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Acute hypoxia enhances the proliferation of brain capillary endothelial cells via upregulation of Ca^{2+} -activated Cl^- channel TMEM16A.

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The blood-brain barrier (BBB) is a physical barrier that limits substance transfer to the brain and maintains the homeostasis of the central nervous system. The breakdown of BBB leads to hypoxic encephalopathy, cerebral infarction, and neurodegenerative diseases. Cerebral ischemia, such as cerebral infarction, causes cell damage from hypoxia. However, it remains unclear how hypoxia affects **brain capillary endothelial cell** (BCEC) functions. Therefore, we focused on the Ca^{2+} -activated Cl^- (Cl_{Ca}) channels, TMEM16A, in an immortalized bovine brain endothelial t-BBEC117 cells. Under hypoxic conditions, the expressions of mRNA and protein of TMEM16A channels in t-BBEC117 cells were upregulated and the activity of Cl_{Ca} currents were increased. Hypoxic stress enhanced cell proliferation and the enhancement was significantly suppressed by 100 μM niflumic acid or TMEM16A siRNA. The expression of HIF-1 α protein downregulated under acute hypoxic conditions. In conclusion, the expression level of TMEM16A is increased and the cell proliferation is enhanced due to hypoxic stress. These findings suggest that TMEM16A channels are involved in the BBB functions during cerebral ischemia.