# Wnt/β-Catenin signaling controls development and maintenance of the blood-brain barrier

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## *Abstract*

The blood-brain barrier (BBB) is confined to the endothelium of brain capillaries and is indispensable for brain fluid homeostasis and neuronal function, but little is known about the molecular basis of its development and maintenance. Here we show that endothelial Wnt/β-catenin signaling is necessary for the induction and maintenance of BBB characteristics. Endothelial β-catenin signaling was observed during embryonic BBB development and its postnatal maturation. Endothelial specific stabilization of β-catenin *in vivo* enhanced barrier maturation, while endothelial specific inactivation of β-catenin caused significant down regulation of claudin-3 and -5 and BBB breakdown. Stabilization of β-catenin in primary brain ECs *in vitro* by N-terminal truncation or Wnt3a treatment, induced claudin-3 expression and BBB-type tight junction formation, as well as a BBB characteristic gene signature. Loss of β-catenin abrogated this effect. In ischemia-induced retinopathy, β-catenin stabilization prevented vascular hyper-permeability. These findings may open new therapeutic avenues for limiting the devastating effects of ischemia induced BBB breakdown.

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