

Title of Research:

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Development of novel method to assess chemical compounds for the risk of cancer stem cell induction with iPS cells

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Summary of Research:

Cancer stem cells are considered to be significantly responsible for growth, metastasis, invasion and recurrence of all cancer. We propose the risk assessment of chemical compounds for their potential of induction of cancer stem cells, while those for carcinogenic activity have been evaluated by mutagenicity test, repeated dose toxicity study, estimating with statistical analysis, and so on.

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 at 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, of which expression is under the control of Nanog promoter, and the shape of colonies everyday for a period of 8 days. Based on these observations, 20 from 75 compounds assessed in the procedure were selected as prospectively positive candidates for converting mouse iPS cells to cancer stem cells. The modification of the method for efficient availability and high sensitivity is under way. We are planning further assessment for the mechanism through which the compounds are inducing the generation of cancer stem cells. The mechanism inducing cancer stem cells is needed to be studied in detail.

Timeline:

March 2012-February 2015

Topics:

Development of novel method to evaluate chemical compounds as the possible inducer of cancer stem cells using iPS cells. The 28th Annual Meeting of the Japanese Society for Alternatives to Animal Experiments. (Dec. 2015, Yokohama)

Publications:

Analysis of the mechanism in the induction of cancer stem cells by signaling inhibitors. BMB 2015 (Dec. 2015, Kobe)

Development of a simple risk assessment of chemical compounds in the induction of cancer stem cells *in vitro*. The 28th Annual Meeting of the Japanese Society for Alternatives to Animal Experiments. (Dec. 2015, Yokohama)