

【Grant-in-Aid for Scientific Research (S)】

Broad Section G



Title of Project : Structural basis of higher-order complexes connecting transcription and its related functions

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Keyword : RNA polymerase, Transcription factors, Nucleosomes, Ribosomes, Cryo-electron microscopy

【Purpose and Background of the Research】

RNA polymerase is a large protein complex, which governs transcription of genetic information in DNA into RNA. It interacts with various molecules in cells, and serves as a hub for many biological processes. In eukaryotes, transcription by RNA polymerase II is tightly linked to important biological functions such as epigenetics, signal transduction, and mRNA processing. In prokaryotes, transcribing RNA polymerase interacts with a translating ribosome, and thereby, transcription and translation are coordinated. However, structural basis of the complexes formed at the interface between transcription and its related functions are largely unknown. Recent advances in cryo-electron microscopy (cryo-EM) methodologies made it possible to address such higher-order complex structures. In this study, through investigating such higher-order complex structures mainly by cryo-EM, we aim to elucidate not only the basic transcription mechanism, but also structural foundations of interplay and coordination between transcription and its related essential biological processes.

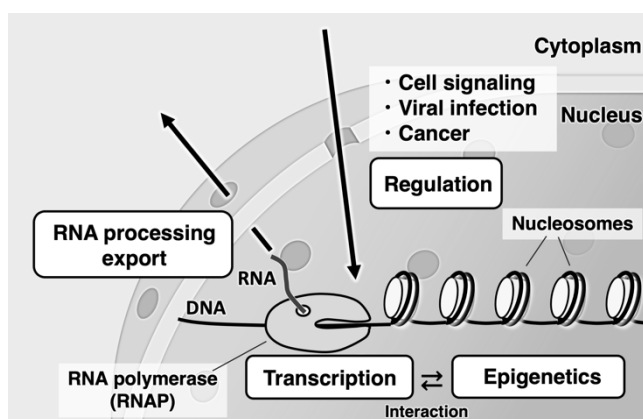


Figure 1. Interplay between transcription and various biological processes/functions

【Research Methods】

We will focus on the molecular mechanisms of the relationship between transcription and epigenetics, transcriptional regulation in higher eukaryotes, the coordination between transcription and mRNA processing, and transcription-translation coupling in bacteria. Key

higher-order complexes involved in these phenomena will be prepared, and their structures will be analyzed by cryo-EM. In combination with biochemical and mutational analyses, we will elucidate the mechanisms of interplay, coordination, and regulation of transcription and its surrounding processes at near-atomic resolution.

【Expected Research Achievements and Scientific Significance】

Little is known about how biological macromolecules interact with each other and form higher-order complexes in cells to support cellular functions. In this study, by analyzing the structures of higher-order complexes, we will elucidate the molecular mechanisms of interconnection between transcription and other important biological functions (epigenetics, gene regulation, mRNA processing, translation, etc.), which will shed new lights on the mechanism of chromatin transcription and regulation. The study of transcriptional regulation in higher eukaryotes will also be expected to provide important insights into the disease mechanisms such as viral infection and cancer.

【Publications Relevant to the Project】

- Ehara, H.,* Kujirai, T.,* Fujino, Y., Shirouzu, M., Kurumizaka, H.† and Sekine, S.† “Structural insight into nucleosome transcription by RNA polymerase II with elongation factors”, *Science* 363, 744-747 (2019).
- Kujirai, T.,* Ehara, T.,* Fujino, Y., Shirouzu, M., Sekine, S.† and Kurumizaka, H.† “Structural basis of the nucleosome transition during RNA polymerase II passage”, *Science* 362, 595-598 (2018).
- Ehara, H., Yokoyama, T., Shigematsu, H., Yokoyama, S., Shirouzu, M. and Sekine, S.† “Structure of the complete elongation complex of RNA polymerase II with basal factors”, *Science* 357, 921-924 (2017).

【Term of Project】 FY2020- 2024

【Budget Allocation】 145,500 Thousand Yen

【Homepage Address and Other Contact Information】

<https://www.bdr.riken.jp/jp/research/labs/sekine-s/index.html>

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