【Abstract of 2011 Grant - in - Aid for Scientific Research on Innovative Areas
(Research in a proposed research area)】

Biological Science

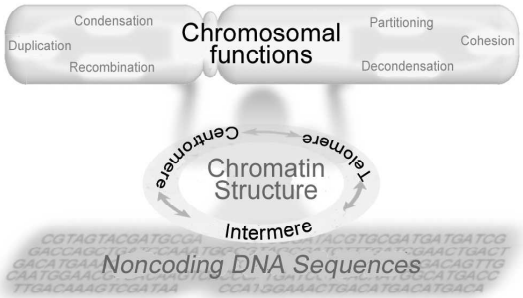
Title of Project : Functions of Non-coding DNA Region for GenomeIntegrity

Takehiko Kobayashi
(National Institute of Genetics / SOKENDAI, Professor)

【Purpose of the Research Project】

Most part of the eukaryotic genome is occupied by noncoding DNA regions that do not encode proteins. Those regions have functions to control all of the chromosomal events (gene expression, initiation of DNA replication, recombination hotspot that causes gene amplification and rearrangement, chromosomal fragile site, chromosome condensation, chromosome segregation, etc.). However, those noncoding DNA regions are so to speak "unexplored regions of the genome" because most part of the regions is occupied by repetitive sequences such as transposons, repeated ribosomal RNA genes, and microsatellites.

By means of experimental and informatical methods in this research project, we will comprehensively identify the functional noncoding DNA sequences we name "intermeres" that scatter in the genome in large numbers. Furthermore we aim to clarify the mechanisms in regulation of chromosomes by noncoding DNA by focusing on the chromatin structure of the intermeres and their network with telomeres and centromeres (three-mere network). Also we will analyze the mechanisms in occurrence of abnormal cellular functions such as oncogenesis and aging caused by malfunctioning regulatory system.



(Fig.) The functional sequences (three-meres: centromere, intermere, and telomere) present in the noncoding DNA regions support the chromosomal functions by forming a network. We will clarify the whole mechanisms in this research project.

【Content of the Research Project】

The following four teams in cooperation will analyze the entity of intermeres that are noncoding functional sequences, and factors related with the three-mere network.

1) The Sequence Team will identify the various DNA sequences in noncoding DNA regions that function in maintaining the chromosomal functions and clarify the role of the associated proteins, RNAs, etc. 2) The Structure Team will identify and analyze arrangement of local nucleosomes regulating chromosomal functions in the hierarchy above intermeres, epigenome modifications such as histone modifications, and change of chromatin structure. The team will also clarify the roles of the factors in maintenance of chromosomes. 3) The Network Team will clarify the entity of network that connects the three-meres through the characteristic chromatin structure. 4) The Pathological Analysis Team will clarify how the failure of chromosome-maintenance system influences the cellular functions and causes oncogenesis and aging.

【Expected Research Achievements and Significance】

In this research project, we will construct a Japanese cooperative research system based on strong relationships of mutual trust. By this, discovery of the third functional sequences following centromere and telomere, and clarification of novel mechanisms that regulate those sequences in an integrated manner are expected, which would let us take the global initiative in this field. The intermere and its network that this research project provokes are definitely essential factors for the chromosome maintenance system. Failure of the system would result in not only chromosomal inversion, translocation and abnormality such as gene amplification, but also increase of cancer incidence through the occurrence of extremely fragile sites of chromosome, inactivation of tumor-suppressor genes, activation of oncogenes, and furthermore association with progressive diseases caused by cell death, aging, etc. Identification of intermere and its network will lead to constructing a basic research for the mechanisms of those diseases, and following development of novel diagnostic methods and treatment techniques.

【Key Words】

Noncoding DNA region: DNA region that is not translated into protein. Repetitive sequences: Sequences repetitively present in the genome such as transposons, ribosomal RNA genes, and microsatellites. They account for approximately half of the human genome. Intermere: Neology. Noncoding functional sequences present in the main body of chromosome except for telomere and centromere. Chromatin: Consisted of a nucleosome structure in which histones are wrapped by DNA. Modification of histones such as acetylation and methylation alters the local chromatin structure.

【Term of Project】 FY2011–2015

【Budget Allocation】 1,189,100 Thousand Yen

【Homepage Address and Other Contact Information】

http://www.cdb.riken.jp/cmd/ncDNA.html
takobaya@lab.nig.ac.jp