Transient middle cerebral artery occlusion mice model

The intraluminal monofilament model of middle cerebral artery occlusion (MCAO) involves the insertion of a surgical filament into the external carotid artery and threading it forward into the internal carotid artery (ICA) until the tip occludes the origin of the MCA, resulting in a cessation of blood flow and subsequent brain infarction in the MCA territory [1]. The technique can be used to model permanent or transient occlusion [2]. If the suture is removed after a certain interval (30 min, 1 h, or 2 h), reperfusion is achieved (transient MCAO); if the filament is left in place (24 h) the procedure is suitable as a model of permanent MCAO. This technique does not require craniectomy, a neurosurgical procedure to remove a portion of skull, which may affect intracranial pressure and temperature [3]. It has become the most frequently used method to mimic permanent and transient focal cerebral ischemia in rats and mice

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In a study, Wu et al. used the transient middle cerebral artery occlusion mice model to investigate the role of circCCDC9 in stroke pathogenesis. They found that the expression of circCCDC9 was significantly decreased in the brains of tMCAO mice. The Evans blue and brain water content were significantly higher in the Pre-IR and Pre-IR+Vector mice, while these patterns were partially reversed by overexpression of circCCDC9. The nitrite content and eNOS expression were decreased in the Pre-IR and Pre-IR+Vector groups, which was restored by circCCDC9 overexpression. Overexpression of circCCDC9 also inhibited the expression of Caspase 3, Bax/Bcl-2 ratio and the expression of Notch1, NICD and Hes1 in tMCAO mice. Knockdown of circCCDC9 increased the expression of Caspase-3, Bax/Bcl-2 ratio, and the expression of Notch1, NICD, and Hes1. In summary, overexpression of circCCDC9 protected the blood-brain barrier and inhibited apoptosis by suppressing the Notch1 signaling pathway, while knockdown of circCCDC9 had the opposite effects. The findings showed that circCCDC9 is a potential novel therapeutic target for cerebrovascular protection in acute ischemic stroke [4].

Pericytes play essential roles in blood-brain barrier (BBB) integrity and dysfunction or degeneration of pericytes is implicated in a set of neurological disorders although the underlying mechanism remains largely unknown. However, the scarcity of material sources hinders the application of BBB models in vitro for pathophysiological studies. Additionally, whether pericytes can be used to treat neurological disorders remains to be elucidated. Here, we generate pericyte-like cells (PCs) from human pluripotent stem cells (hPSCs) through the intermediate stage of the cranial neural crest (CNC) and reveal that the cranial neural crest-derived pericyte-like cells (hPSC-CNC PCs) express typical pericyte markers including PDGFRβ, CD146, NG2, CD13, Caldesmon, and Vimentin, and display distinct contractile properties, vasculogenic potential and endothelial barrier function. More importantly, when transplanted into a murine model of transient middle cerebral artery occlusion (tMCAO) with BBB disruption, hPSC-CNC PCs efficiently promote neurological functional recovery in tMCAO mice by reconstructing the BBB integrity and preventing of neuronal apoptosis. Our results indicate that hPSC-CNC PCs may represent an ideal cell source for the treatment of BBB dysfunction-related disorders and help to model the human BBB in vitro for the study of the pathogenesis of such neurological diseases [5].

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