第 424 回　難研セミナー

[演題]

Induction of Pluripotency in Adult Somatic and Germline Stem Cells: iPS, piPS and gPS

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[講演要旨]

Mammalian development requires the specification of over 200 cell types from a single totipotent cell. Investigation of the regulatory networks that are responsible for pluripotency in embryo-derived stem cells is fundamental to understanding mammalian development and realizing therapeutic potential. Reprogramming of mouse and human somatic cells into pluripotent stem cells, designated as induced pluripotent stem (iPS) cells, was first described for fibroblasts and required the introduction of the virally-expressed transcription factor quartet Oct4, Sox2, c-Myc, and Klf4. I will present how we reduce the number of critical factors in adult somatic stem cells. Furthermore, I will present data showing that mouse pluripotent stem cells can be derived from established adult unipotent stem cell lines without exogenously introduced transcription factors. Germline stem cells (GSCs) are unipotent cells of the testis capable of self-renewing and of giving rise to sperm. GSCs express endogenous levels of Oct4 and Klf4 similar to that of embryonic stem cells (ESCs), while they express lower levels of Sox2. Genome-wide gene expression profiling demonstrates that GSCs are more closely related to ESCs than other cell types that had been previously reprogrammed, which puts germline-derived pluripotent stem (gPS) cells converted from GSCs even closer to ESCs than iPS cells. gPS cells were also derived after clonal expansion from single GSCs. Pluripotency of gPS cells was confirmed by in vitro and in vivo differentiation analyses, including germ cell contribution and germ cell transmission. We also showed that functional cardiomyocytes and neural cells could be derived by in vitro differentiation of gPS cells.

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