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

Section Ⅲ

Title of Project： Genome modality: understanding physical properties of the genome

NISHIYAMA Tomoko
(Nagoya University, Graduate School of Science, Associate Professor)

Number of Research Area：20A305 Researcher Number：90615535

【Purpose of the Research Project】

Since the discovery of DNA double helix, genome study has been expanded and our knowledge of the genome was enormously progressed; Meanwhile whole genome has been sequenced in many model organisms and nowadays genome editing technology is widely and rapidly spread. The past genome researches have mainly forced on its informational aspects, such as replication, repair, recombination, and division of the genomic information and further highlighted epigenetic regulations to explain genetic phenomena. On the other hand, physical properties of the DNA, such as stiffness, torsion, supercoiling and so on, have been much less understood, although it is the most important properties directly affecting the genome structure. In this project, we will focus on physical properties of genome/DNA to understand how the genome builds its structure and how it functions. We define "genome modality" as a multi-dimensional mode to organize the structure and function of the genome. We will uncover bona fide figure of the genome from the perspective of genome modality. To this end, we utilize methods of biochemistry, cell biology, genome science, and polymer physics and create new field to study "genome modality."

【Content of the Research Project】

Objects of this project range from nano-scale DNA/nucleosome structures to organisms (Figure 1). Regulators of genome modality would include nucleoplasmic/cytoplasmic environments, physical properties of proteins, and physicochemical reactions such as liquid-liquid phase separation, as well as physical properties of DNA. How do they regulate genome modality in each scale and define chromosome- or chromatin-dynamics, and how does dysfunction of the factors result in disorganization of cellular functions and causes diseases? We will address these questions from different approaches including theoretical physics, measurements of biophysical properties, reconstitutions, and genomics as well.

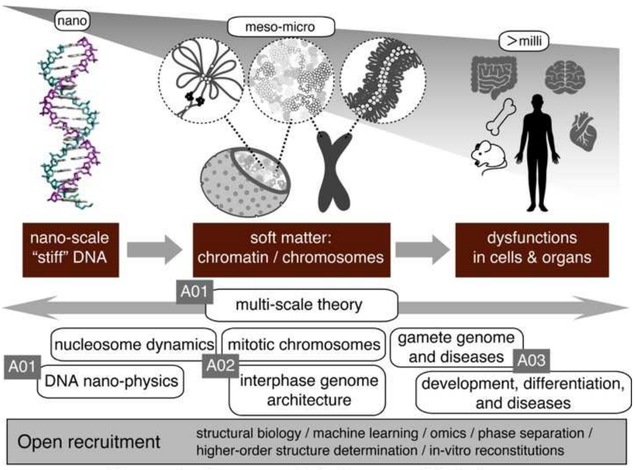

Figure 1 Framework in Genome Modality

In the framework, there are 3 major categories as follows. A01: Physics of genome modality, where we uncover nano-scale genome structure and properties, and also build multi-scale theoretical model of the genome. A02: Meso-scale genome modality, where we focus on meso-scale structure including nucleosome, DNA loops, and chromatin fibers/domains, and figure out how these structures are formed. A03: Disorders of genome modality, where we address the questions how dysfunction of genome modality-regulating factors causes diseases.

【Expected Research Achievements and Scientific Significance】

First, we will discover novel genome organizers, which can regulate physical properties of DNA. This will be possible only when both genome biology and polymer physics fields work together collaboratively in our consortium, and will establish a novel concept of genome organization based on physical properties of DNA. Second, we will create "Genome Modality Suite", an integrative platform, where all new information coming from this project are combined, so that nano-scale disorders of the genome can be linked to whole-genome behavior and resulting diseases. This platform will be opened for public as a useful tool in the future.

【Key Words】

Genome modality: A multi-dimensional mode to organize/regulate the structure and function of the genome.

【Term of Project】 FY2020-2024

【Budget Allocation】 1,140,400 Thousand Yen

【Homepage Address and Other Contact Information】

https://www.genome-modality.com
nishiyama@bio.nagoya-u.ac.jp