Ca^{2+}-activated Cl^- channels are involved in the proliferation and migration of brain capillary endothelial cells.

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The blood-brain barrier (BBB) contributes to the maintenance of homeostasis in the brain. Brain capillary endothelial cells (BCECs) are a major component of the BBB and, thus a delicate balance between their proliferation and death is required. Although the activity of ion channels in BCECs is involved in BBB functions, the underlying mechanisms remain unclear. In this study, the molecular components of Ca^{2+}-activated Cl^- (Cl_{Ca}) channels and their physiological role were examined using the cell line derived from bovine BCECs, t-BBEC117. Expression analyses revealed that TMEM16A was predominantly expressed in t-BBEC117 cells. Whole-cell Cl^- currents were sensitive to Cl_{Ca} channel blockers, niflumic acid and $T16A_{inh}$-A01, and markedly reduced by the siRNA knockdown of TMEM16A. The blockade of Cl_{Ca} channel activity with Cl_{Ca} channel blockers or TMEM16A siRNA induced a significant membrane hyperpolarization. The treatment with TMEM16A siRNA caused an increase in cytosolic Ca^{2+} concentration ($[Ca^{2+}]_{cyt}$) at the resting level. $T16A_{inh}$-A01 inhibited cell viability in a dose-dependent manner, and Cl_{Ca} channel blockers and TMEM16A siRNA also blocked cell proliferation. In addition, Cl_{Ca} channel blockers and TMEM16A siRNA clearly attenuated cell migration. These results indicate that TMEM16A contributes to Cl_{Ca} channel conductance and its activity regulates the resting membrane potential of and $[Ca^{2+}]_{cyt}$ in BCECs, TMEM16A Cl_{Ca} channel are involved in the maintenance of BBB functions, including the proliferation and migration of BCECs.