

Microglia enhance the functional maturation of blood-brain barrier.

Yukari Shigemoto-Mogami, Kazue Hoshikawa, Kimiko Kitamura, Kaoru Sato

Lab. of Neuropharmacol, Divi. Pharmacol, NIHS

The blood-brain barrier (BBB) restricts the transport of substances between vasculature and brain. Recent studies have clarified that various kinds of cells in neurovascular unit are related to the BBB functions. In this study, we investigated the roles of microglia in BBB functional maturation using *in vitro* BBB model comprised of endothelial cells, pericytes, and astrocytes (C^opharmacocell). When we added primary microglia to the brain side of the model during the maturation period, trans-endothelial electrical resistance (TEER) and the expression level of claudin-5, were significantly increased. On the other hand, when we added LPS-activated microglia, the TEER and the expression levels of tight junction proteins (TJs) were significantly decreased. We next investigated involvement of cytokines/chemokines in the effects of microglia. We clarified that microglia-induced increase in TEER was mediated by VEGF, while the increases in TJs were mediated by the inhibition of fractalkine signaling. In the developing brain, a lot of microglia surround the capillaries. Our data suggest that microglia contribute to the developmental maturation of the BBB. We are currently investigating the accurate time course of BBB maturation and the roles of microglia in the BBB maturation at the developmental stage by *in vivo* experiments.