【Grant-in-Aid for Transformative Research Areas（A）】

Dynamic reproductive lifespan: Life-long changes and fluctuations in germ cell function and risk for next generation（Reproductive lifespan）

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Research Area Information	Number of Research Area : 23A304 Project Period (FY) : 2023-2027 Keywords : Germ cell, Gamete, Genome inheritance, Reproduction	

Purpose and Background of the Research

●Outline of the Research

This Research Area will transform the classical concept of reproductive lifespan into a new concept, "dynamic reproductive lifespan". In this new concept, germ cell functionality and safety for the next generation dynamically change and fluctuate throughout the lifespan, mediating the acquisition, maintenance, adaptation, and decline of reproductive function. To elucidate the changes and fluctuations exhibited by germ cells, we will develop innovative techniques for quantitative analysis of the long-term dynamics of germ cells. By bringing together a wide range of scientists in the fields of germ cell research and the life sciences, we will transform the field of germ cell research into one with a scientific scope that encompasses the entire lifespan, from development to adulthood and aging, and provide a foundation for manipulating the reproductive lifespan.

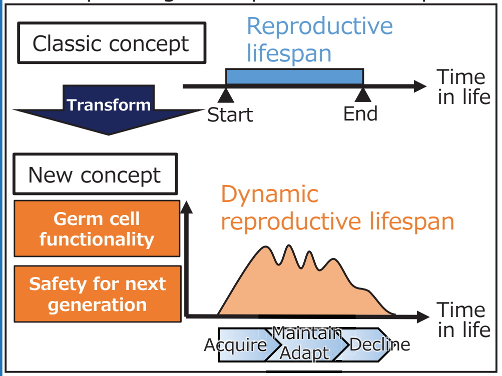

Figure 1. Dynamic reproductive lifespan

●Background

Reproductive lifespan has been classically viewed as a period during which an individual has the ability to produce the next generation (reproductive capacity). This view is based on the qualitative idea that reproductive capacity is switched on and off in a binary manner at physiological turning points (Figure 1). However, as recent technological innovations have quantitatively revealed the functions and properties of germ cells at the cellular level, it has become clear that they exhibit life-course-dependent changes and fluctuations in reproductive capacity and risk to the next generation. However, such changes and fluctuations have not been systematically studied, and the underlying mechanisms are not clear. It is likely that male and female germ cells have different strategies for maintaining their ability to pass on their genetic information to the next generation throughout the adult stage, which is of our particular interest (Figure 2).

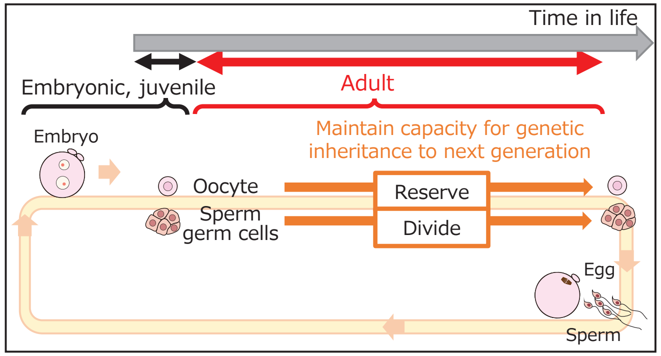

Figure 2 Germ-cell-mediated reproductive cycle including the adult stage

●Aim

To define the dynamic reproductive lifespan, we set the horizontal axis as time in lifespan, the first vertical axis as germ cell functionality, and the second vertical axis as safety for the next generation (Figure 1). To analyze germ cell functionality and safety for the next generation, it is important to have new technologies such as live imaging, single-cell omics, and culture techniques that provide spatiotemporal information at the cellular level in vitro and in vivo. Therefore, we are bringing together scientists with new technologies from a wide range of life science fields and those in the field of germ cell research. Using these technologies, we will analyze life-dependent changes and fluctuations in the functions and properties of germ cells throughout the lifespan, and elucidate the underlying mechanisms.

Expected Research Achievements

●Reproductive lifespan by germ cell functionality

We will reveal the acquisition, maintenance, adaptation, and decline of germ cell functionality throughout the lifespan (Figure 3). The germ cell functionality that defines the dynamic reproductive lifespan is likely to consist of a number of elements. Critical elements include chromosome functions and developmental quiescence of oocytes and intracellular metabolic regulation of the reproductive organs. We will quantitatively analyze the changes and fluctuations of each element throughout across the lifespan and elucidate the underlying mechanisms.

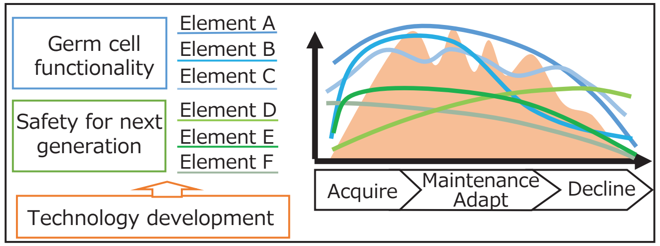

Figure 3: Quantify and elucidate changes and fluctuations in each element of the dynamic reproductive lifespan.

●Reproductive lifespan for next generation

Preventing the transmission of risky genetic information to the next generation ("Safety for next generation") is critical for reproductive cycle (Figure 3). Important elements include the genome integrity and clonal dynamics of sperm stem cells and the prevention of mitochondrial mutation transmission. We will quantitatively analyze the changes and fluctuations in each of these elements across the lifespan and elucidate their mechanisms.

●Technology development for reproductive lifespan research

Quantitative measurement of germ cells and their changes at the cellular level in adult reproductive organs is technically challenging. Therefore, we will develop technologies such as in vitro germ cell development, long-term in vivo imaging, genome analysis, cell clonal analysis, spatial omics, metabolomics, and molecular turnover measurement. In addition, we will develop technologies to manipulate the reproductive lifespan, including advanced reproductive engineering technologies.

●Establishment of a germ cell research field that brings together a wide range of life scientists

Germ cell research has been strongly driven by developmental biology approaches. With this strength as a core, we will establish a new research field that focuses on germ cells throughout the entire life span, including not only developmental stages but also adult and aging stages, by incorporating scientists with new approaches and technologies that are emerging from a wide range of fields in the life sciences.

Homepage Address, etc.	https://reproductivelifespan.jp/en/