No. 1122

Analysis of Ion Transporters in Cancer Stem Cells

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Summary

Recent evidences have demonstrated that most cancers are composed of a heterogeneous population of cells, and that a small minority of cancer cells have the capacity to proliferate extensively and form new tumors. These tumorigenic cells are defined as cancer stem cells (CSCs). This small population of CSCs, which generates non-cancer stem cell (non-CSC) cancer cells and relapses cancers, exists in the hypoxic niche. It is an urgent issue for cancer therapy to develop an agent attacking CSCs.

Cancer cells produce ATP through glycolysis even under a normoxic condition (Warburg's effect), and cancer cells generate excessive lactic acid in their cytoplasm. To maintain their metabolism and intracellular pH at normal level, cancer cells secrete H^+ to the outside of cells and acidify their extracellular environment. The previous reports indicate that CSCs exist in the hypoxic area of the tumor tissue.

We hypothesize that the regulation of ion transporter function in CSCs can regulate the survival of CSCs via controlling intracellular pH. In this study, we investigate the expression of ion transporters in CSCs compared to non-CSC cancer cells. We demonstrated that the transcripts of *Na^+/H^+ exchanger 2* (*NHE2*) mRNA are expressed more in the CSCs generated from glioblastoma cells compared to those in the parental cells, suggesting that NHE2 could be one of the biomarkers to maintain the CSCs in glioblastomas. We next clarify the functions of NHE2 in glioblastoma CSCs as well as those in CSCs generated from other kinds of cancers. In near future, we discover the novel therapeutic targets against CSCs.