【Grant-in-Aid for Scientific Research(S)】
Integrated Science and Innovative Science (New multidisciplinary fields)

Title of Project：A novel approach for the understanding of basic structure and behavior of human chromosomes

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Research Area：Genome Science

Keyword：Chromosome Informatics, Chromosome Dynamics, Chromosome Structure

【Purpose and Background of the Research】

Chromosome is a platform of life and various functions are integrated into a single chromosome molecule (Figure1). To understand the molecular mechanism that guarantees the proper function of chromosome, it is essential to study the process of chromosome dynamics (i.e., replication, recombination, repair, and partition) using a genomic approach. Genetic and biochemical approaches have so far identified hundreds of proteins that function in some aspects of chromosome dynamics. Now, genomic

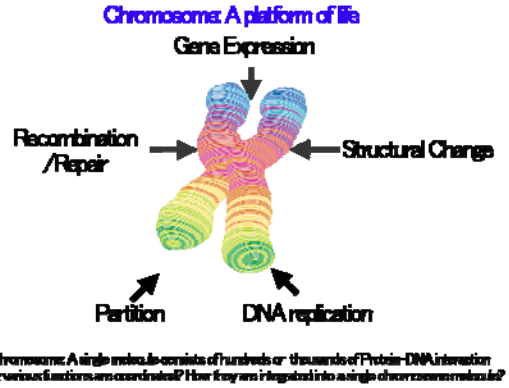

Figure1: Chromosome is a platform of life

approaches are able to show us how these proteins are integrated in the process of whole chromosomal dynamics, that is, how each elemental process is connected to make a complex network in order to guarantee the faithful maintenance of genomes. The goal of this proposal is to build up an analytical system to understand the structure and function of the human chromosome through a genomic approach. Our genomic approach (ChIP-seq technology; Chromatin Immuno-precipitation combined with next generation sequencer technology) has made us to know how protein-DNA interactions are actually integrated into the chromosome functions, and how each function is connected to make a huge network for the faithful maintenance of genome.

【Expected results】

The system we develop will tell us not only the molecular basis of functional elements of human chromosomes (replication origins, cohesin sites, centromeres and so on.), but also how these functional elements are organized to construct the flexible, dynamic, and huge chromosome structure, that is a specific feature of mammalian chrmosome (Figure2).

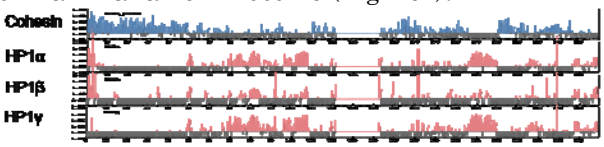

Figure2: Binding profiles of cohesin, HP1α, β, and γ on human chromosome1 revealed by ChIP-seq methods. Large heterochromatic (HP1) and euchromatic (cohesin) domain on chromosome1 are visualized.

【Research Methods】

Using HeLa and RPE cell lines, we will explore cell cycle dependent and senescence dependent changes of chromosome structure by monitoring binding profiles of more than 40 proteins by ChIP-seq. 3D chromosome folding structure will be examined by Hi-C technique. We will newly develop an algorithm to interpret ChIP-seq data and to investigate the correlation among protein binding profile and Hi-C maps. New chromosome functions and functional networks will be predicted and proved experimentally.

【Expected Research Achievements and Scientific Significance】

An entirely new picture for the molecular basis of human chromosome structure and dynamics will be revealed. The analytical system constructed in this study will open to public and be useful not only to basic fields of biosciences but to applied scientific fields like regenerative medicine and predictive medicine.

【Publications Relevant to the Project】

・T. Sutani, et al.. Curr. Biol. 19, 492-497, (2009)
・K. S. Wendt et al. Nature (article). 451, 796-801, (2008)

【Term of Project】 FY2010-2014
【Budget Allocation】 172,700 Thousand Yen

【Homepage Address and Other Contact Information】

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