【Grant-in-Aid for Specially Promoted Research】

Biological Sciences

Title of Project : Investigation for mechanisms underlying cell cycle regulation and metabolism in stem cells

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Research Project Number : 18H05215 Researcher Number : 80291508
Keyword : Stem cell, Cell cycle, Metabolism

【Purpose and Background of the Research】

The cell cycle in adult stem cells (ASCs) is arrested, and therefore regeneration of nerves and cardiomyocytes after injury is limited. Understanding the mechanism underlying cell cycle arrest will lead to the development of strategies for tissue regeneration. In contrast, embryonic stem cells (ESCs) proliferate rapidly. We have recently discovered that this difference is attributable to the expression of CDK inhibitor p57 and ubiquitin ligase component Skp2.

The aims of this study are 1) to decipher the mechanisms underlying transcriptional regulation of p57 and Skp2 genes in ASCs and ESCs, 2) to identify the molecular connection between cell cycle and metabolism by the next-generation proteomics, and 3) to develop new methods to reactivate cell cycle in ASCs for tissue regeneration after injury.

【Research Methods】

In this study, we will elucidate the mechanism underlying transcriptional regulation of p57 and Skp2 genes in stem cells. Transacting factors identified will be ablated in mice to examine the biological significance of these factors. Furthermore, the next-generation proteomics platform termed iMPAQT (Fig. 1) will be applied to delineate the entire landscape of metabolic pathways in ASCs and ESCs, which will lead to identification of molecules connecting cell cycle and metabolism.

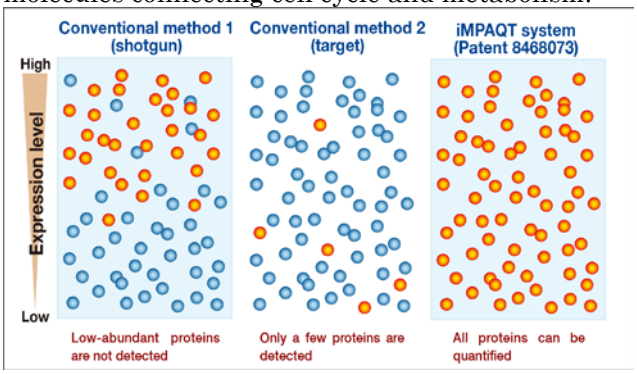

Fig. 1 iMPAQT system can measure all proteins

【Expected Research Achievements and Scientific Significance】

Elucidation of the mechanism for cell cycle arrest in ASCs and identification of key molecules are expected to promote development of new strategies for tissue regeneration after injury by cerebrovascular disorder, neurodegenerative diseases, ischemic heart disease, hepatic cirrhosis, and other diseases. In contrast, cell cycle activation by targeting p57 might promote proliferation of cancer stem cells (CSCs), which can sensitize them to anticancer drugs (Fig. 2).

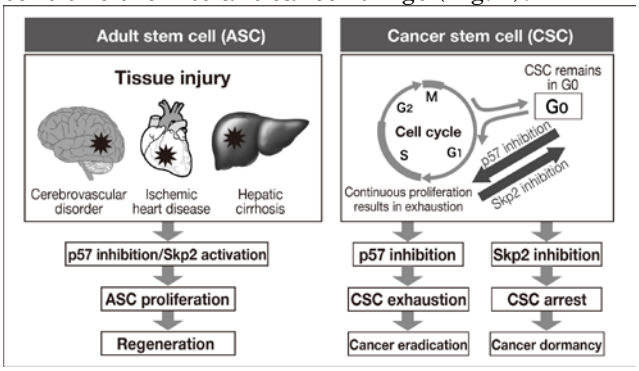

Fig. 2 Expected research achievements

【Publications Relevant to the Project】

・Matsumoto, M., et al., Nakayama, K., Nakayama, K.I.: A large-scale targeted proteomics assay resource based on an in vitro human proteome. ***Nature Methods*** 14: 251-258 (2017).
・Takeishi, S., et al., Nakayama, K.I.: Ablation of Fbxw7 eliminates leukemia-initiating cells by preventing quiescence. ***Cancer Cell*** 23: 347-361 (2013).

【Term of Project】 FY2018-2022

【Budget Allocation】 394,400 Thousand Yen

【Homepage Address and Other Contact Information】

http://www.bioreg.kyushu-u.ac.jp/saibou/index.html