2SBP-06 一回膜貫通型サイトカイン受容体 Mpl 二量体化の一分子蛍光解析**Single-molecule fluorescence analysis of the single-transmembrane cytokine receptor Mpl dimerization**

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Mpl is a single-transmembrane cytokine receptor that regulates platelet production and early hematopoiesis. In the previous meeting, we proposed a positive feedback regulation of Mpl phosphorylation by the stabilization of the Mpl dimer. In this model, Mpl dimers are stabilized by their phosphorylation, and the stabilized Mpl dimers in turn promote their phosphorylation, which should contribute to the effective stimulation of Mpl-expressing cells. Although this model is based on our understanding of Mpl dimerization, the single-molecule analysis of the Mpl dimer has been difficult because of the diffraction limit. Here, we solve this problem by single-molecule super-resolution microscopy using compressed sensing and the à trous wavelet transform.

2SCP-01 スクレオソーム DNA 弛緩状態の自由エネルギープロファイル**Free Energy Profile for Nucleosomal DNA unwrapping**

Hidetoshi Kono, Yoshiteru Yonetani, Jinzen Ikebe, Shun Sakuraba, Hisashi Ishida (*Molecular Modeling and Simulation, JAEA*)

Eukaryotic Genome is stored in a nucleus in the form of chromatin. Along with DNA binding proteins, this chromatin structure plays a key role in gene regulation. The chromatin has the fundamental structural unit called nucleosome which is composed of two copies of histones H2A, H2B, H3 and H4 and DNA wrapped around the histone proteins almost twice. Transcription does not occur until nucleosome is unwrapped to expose DNA, which can then be recognized by regulatory proteins. To understand this unwrapping process, MD simulations were performed on two nucleosomes: the canonical H3 and the H3 variant called CENP-A, essential for the kinetochore assembly. In the talk, how these nucleosomes are different in free energy profiles and what causes the differences are discussed.

2SCP-02 クロマチン高次構造形成におけるスクレオソーム構造多様性
Structural versatility of nucleosomes in higher order chromatin

Hitoshi Kurumizaka (*Waseda University, Faculty of Science and Engineering*)

In eukaryotes, genomic DNA is highly compacted and packaged into nucleus as chromatin, in which nucleosome is the basic repeating unit. Nucleosome accommodates about 145-147 base pairs of DNA, which are wrapped around a histone octamer composed of two of each histones H2A, H2B, H3, and H4. It has recently been revealed that nucleosomes are not structurally homogeneous, and the nucleosome versatility in structure and dynamics play essential roles in gene regulation in eukaryotes. The nucleosome structures and dynamics are regulated by histone variants and post-translational modifications. In this symposium, I will discuss about structural basis of regulation of higher-order chromatin architecture and dynamics by histone variants and modifications.

2SCP-03 モデルクロマチンの構造と転写因子ダイナミクスの粗視化シミュレーション研究**Structure of model chromatin and dynamics of transcription factors studied by coarse-grained simulations**

Shoji Takada (*Department of Biophysics, Graduate School of Science, Kyoto University*)

In eukaryotic cells, genome is stored in highly condensed form of chromatin. How nucleosomes are arranged and how DNA-binding proteins seek cognate sequences in condensed chromatin is unclear. Using multiscale methods, we have been simulating structure and dynamics of mono- and poly-nucleosome model chromatin systems and dynamics of transcription factors on them. Some of these recent works are presented.

2SCP-04 スクレオソームの線維は細胞内でどのように収納されているのか？**How is nucleosome fiber organized in the cell?**

Kazuhiro Maeshima (*National Institute of Genetics*)

DNA is wrapped around core histones and forms a nucleosome fiber. This nucleosome fiber has long been assumed to be folded into a 30-nm chromatin fiber, and a further helically folded larger fiber. However, when we observed human mitotic cells using cryoelectron microscopy, no higher-order structures including 30-nm chromatin fibers were found. Furthermore, our small-angle x-ray scattering analysis, which can detect periodic structures in noncrystalline materials in solution, demonstrated no structural feature larger than 11 nm. We also found a similar scattering pattern in interphase nuclei of human cells. Our findings suggest a common structural feature in interphase and mitotic chromatin: compact and irregular folding of nucleosome fibers.

2SCP-05 Diffusion-controlled reaction rate-laws in intracellular environment with molecular crowding: A single-particle-level simulation study

Kazunari Kaizu, Koichi Takahashi (*Laboratory for Biochemical Simulation, RIKEN Quantitative Biology Center (QBiC)*)

Although intracellular environment is significantly different from the ideal conditions expected in conventional biochemical simulations, the effect is poorly understood. In particular, there is no general quantitative theory for the reaction kinetics with molecular crowding. To derive the practical theory, we quantified the effect of molecular crowding on a rate-law in various conditions by using a single-particle-level simulation. In contrast to the common theory for diffusion-controlled reactions like Collins-Kimball's, the recombination probability was evaluated as a kinetic parameter. The rate-law revised on the basis of these calculations allowed simulations of intracellular signaling pathways and revealed the impact of crowding on cellular responses.