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

Deciphering the epicode of chromatin, which controls cell fate decisions in organisms

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Research Area Information	Number of Research Area : 24A306　Project Period (FY) : 2024-2028 Keywords : chromatin, development, differentiation, gene expression

Purpose and Background of the Research

●Outline of the Research

Chromatin plays a key role in the regulation of gene expression. However, it is unclear how gene expression during development and differentiation is regulated through chromatin structure to determine the cell fate. A higher-order chromatin structure organized by multiple regulatory layers in specific cell types can be an acquired code, or “epicode”. We are aiming to reveal how epicode is established and defines the cell fate. Our research will lead to a paradigm shift in the concept of chromatin regulation, from the basis of transcription to the determinant of cell fate.

Epicode: the acquired cipher that determines the cell fate in individual

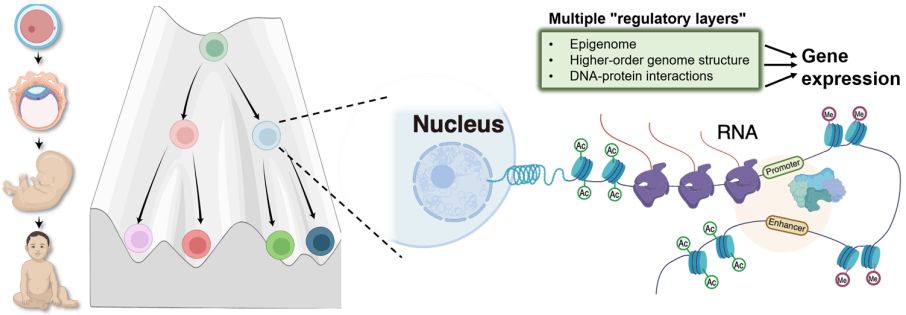


Figure 1. Epicode: the code of chromatin responsible for cell fate decision

●Background

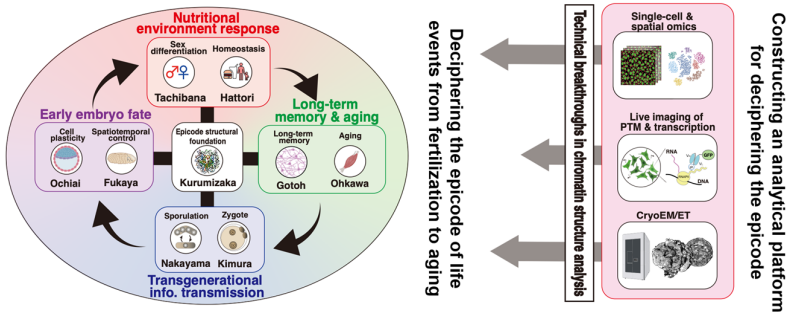
Our bodies are constructed through the various processes of cell fate decisions. Cell type-specific gene expression a pattern is induced in these processes. It is thought that multiple nuclear regulatory layers are interdependently involved in the cell fate decisions, such as the epigenome, the higher-order genomic structure, and DNA/protein interactions. However, the actual picture of how these layers contribute to the cell fate decisions is still unclear. We define these multiple layers of chromatin structure as **“epicode"** that is responsible for cell fate decision (Fig. 1).

●Research content

In this research group, we decipher the epicodes responsible for biological events throughout life: **Transgenerational information transmission**, **Early embryo fate**, **Nutritional environment response**, **Long-term memory and aging** (Fig. 2).

To analyze epicodes in a limited number of cells in vivo, a technical breakthrough in chromatin analysis is required. We will build three innovative chromatin analysis platforms: **Single-cell and spatial omics**, **Live imaging of posttranslational modification (PTM) and transcription**, and **Cryo-electron microscopy and tomography (CryoEM/ET)** (Fig. 2). Based on the information on chromatin and nuclear structures obtained by these techniques, we will perform mutant analysis in vivo. By linking the corresponding mutant phenotype with the changes in chromatin and nuclear structures, the epicodes for cell fate decision will be obtained.

Deciphering the epicode that orchestrates events throughout the lifespan of an organism



Realized through close collaboration between developmental and differentiation researchers and chromatin researchers

Figure 2. Deciphering the epicode by technical breakthrough in chromatin analysis

Expected Research Achievements

●Goal of the Research

We will prove that the multi-layered nuclear information acts as a code for cell fate decisions. Through these research activities, we hope to generate a new paradigm in the field of gene regulation through the lens of 'epicode' (Fig. 3). These activities are expected to have a significant international impact and contribute to the expansion of life sciences.

Establishing and generalizing the concept of the Cell Fate Code (Epicode)

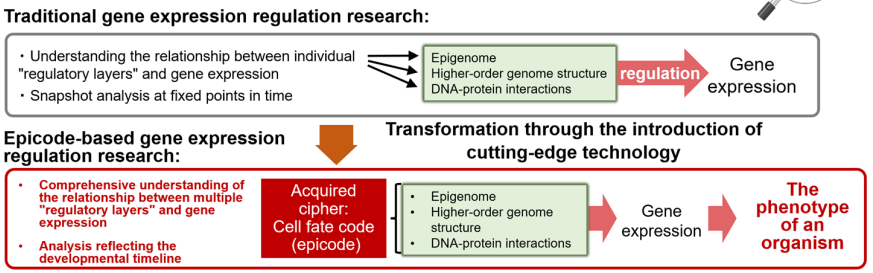


Figure 3. Goals of the research area, “Cell Fate Code”

Homepage Address, etc.	https://www.bioreg.kyushu-u.ac.jp/ext/epicode/home-en/