

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

## Biological Sciences (Biology)



**Title of Project : Molecular mechanism underlying sexual development of male germ cells**

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Research Area : Developmental Biology

Keyword : Nanos, RNA, meiosis, stem cell, spermatogenesis

### 【Purpose and Background of the Research】

Germ cells are only cells that have ability to transmit their genetic information into the next generation. In mammal, germ cells are set aside from somatic cells during early embryonic stage and establish their unique system to maintain their identity. During embryonic stage, germ cells sexually differentiate into eggs or sperms according to sex of individual organisms. We have been investigating functions of RNA binding proteins, Nanos2 and Nanos3 and found that Nanos2 is involved in the sexual differentiation of male germ cells during embryogenesis. In addition, Nanos2 has crucial function in the maintenance of spermatogonial stem cells after birth. We are interested in the mechanisms how these germ cells establish and maintain their unique characteristics by the aspect of both genetic and epigenetic regulation. The specific aims of our studies are 1) To understand genetic cascade leading to the sexual differentiation of male germ cells during embryogenesis and 2) To understand mechanisms to make sure the cyclic continuation of spermatogenesis throughout life. The elucidating mechanisms of germ cell differentiation provides not only bases of germ cell development but also valuable information for the understanding of stem cell system.

### 【Research Methods】

We are planning to conduct following four experiments to understand molecular mechanism of sexual differentiation of germ cells and the maintenance mechanism of spermatogonial stem cells during spermatogenesis.

#### Research plan 1) Regulation of sexual differentiation of germ cells

Nanos2 is specifically expressed in male germ cells and plays an essential role in their sexual differentiation. Nanos2 induce male program by suppressing female genetic cascade. We analyze both upstream and downstream events of Nanos2 action to elucidate the genetic cascade toward sexual development of germ cells.

#### Research plan 2) The maintenance mechanism of spermatogonial stem cells

Nanos2 is also expressed in spermatogonial stem cells during spermatogenesis after birth. We like to elucidate the mechanism how Nanos2 maintains spermatogonial stem cell pools.

#### Research plan 3) Regulation of cyclic gene expression of Sertoli cells in spermatogenesis

Sertoli cells play important roles to support cyclic spermatogenic process. Sertoli cells also have cyclic gene expression pattern depending on the spermatogenic stage. We like to identify the genes involved in the cyclic state of Sertoli cells and analyze possible functions of these genes during spermatogenesis.

#### Research plan 4) Molecular mechanism of Nanos2 action as an RNA-binding protein

By immunoprecipitation using anti-Nanos2 antibody, we like to identify the interacting proteins of Nanos2 to understand molecular mechanism of the Nanos2 action. We also try to identify target RNAs exist in the Nanos2 protein complex, which is essentially important to clarify Nanos2 function.

### 【Expected Research Achievements and Scientific Significance】

Accurate and detailed understanding of germ cell differentiation pathway would provide valuable bases for establishing a method to deliver functional germ cells from ES and iPS cells in vitro culture system.

### 【Publications Relevant to the Project】

- Suzuki A, Saga Y. Nanos2 suppresses meiosis and promotes male germ cell differentiation. *Genes & Develop.* 22, 430-435, 200
- Tsuda, T. Sasaoka, Y. Kiso, M. Abe, K. Haraguchi, S. Kobayashi, S. and Saga, Y. Conserved role of nanos proteins in germ cell development. *Science* 301:1239-1241, 2003.

【Term of Project】 FY2009-2013

【Budget Allocation】 160,000 Thousand Yen

### 【Homepage Address and Other Contact Information】

<http://www.nig.ac.jp/labs/MamDev/home-j.html>