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

Section II

Title of Project： Elucidation of the mechanism for dimensional response genome across species regulated by nucleic acid structures

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【Purpose of the Research Project】

Nucleic acids are the genome component considered to be responsible for genetic information. In contrast, proteins are considered to regulate and control gene expression. In recent years, several reports have described that non-canonical structures (e.g., triplex and G-quadruplex) in human cells regulate gene expression. These findings could overturn the preconceived notion of nucleic acids and proteins. The formation of nucleic acid structures is greatly influenced by the surrounding environment. Therefore, it is possible that nucleic acids sense the surrounding environment and change their structure in a multidimensional manner to proactively regulate gene expression. However, all organisms have genomes, and from a physicochemical point of view, the mechanism for ordered structure formation of nucleic acids should be species-independent. Furthermore, taking into account the characteristics of each organism, organisms other than humans, such as bacteria and plants, can change the structure of nucleic acids more easily than humans because the intracellular molecular environment changes greatly depending on the growth environment, and may be able to control biological reactions more efficiently through nucleic acid structures. No studies have analyzed the similarities and differences in gene expression mechanisms by non-canonical structures beyond the framework of biological species.

【Content of the Research Project】

In this research project, we will clarify the molecular mechanism of the "dimensional response genome" and its physiological significance. To this end, we will integrate research approaches from other fields and promote the following research in a stepwise manner (Figure 1).

[1] Using analytical chemistry and information science approaches, we will analyze the information from various organisms whose whole genome sequences have been deciphered and which can form the non-canonical structure of nucleic acids. The "structural information" of nucleic acids that show multiple responses will be determined.

[2] Using physical chemistry, biochemistry, and inorganic materials science approaches, we will understand the "molecular mechanism" of nucleic acid structure-dependent dimensional responses based on direct observation of non-canonical structures in living cells and physicochemical parameters of nucleic acid structure changes in response to environmental changes in cellular model systems.

[3] Using molecular biology and phytochemistry approaches, we will analyze gene expression changes in response to non-canonical structures and correlate them with phenotypic changes in cells and individuals to understand the "regulatory function" of biological phenomena by multiple responses.

The findings will be integrated to create the Dimension Responsive Genome Bank (DiR-GB) — the first data bank of nucleic acid structures that show dimensional responses in various species.

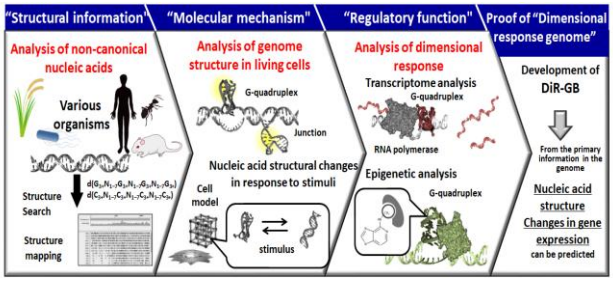

Figure 1. Research plan for elucidating the mechanism of "dimensional responsive genomics," in which nucleic acid structures regulate cellular functions in dimensional response.

【Expected Research Achievements and Scientific Significance】

The unified expression regulation mechanisms of all genes will be elucidated. Furthermore, by utilizing the constructed DiR-GB genome bank for multiple responses, we will be able to predict "dimensional responses" by nucleic acid structures based on genome sequences. The information on the regulatory mechanisms of genes will make it possible to control the biological phenomena of targeted genes in humans as well as in viruses and plants, using chemical approaches. This will have value in a wide range of fields, including medical engineering, agriculture, and materials chemistry.

【Key Words】

Non-canonical structures: A general term for structures other than the canonical structure (duplex) of nucleic acids, including triplex, quadruplex, cruciform structure, and others. Nucleic acids change their structure in response to changes in the surrounding environment, even if the base sequences are identical.

Dimensional response: A mechanism (which this research aims to elucidate) for regulating gene expression that depends on nucleic acid structures that change in a multidimensional manner in response to the environment

【Project Term: FY2021-2023

【Budget Allocation】105,000 Thousand Yen

【Homepage Address and Other Contact Information】

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