Laboratory of RNA biofunction

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Post-genome analysis at the beginning of 21st century revealed that large numbers of non-coding RNAs (ncRNAs) are produced from the large non-coding regions of the genome, and their functions have attracted considerable attention. Our laboratory aims to reconstruct the concept of genome function by clarifying the biological functions of these ncRNAs and elucidating new genetic code rules that govern their functions. In particular, we are studying the formation mechanism of intracellular structures and its role controlled by the ncRNA mediated phase separation phenomenon, which we have revealed so far, by incorporating biophysical and bioinformatics methods into basic molecular and cell biological studies.

Decoding of non-coding RNA codes

Only 2% of the human genome encodes protein information. And the remaining 98% non-coding region produces tens of thousands of different ncRNAs (Figure 1). The protein-coding genes work according to a textbook genetic code, however, this code works for only 2% of the genome. On the other hand, what sequence rules (or genetic code) are necessary for ncRNAs to function remains a mystery. Therefore, our laboratory is working to decipher the new genetic code that governs the function of ncRNAs. ncRNAs, without exception, form complexes with multiple RNA-binding proteins (RBPs) to form an operating apparatus. In order to decipher a new genetic code (ncRNA code) that specifies ncRNA functions, we are trying to clarify what kind of ncRNA sequences and structures are recognized by the RBPs that form the ncRNA machinery, and how such sequences were acquired during evolution.

Analysis of non-coding RNA-induced intracellular phase separation

As a function specified by the ncRNA code, we focus on the function of ncRNAs to build intracellular structures. In the nucleus of eukaryotic cells, there are many membraneless structures that fulfill important functions (Fig. 2). Our research has revealed that some of these structures are constructed using ncRNAs as a structural scaffolds (Fig. 3). Recently, it has been found that these membraneless structures have droplet or gel-like properties and are formed by a physical phenomenon called "liquid-liquid phase separation (LLPS). In other words, ncRNAs seem to act as seed molecules that induce LLPS in the nuclear space. Therefore, we are trying to understand how the massive and ordered membraneless structures are formed through LLPS, especially to elucidate the functions of intrinsically disordered proteins directly responsible for LLPS and to decipher the ncRNA code to consolidate these proteins.

Research on the significance of intracellular phase separation

LLPS is a clever mechanism for compartmentalizing intracellular space without the use of membranes (Figure 3). What is happening in the structure formed by LLPS? What is the significance of using RNA molecules as a structural scaffolds? We are trying to elucidate LLPS-related intracellular phenomena through understanding the ncRNA functions.

RNA research has rewritten the fundamental rules of biology and set new research trends. In this century, a new RNA world full of mysteries has emerged. We welcome romantic and energetic students who are willing to challenge this mystery.

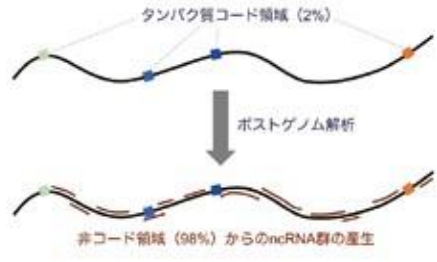

Figure 1. Post-genome analyses have revealed that tens of thousands of ncRNAs are produced from non-coding regions that make up 98% of the human genome. Their functions remain largely unknown.

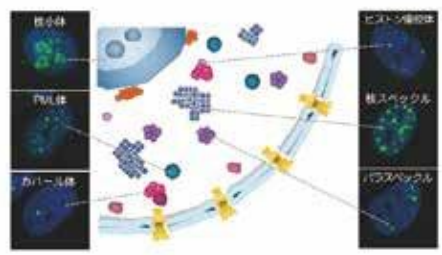

Figure 2: Schematic diagram of membraneless structures in mammalian cell nuclei

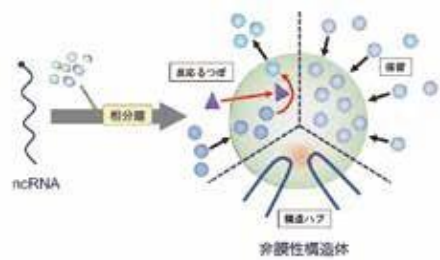

Figure 3. ncRNAs gather a group of intrinsically disordered proteins to induce LLPS and form membraneless structures. Three regulatory functions have been proposed for the membraneless structures: reaction crucible, molecular sponge, and structural hub.

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