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

Biological Sciences (Biology)

Title of Project： Molecular mechanisms for centromere formation

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Research Project Number：17H06167　　Researcher Number：60321600
Research Area：　Chromosome Dynamics
Keyword：　Centromere, Chromosome segregation, Chromosome function, Epigenetics

【Purpose and Background of the Research】

Chromosome segregation during mitosis is critical to transfer genetic information to daughter cells in all organisms. If errors of chromosome segregation occurred, chromosome instability would be caused. Therefore, it is one of the most important topics in genetics to understand mechanisms how chromosomes are faithfully segregated.

In this project, we focus on centromere, which is a critical genome region for chromosome segregation, and aim to define the molecular mechanisms how centromeres are formed.

【Research Methods】

I) Protein interaction network during progression of cell cycle

We have previously found that centromere proteins dynamically interact each other during progression of cell cycle. It is critical to address how such dynamic changes for protein-protein interaction in centromeres occur. In this project, we focus on phosphorylation of centromere proteins and try to clarify how the phosphorylation regulates the dynamic changes of protein-protein interaction in centromeres.

In addition to this, as shown in Fig.1, we proposed that the Ndc80 complex is recruited to centromeres by two pathways. We also clarify how and why these two pathways exist.

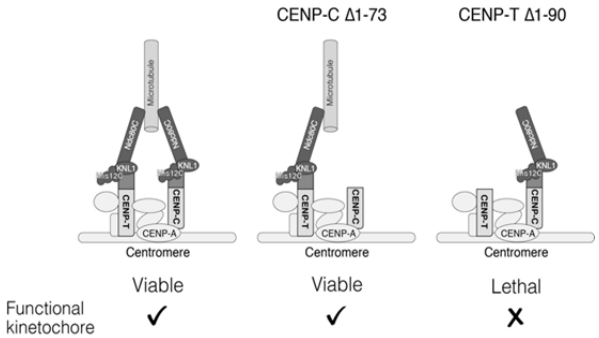

Fig 1. Model of kinetochore assembly. The Ndc80 complex is recruited by both CENP-T- and CENP-C-pathway (left). CENP-C Δ 1-73 cells, in which only CENP-T pathway is active, create kinetochore (middle), but CENP-T Δ 1-90 cells, in which only CENP-C pathway is active, do not form kinetochore (right).

II) Genome organization of centromeres

We have identified centromere-specific histone modifications utilizing non-repetitive centromeres. In this project, we will try to identify additional histone modifications in centromeres and clarify biological significance of such modifications for centromere specification and assembly.

III) Structural analysis of centromere protein complexes using Cryo-EM

Addition to functional analyses of centromere proteins, it is important to solve high-resolution structure of centromere protein complexes. In this project, we try to solve some of centromere protein complexes using Cryo-EM. This information would be useful to understand centromere architecture.

【Expected Research Achievements and Scientific Significance】

We propose this project based our achievements in centromere study. Combined our previous knowledge with results in this project, we expect to clarify mechanism how centromeres are formed. As we can perform various experiments using our own original assay, we are standing a good position to lead the research-field of centromere biology.

【Publications Relevant to the Project】

・Fukagawa T et al., The centromere: chromatin foundation for the kinetochore machinery. Dev. Cell, 30, 496-508 (2014).
・Nishino T et al., CENP-T-W-S-X forms a unique centromeric chromatin structure with a histone-like fold. Cell, 148, 487-501 (2012).

【Term of Project】 FY2017-2021

【Budget Allocation】 157,100 Thousand Yen

【Homepage Address and Other Contact Information】

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