Biological Sciences

Title of Project：Program of totipotency: From decoding to designing

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【Purpose of the Research Project】

The genomes of terminally differentiated germ cells, spermatozoa and oocytes, acquire totipotency following genomic reprogramming at fertilization. This genomic reprogramming is the most large-scale one among those during the germline cycle. Totipotency is the most undifferentiated genomic status and the ability to contribute all the tissues and cells that constitute the body of newborns as well as the products during development such as placentas (**Fig. 1**). We aim to understand the mechanisms that ensure totipotency and to regulate and construct totipotency. Through these activities, in combination with cutting-edge analytical tools and unique reproductive engineering technologies, we will establish a new research core for totipotency study.

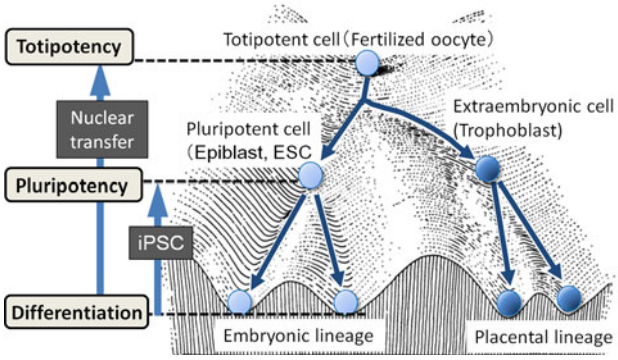

Fig. 1. Totipotency of mammalian development. The totipotent cell (fertilized oocyte) can contribute to both the embryonic and extraembryonic (placental) lineages. The pluripotent cells such as ESCs and iPSCs are at the early differentiating state, being exclusively destined to the embryonic lineage.

【Content of the Research Project】

Although more than 100 years have passed since the concept of "totipotency" was proposed, its underlying molecular mechanisms are unclear. Totipotency can be considered to be a feature in which multi-scale and multi-factor relationships are complicatedly involved. Therefore, for understanding the nature of totipotency, it may be the best way to identify the conditions or factors that are indispensable for the maintenance of totipotency. Our project consists of two research items; i.e., A01 "Decoding of the totipotent program" and A02 "Regulation and construction of totipotency" (**Fig. 2**). A01 aims to identify the basic mechanisms of totipotency including the genomic status, gene expressions, maternal factors, embryonic factors, and nuclear structure, which ensure the perfect developmental ability of fertilized oocytes. The time-dependent changes of these factors are also analyzed. A02 aims to verify the achievements of A01 by regulating or reconstructing the totipotent status or totipotent cells in vitro. To this end, we will maximize synergistic effects of our expertise through active intra-project collaborations.

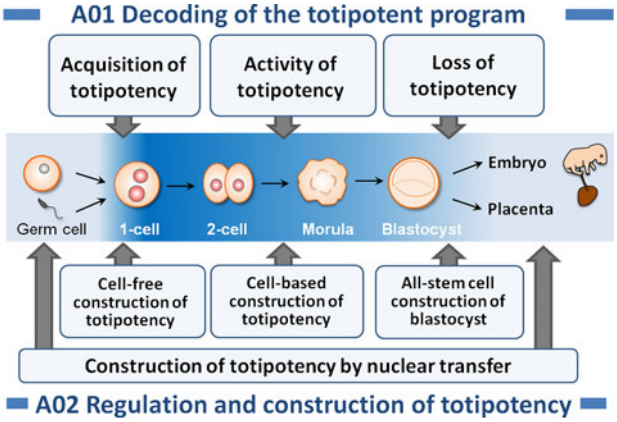

Fig. 2. Research subjects of our project. It consists of 2 items (A01 and A02), which are each divided into three subjects according to the developmental time course.

【Expected Research Achievements and Scientific Significance】

As there may be some common mechanisms exist in the totipotent state of different species, our achievements would contribute, at least partially, to better understanding of the principal molecular basis of totipotency. Moreover, through regulation of totipotency, a wide variety of applications could become practical; e.g., development of new reproductive engineering technologies will promote stock breeding, pharmaceutical industry, generation of primate models for human diseases, and conservation of endangered species. Our research achievements would also contribute to development of more effective assisted reproductive technology in humans.

【Key Words】

Totipotency: The genomic status of a cell that can contribute to the entire tissue/cells of newborns including appendix products such as the placenta.

【Term of Project】

FY2019-2023

【Budget Allocation】

1,139,100 Thousand Yen

【Homepage Address and Other Contact Information】

https://totipotency.biken.osaka-u.ac.jp