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

Section III

Title of Project： Elucidation of the mechanisms of transcriptional unity by understanding spatiotemporal multifactorial interactions

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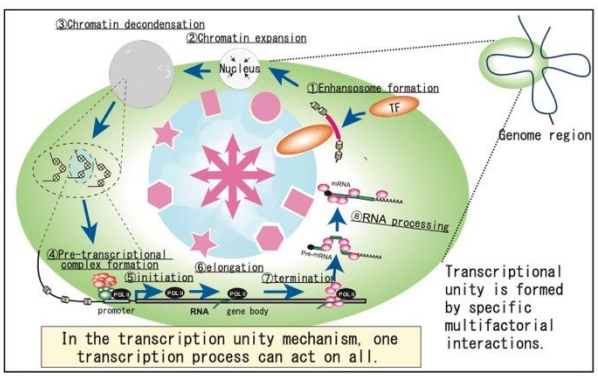
【Purpose of the Research Project】

Our previous studies have shown that not only genomic DNA, including transcriptional regulatory regions such as enhancers and gene regions, but also RNAs such as nascent RNAs and non-coding RNAs, which are transcription products, form multifactorial interactions by interacting with proteins and are thought to be involved in the transcriptional unity mechanism. In addition, RNAs such as nascent RNAs and non-coding RNAs are thought to be involved in the transcriptional unity mechanism by forming multifactorial interactions through interactions with proteins (see Fig. 1). In order to elucidate the transcriptional unity mechanism by such spatiotemporal multifactorial interactions, it is necessary to understand not only the interactions based on the biochemical analysis of protein complexes, which has been important in conventional transcriptional research, but also the complex interactions formed among multifactorial factors including proteins, genomic DNA, new RNAs, and non-coding RNAs. In addition, it is necessary to elucidate the complex and diverse interactions among multiple factors, including proteins, genomic DNA, new RNAs and non-coding RNAs, in a spatio-temporal manner. In this study, we will establish a comprehensive method for the identification of multifactorial interactions by in situ biotinylation in order to capture multifactorial interactions spatially and comprehensively. Furthermore, in order to quantify the spatiotemporally and comprehensively identified multifactorial binding, we will establish a spatial quantification method of multifactorial interactions using antibody barcoding. This research aims to elucidate the transcriptional unity mechanism of multifactorial interactions from the structural to the molecular, cellular, tissue, and individual levels, and to elucidate the disease mechanism caused by its disruption.

Fig 1. Multifactor Interactions to Build



【Content of the Research Project】

In this research, we will promote research through collaboration within the field as shown below.
In research group A01, we will establish a comprehensive identification method for multifactor interactions by in situ biotinylation, and comprehensively identify multifactors that constitute the transcriptional unity. In research group A02, we will establish a new technique, "Spatial quantification of multifactorial interactions using antibody barcoding", and quantify the multifactorial interactions that constitute transcriptional unity. In research group A03, we will structurally elucidate the multifactorial interactions constituting the transcriptional unity by Cryo-EM analysis and X-ray crystallography. Thus, this research area aims to elucidate the "transcriptional unity mechanism by multifactor interactions" from the structural analysis to the molecular network, and then to the cellular, tissue, and individual levels, and to elucidate the disease mechanism caused by its defects.

【Expected Research Achievements and Scientific Significance】

The methods of "comprehensive identification of multifactor interactions by in situ biotinylation" and “protein-protein interactions using antibody barcoding” developed in this research area will comprehensively identify multifactor interactions in the whole cell. If the transcriptional unity mechanism formed by multifactorial interactions can be clarified through this research, it will be a rewrite of the textbook in the field of gene expression regulation.

【Key Words】

Transcription: A reaction in which RNA is synthesized from DNA. The interaction of many factors regulates the amount of mRNA synthesized from a gene and its processing.

【Term of Project】 FY2021-2023

【Budget Allocation】 105,000 Thousand Yen

【Homepage Address and Other Contact Information】

https://www.med.osaka-u.ac.jp/pub/gts/TranscriptionUnity/
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