

Coordinating of blood–brain barrier development: A new role of CD146 in cerebral vasculo–angiogenesis

Recently, with the support of the National Natural Science Foundation of China, scientists from Prof. Yan Xiyun's (阎锡蕴) group at the Institute of Biophysics of the Chinese Academy of Sciences, in cooperation with Prof. Zhang Jingjing's (张晶晶) group of the Affiliated Hospital of Guangdong Medical University have made significant progress in understanding the molecular regulation of BBB development, where a single cell adhesion receptor, CD146, could spatio-temporally coordinate the brain endothelial cell-pericyte communication and contribute to the functional formation of BBB during embryogenesis. This research article entitled "CD146 coordinates brain endothelial cell-pericyte communication for blood-brain barrier development" was published in *PNAS* (2017, 114(36): E7622–E7631).

The blood-brain barrier (BBB) is a highly regulated multicellular partition including monolayer endothelial cells, pericytes and basement membrane, which protectively separates blood from the brain parenchyma. Disruption of BBB has been tightly related to neurological disorders and neuroinflammation during CNS injuries, including brain tumors, stroke, CNS infections, and neurodegenerative diseases. However, till now, the molecular mechanisms controlling BBB formation remain incompletely unknown.

In this study, scientists show that early in embryonic development, endothelial CD146 promotes barrier induction by regulating the expression of claudin-5. Subsequently, pericyte-expressed CD146 controls pericyte recruitment to BECs. Accompanied by the pericyte recruitment, endothelial CD146 is finally downregulated by pericyte-secreted transforming growth factor-beta 1, contributing to further BBB maturation. The work links the low CD146 expression in BECs of the mature BBB to a quiescent CNS immune state. Previous studies by Yan's lab and others show that CD146 is significantly elevated in BECs to promote neuroinflammation in multiple sclerosis. CD146 could be a key regulator to CNS immune surveillance, and a potential therapeutic target for treating neuroinflammatory diseases associated with BBB breakdown.

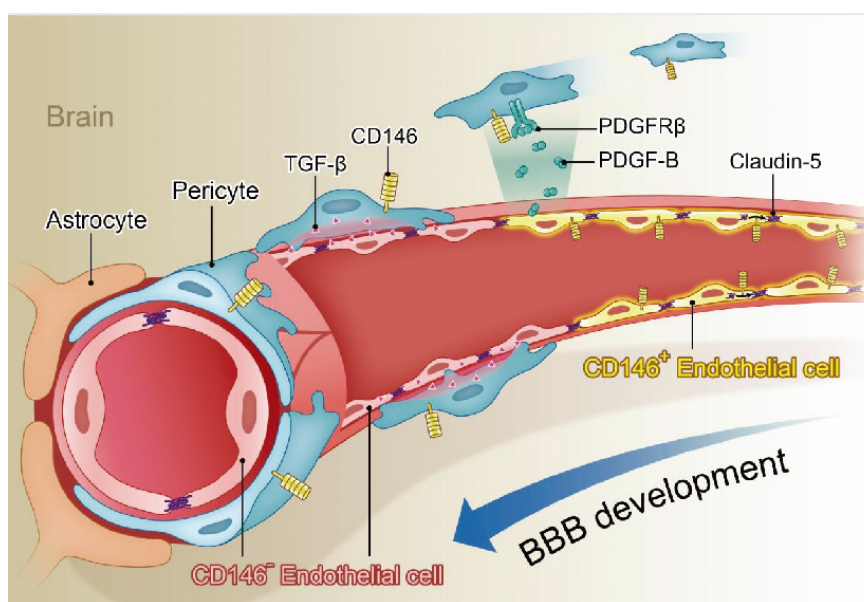


Figure CD146 coordinates brain endothelial cell-pericyte communication during the development of blood-brain barrier.