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

Biological Sciences (Biology)

Title of Project： Mechanism of sex differentiation of germ cells

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Research Project Number：17H06166　Researcher Number：50221271
Research Area：　Developmental Biology
Keyword：　Germ cells

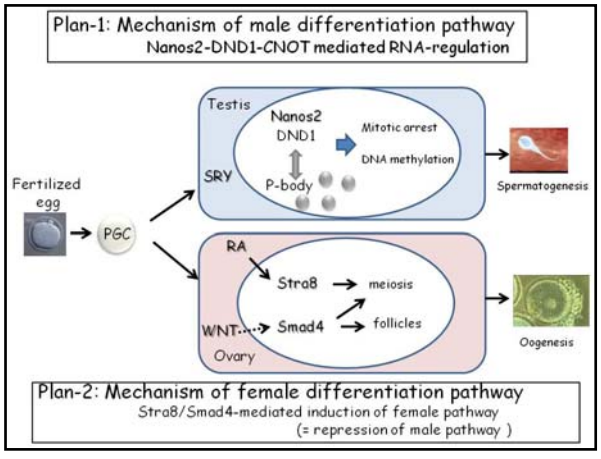
【Purpose and Background of the Research】

The differential programming of sperm and eggs in gonads is a fundamental topic in reproductive biology. Although the sexual fate of germ cells is believed to be determined by signaling factors from sexually differentiated somatic cells in fetal gonads, the molecular mechanism that determines germ cell fate is poorly understood.

We aim to elucidate the molecular mechanism of sex differentiation of germ cells. With regard to male differentiation pathway, we will clarify the mechanism how Nanos2-DND1-CNOT recognizes and suppresses target RNAs. We try to reconstruct the germ cell system using somatic cells. Regarding the feminization mechanism, we clarify the targets of Smad4 and Stra8 which are determinants for feminization, and clarify the molecular mechanism of feminization mediated by these genes by performing in vivo function analysis.

【Research Methods】

Research plan 1: Analysis of RNA regulatory mechanism involved in male pathway. We focus on Nanos2-DND1-CNOT1 complex localized in the P-body, the center of RNA metabolism. I will perform the following experiment. 1) Identify the necessity of P-body for Nanos2 function.
2) Identify factors required for reconstruct Nanos 2-DND1-CNOT function even in the somatic cells to clarify target RNA recognition mechanism.



Research plan 2: We aim to elucidate feminization mechanism of germ cells by focusing two factors Smad4 and Stra8. We will identify targets of Smad4 and conduct function assay to ask whether the deficiency induces sexual fate change from female to male in the absence of Stra8.

【Expected Research Achievements and Scientific Significance】

Nanos2-mediated germ cell specific RNA machinery is required for masculinization of mammalian germ cells. If you can elucidate the RNA regulatory mechanism and reproduce the RNA machinery in somatic cells, it will be useful to identify and verify the target RNAs. It may help to make germ cell from somatic cells via RNA regulation. It also contributes to the innovation of RNA manipulation technology.

Clarification of the feminization mechanism may lead to the understanding of sex determination of germ cells. We recently showed that germ cells could take male pathway even in the ovary if two genes were knocked out. This suggests that induction of feminization is essential for sex determination, and elucidation of its molecular mechanism greatly contribute to understanding of germ cell sex determination mechanism.

【Publications Relevant to the Project】

・Suzuki A, Niimi Y, Shinmyozu K, Zhou Z, Kiso M, Saga Y. Dead end1 is an essential partner of NANOS2 for selective binding of target RNAs in male germ cell development. ***EMBO Rep.*** 17(1):37-46 (2016).
・Wu Q, Fukuda K, Kato Y, Zhou Z, Deng C-X, Saga Y. Sexual Fate Change of XX Germ Cells Caused by the Deletion of SMAD4 and STRA8 Independent of Somatic Sex Reprogramming. ***PLOS Biol.*** 14(9):e1002553 (2016)

【Term of Project】FY2017-2021

【Budget Allocation】　156,200 Thousand Yen

【Homepage Address and Other Contact Information】

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