Title of Research:

13_S01-01-3

Development of novel method to evaluate the indicibility of cancer stem cells from iPS cells in chemical compounds

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Summary of Research:

Cancer stem cells are typically characterized by continuous proliferation self-renewal as well as by differentiation potential, while stem cells are considered to differentiate into tissue specific phenotype of mature cells under the influence of microenvironment. Cancer stem cells can be traced back to the stem cells under specific influences of microenvironment, so called ‘cancerous niche’, which induces malignant tumors. We have very recently demonstrated the induction of cancer stem cells from mouse iPS cells culturing in the conditioned medium derived from cancer cells, although the details of the mechanisms of differentiation is not very well known as of yet.

In this study, we aim for the development of novel method to evaluate the risk of chemical compounds for the potential to induce cancer stem cells from iPS cells in vitro in a short period. Briefly, mouse iPS cells are suspended in the conditioned medium. The cells are further replenished with the growth medium with the compounds to be assessed.

We are currently observing the fluorescence intensity of GFP, which corresponds to the active Nanog promoter, and establishing the method for detecting the risk of compounds which accrete CSC conversion. The modification for usable method and high sensibility is under way. We are investigating the epigenetic analysis by RRBS (Reduced Representation Bisulfite Sequencing) and DMR (Differentially methylated regions) analysis.

Timeline:

March 2012-February 2016

Publications:

1. Prieto-Vila M, Yan T, Calle AS, Nair N, Hurley L, Kasai T, Kakuta H, Masuda J, Murakami H, Mizutani A, Seno M. iPSC-derived cancer stem cells provide a model of tumor vasculature. Am J Cancer Res. 2016 Sep 1;6(9):1906-1921.
2. Seno A, Kasai T, Ikeda M, Vaidyanath A, Masuda J, Mizutani A, Murakami H, Ishikawa T, Seno M. Characterization of Gene Expression Patterns among Artificially Developed Cancer Stem Cells Using Spherical Self-Organizing Map. Cancer Inform. 2016 Aug 16;15:163-178.
3. Calle AS, Nair N, Oo AK, Prieto-Vila M, Koga M, Khayrani AC, Hussein M, Hurley L, Vaidyanath A, Seno A, Iwasaki Y, Calle M, Kasai T, Seno M. A new PDAC mouse model originated from iPSCs-converted pancreatic cancer stem cells (CSCcm). Am J Cancer Res. 2016 Dec 1;6(12):2799-2815.

Conferences:

1. Takayuki Kudoh, Saki Sasada, Junko Masuda, Masashi Ikeda, Takuma Matsumoto, Anna Sanchez Calle, Neha Nair, Mami Asakura, Tomonari Kasai, Masaharu Seno. Exploration of Target Molecules and Related Pathways Affecting the Conversion of iPSCs into Cancer Stem Cells by Chemical Compounds. IIBMP 2016, (Sep 29-Oct 1,Tokyo)
2. Matumoto T, Sasada S, Ikeda M, Calle AS, Kasai T, Seno M. Elucidation of inducible mechanism of cancer stem cells with chemical compounds. MBSJ 2016, 39 th (Nov 30-Dec 2, Yokohama)