



**Title of Project: Ensuring integrity in gametogenesis**

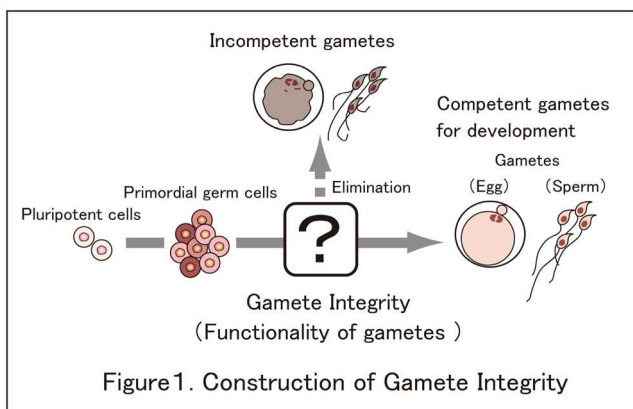
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**【Purpose of the Research Project】**

Gametes are highly specialized cells for the creation of new individuals. To finally become functional gametes, the germ cell lineage including the precursors undergoes a unique series of differentiation processes. Quality of germ cell lineage closely relate to viability of embryos and individuals. The aim of this project is to understand how the functionality of gametes, named “gamete integrity”, is established during gametogenesis *in vivo*. Based on this knowledge, the project also aims to reconstitute the process *in vitro*.

Recently, the research members in this project succeeded in production of functional gametes *in vitro* (*in vitro* gametogenesis) by culturing reproductive organs or inducing differentiation of pluripotent stem cells. However, the developmental potential of the gametes from *in vitro* gametogenesis was extremely limited, suggesting that gamete integrity was not properly reconstituted in culture. Therefore, this project will try to understand the molecular mechanisms and biological processes for construction of gamete integrity *in vivo*. The project includes the technological development of a non-invasive system to evaluate gametes. Based on this knowledge, we try to establish *in vitro* gametogenesis that can firmly and stably reconstitute gamete integrity.



**【Content of the Research Project】**

This project is composed of three subjects (A01-A03) to achieve the aim. In A01, we focus on the development of the culture system to reconstitute gamete integrity. In A02, we plan to identify the molecules regulating gamete

integrity, which includes development of the non-invasive system. In A03, we want to understand the biological process needed for selection of competent gametes (and eliminate incompetent gametes).

A01 will optimize culture conditions, develop novel culture devices, purify proteins and substances required for gametogenesis, and produce supporting somatic cells from pluripotent stem cells. A02 will identify genes regulating gamete integrity by comparison between competent and incompetent gametes, which are sorted by the non-invasive system. A03 will identify the heterogeneity of the germ cell population, analyze gene expression at the single cell level, and understand the biological significance of the heterogeneity.

By combining all the knowledge, we will gain deep insights into gamete integrity and reconstitute it *in vitro*.

**【Expected Research Achievements and Scientific Significance】**

We expect to identify molecules (genes, proteins and other substances) that have critical roles on gametogenesis. Understanding of the biological process for gamete selection will provide important information for the field of biology, in particular reproductive biology, developmental biology and evolutionary biology. The establishment of *in vitro* gametogenesis that efficiently produces competent gametes will have many experimental applications. Finally, this project will provide scientific evidence to apply to human *in vitro* gametogenesis.

**【Key Words】**

Gamete integrity, Developmental potential, *in vitro* gametogenesis, non-invasive system, heterogeneity

**【Term of Project】** FY2018-2022

**【Budget Allocation】** 1,181,700 Thousand Yen

**【Homepage Address and Other Contact Information】**

<https://www.gamete-integrity.com>