

**TITLE:** “Blood-Brain Barrier Function in Epilepsy: New Targets for Therapy?”

**PRESENTER:** Björn Bauer, College of Pharmacy, University of Minnesota

The blood-brain barrier is severely altered in epilepsy. Alterations include changes in expression of efflux and influx transporters, metabolic enzymes, and development of barrier leakage that have been linked to antiepileptic drug resistance and seizure genesis. Recent findings suggest that seizure-induced glutamate release is, at least in part, responsible for altered barrier function in epilepsy and contributes to seizure genesis and antiepileptic drug resistance. However, the molecular mechanism(s) and signaling molecules responsible for these pathologies are currently unknown.

We hypothesize that glutamate signals through the two-arm LOX/COX pathway, thereby changing expression of efflux and influx transporters, metabolic enzymes, and causing barrier leakage. This hypothesis is based on preliminary data showing that: 1) glutamate decreases expression of influx transporters, increases expression of efflux transporters and metabolic enzymes in brain capillaries, and inhibiting the COX pathway blocks these effects; 2) glutamate activation of the LOX pathway triggers barrier leakage; and 3) blocking the LOX/COX pathway abolishes the glutamate-induced changes in transporter and enzyme expression levels and prevents barrier leakage.

Together, our findings suggest new therapeutic targets that could potentially be used to design a novel strategy to improve epilepsy treatment and better control seizures in patients.