

**Title of Research:**

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**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 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 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, seeded at a density of 1,000 or 2,000 cells/well in 96-well plates and incubated for 24 hrs. 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 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 for usable method and high sensibility is under way. We plan to further assess the mechanism through which the compounds are inducing the cancer stem cells generation. The clarification of the mechanisms of cancer stem cells derivation is needed.

**Timeline:**

March 2014-February 2015

**Topics:**

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**Publications:**

Masaharu Seno. Development of novel method to evaluate chemical compounds as the possible inducer of cancer stem cells using mouse iPS cells. The 27th Annual Meeting of the Japanese Society for Alternatives to Animal Experiments. (Dec. 2014, Yokohama)