Cancer heterogeneity and plasticity based on cancer stem cell biology

Author(s)

Hideyuki Saya

Authors affiliation(s)

Division of Gene Regulation, Institute for Advanced Medical Research, Keio University School of Medicine, Tokyo, Japan

Abstract

For several types of cancer, it is considered that a select subpopulation with stem-cell like properties gives rise to all other cells in the tumor mass. Cancer stem cells (CSCs) are therefore, by definition, a major contributor to tumor heterogeneity. However, CSCs themselves can display both intra- and intertumoral diversity and undergo phenotypic reprogramming in response to environmental cues.

The present study explores the metabolic characteristics of brain tumor stem cells, with a specific focus on their adaptation to nutrient and oxygen availability. We present our findings from an induced cancer stem cell model of glioma, based on orthotopic implantation of murine *Ink4a/Arf* -/- neural stem cells overexpressing HRasV12 into the brains of syngeneic mice. Our results show that brain tumors can contain stem cells with different metabolic characteristics and that this diversity can help survival in conditions of nutrient limitation. Moreover, in a subgroup of tumor stem cells, hypoxia can induce a reversible change of the main metabolic pathway.

In addition, we have recently found that differentiation property is a critical factor for tumorigenic activity of cancer stem cells. Based on our findings, we attempted to establish the transdifferentiation approach for treatment of cancer stem cells by using mouse osteosarcoma stem cell model.