【Grant-in-Aid for Scientific Research (S)】

Broad Section I

Title of Project : Molecular Analysis of Spermatogonial Stem Cell Aging

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Keyword : spermatogenesis, stem cells, aging

【Purpose and Background of the Research】

Germline stem (GS) cells proliferate in vitro as clumps of spermatogonia, but they can reinitiate spermatogenesis following spermatogonial transplantation. Unlike embryonic stem (ES) cells, GS cells are resistant to reactive oxygen species (ROS) and have a lower mutation frequency. Moreover, although GS cells express telomerase, their telomeres become shorter during two years of consecutive culture. These results suggest that GS cells have anti-aging machinery, which is different from those found in ES cells or somatic cells. We will analyze 1) the mechanism underlying telomere regulation in GS cells, 2) DNA repair or ROS resistance and 3) identify aging-inducing signals from somatic cells.

【Research Methods】

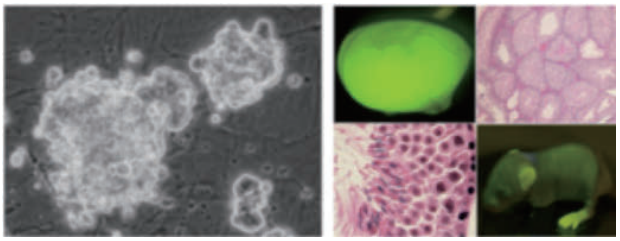

Figure 1 GS cells can differentiate into sperm

1) Analysis of telomere maintenance in GS cells
We will visualize the telomeres in GS cells and analyze the spatiotemporal distribution of telomeres. We will identify molecules involved in telomere maintenance in GS cells.
2) Analysis of DNA repair machinery and ROS level regulation in GS cells.
Cells in the germline lineage have a lower mutation frequency compared with somatic cells. However molecules involved in genome quality control have not been identified. We will analyze the impact of aging on mutation frequency and identify molecules involved in DNA repair.
3) Identification of aging inducing signals from somatic cells
Because germ cells do not show circadian rhythms. it is possible that testicular somatic cells induces germ cell aging. To identify these molecules, we will analyze gene expression patterns in aged animals from several species and identify genes responsible for testis aging.

【Expected Research Achievements and Scientific Significance】

Identification of telomere regulatory factors will bring new insight into telomere biology. Moreover, understanding the mechanism underlying the low mutation frequency in GS cells will open up a new field of germline genome quality control. The identification of aging-inducing signals from somatic cells will promote development of new strategies of male infertility treatment.

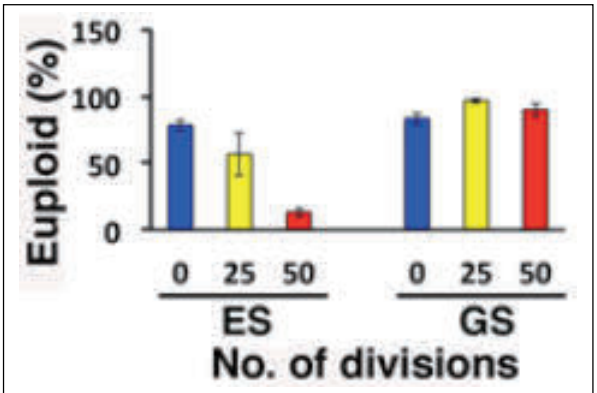

Figure 2 Karyotype stability of GS cells

【Publications Relevant to the Project】

・ Kanatsu-Shinohara, M.. et al. Nonrandom germline transmission of mouse spermatogonial stem cells. Dev. Cell 2016;38: 248-261.

【Term of Project】 FY2018-2022

【Budget Allocation】 148,800 Thousand Yen

【Homepage Address and Other Contact Information】

http://www2.mfour.med.kyoto-u.ac.jp/~molgen/research_summary.html