

Biological Sciences



Title of Project : Mechanisms underlying replication of non-genomic codes that mediate plasticity and robustness for cellular inheritance

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【Purpose of the Research Project】

Multicellular organisms consists of cells with diverse phenotypes even though their genomic information is essentially the same. The diversity of these cells is defined by non-genomic codes. Non-genomic information is coded by multi-layered mechanisms, such as DNA and histone modifications, non-coding RNA, higher ordered chromatin structures and transcription factor networks as well as the interconnections of these layers. Recent advances in understanding DNA replication and repair systems have made great contributions to the progression of many biological fields. In contrast, mechanisms underlying replication of non-genomic codes during cellular replication are largely unknown. In this research project, we focus on the elucidation of the mechanisms underlying replication of non-genomic codes such as DNA methylation and histone modifications during mitotic and meiotic cell cycle. We are also interested in the interconnections of multi-layered non-genomic mechanisms and biological processes regulated by these mechanisms such as cellular differentiation (Fig. 1).

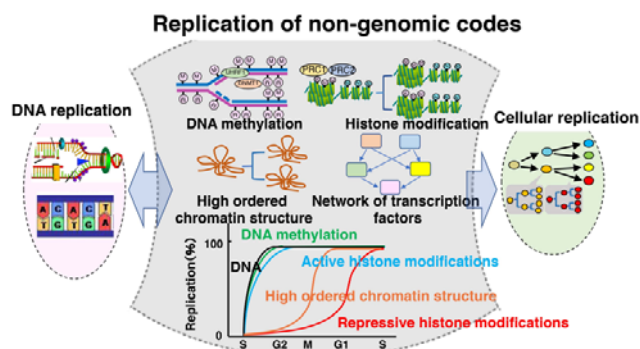


Fig. 1 Scheme of cellular replication regulated by DNA replication and replication of non-genomic codes

【Content of the Research Project】

In order to understand the mechanisms underlying replication of non-genomic codes comprehensively and systematically, the project focuses on two subjects (A01: Basic molecular mechanisms underlying replication of non-genomic codes and A02: Regulatory mechanisms of cellular function by replication of non-genomic codes). The main theme of A01 is to understand the replication mechanisms of non-genomic codes, such as DNA methylation, histone modifications, non-coding RNA, high ordered chromatin structures, and transcriptional networks. The structural analyses of the replication machineries are involved in this subject. The development of highly

sensitive analytical methods, such as single cell analysis and single molecule analysis of non-genomic codes, are also involved.

In A02 subject, we aim to uncover the molecular basis of how replication mechanisms of non-genomic codes regulate plasticity and robustness of differentiated cells in multicellular organisms. These mechanisms should include stem cell renewal, maintenance of stemness, and cellular differentiation during symmetric and asymmetric divisions. By the use of mathematical and simulation analyses, the development of the methods to be able to consolidate big data from multiple layers into a single data store is also involved in this subject.

【Expected Research Achievements and Scientific Significance】

The diversity of cells in multicellular organisms is defined by non-genomic codes. The differentiated cells possess their specific non-genomic code patterns to maintain their specific cellular function. Therefore, non-genomic codes as well as DNA sequence have to be precisely replicated during proliferation of the differentiated cells. A better understanding of the mechanisms underlying replication of non-genomic codes will provide a cue to address the molecular basis of how cells regulate plasticity and robustness in multicellular organisms. Thus, we are confident that our findings will make significant contributions to advancing a variety of biological fields such as developmental biology, regenerative medicine, oncology, and gerontology.

【Key Words】

Non-genomic information: The factors regulating gene activities regardless of DNA sequences.

【Term of Project】 FY2019-2023

【Budget Allocation】 1,168,000 Thousand Yen

【Homepage Address and Other Contact Information】

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