMP-2 (left), MMP-9 (middle) and the negative control (right; overlay of green, blue and transmitted light channels) in isolated rat brain capillaries. MMPs are shown in green; nuclei were counterstained with DAPI (blue). Credit: Rempe et al., *JNeurosci* (2018)

Blocking the activity of an enzyme that has a key role in the generation of recurring seizures may provide a new way to treat epilepsy that is resistant to anti-seizure drugs, according to a study of rats and mice published in *JNeurosci*.

One-third of people with epilepsy, one of the most common neurological disorders, do not respond well to current treatments for managing seizures. Part of this challenge is that seizures erode the lining of

capillaries in the brain that let nutrients in and keeps toxins out. A "leaky" blood-brain barrier, in turn, leads to more seizures. Understanding how this cycle occurs is necessary in order to develop strategies to plug the leak.

In their study of rodent brain capillaries, Björn Bauer and colleagues identified a seizure-triggered pathway that contributes to blood-brain barrier dysfunction in epilepsy. The neurotransmitter glutamate, released during seizures, increased the activity of two types of enzymes belonging to a group called matrix-metalloproteinase (MMP-2, MMP-9) and degraded the tightly-packed proteins that form a critical component of the blood-brain barrier.

Blocking another enzyme called cytosolic phospholipase A2 (cPLA2) in rats with induced seizures and genetically deleting CPLA2 in mice prevented these changes and the associated capillary leakage.

More information: Matrix Metalloproteinase-Mediated Blood-Brain Barrier Dysfunction in Epilepsy, *JNeurosci* (2018). DOI: 10.1523/JNEUROSCI.2751-17.2018

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