

【Grant-in-Aid for Specially Promoted Research】

Biological Sciences



Title of Project : Mechanism and Reconstitution In Vitro of Human Germ Cell Development

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Research Project Number : 17H06098 Researcher Number : 80373306

Research Area : Medicine, dentistry, and pharmacy

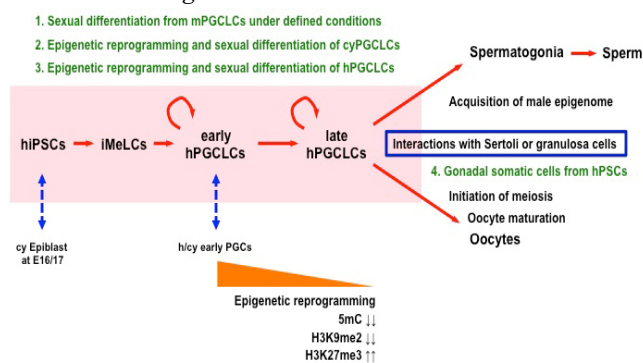
Keyword : Germ Cells, Developmental medicine, Genome, Regulation of gene expression, Evolution

【Purpose and Background of the Research】

The germ cell lineage ensures the creation of new individuals, perpetuating/diversifying the genetic and epigenetic information across generations. Using mouse embryonic stem cells (mESCs)/induced pluripotent stem cells (miPSCs)], we have succeeded in reconstituting the development of germ cells in culture both in males and females: mESCs/miPSCs are induced into primordial germ cell-like cells (mPGCLCs), which contribute to spermatogenesis and oogenesis and to fertile offspring. We have also shown that human iPSCs (hiPSCs) with a primed pluripotency can differentiate into incipient mesoderm-like cells (iMeLCs) that robustly generate human PGCLCs (hPGCLCs). By combining the research using mice, cynomolgus monkeys, and humans, this project aims to further develop the in vitro reconstitution of human germ cell development.

【Research Methods】

We will perform four lines of highly related research sub-projects: 1) Establishment of a strategy for differentiating mPGCLCs into pro-spermatogonia or primary oocytes under defined conditions, 2) Induction of epigenetic reprogramming and sexually dimorphic differentiation of cynomolgus monkey PGCLCs, 3) Induction of epigenetic reprogramming and sexually dimorphic differentiation of hPGCLCs, 4) Induction of gonadal somatic cells from hPSCs.



sub-projects will provide a strong foundation for human germ cell research (Figure 1).

【Expected Research Achievements and Scientific Significance】

The project is expected to generate robust foundations not only for extending our understanding of human germ cell development, but also for creating novel layers in human genetics and epigenetics; as such, its impact on the relevant fields is considered very high.

【Publications Relevant to the Project】

Nakamura, T., Okamoto, I., Sasaki, K., Yabuta, Y., Iwatani, C., Tsuchiya, H., Seita, Y., Nakamura, S., Yamamoto, T., and Saitou, M. (2016). A developmental coordinate of pluripotency among mice, monkeys, and humans, *Nature*, **537**, 57-62.

Sasaki, K., Yokobayashi, S., Nakamura, T., Okamoto, I., Yabuta, Y., Kurimoto, K., Ohta, H., Moritoki, Y., Iwatani, C., Tsuchiya, H., Nakamura, S., Sekiguchi, K., Sakuma, T., Yamamoto, T., Mori, T., Woltjen, K., Nakagawa, M., Yamamoto, T., Takahashi, K., Yamanaka, S., and Saitou, M. (2015). Robust In Vitro Induction of Human Germ Cell Fate from Pluripotent Stem Cells, *Cell Stem Cell*, **17**, 178-194.

【Term of Project】 FY2017-2021

【Budget Allocation】 435,300 Thousand Yen

【Homepage Address and Other Contact Information】

<http://anat.cell.med.kyoto-u.ac.jp/index.html>

The combined achievements from these four lines of