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

Broad Section G

Title of Project：Molecular mechanisms of condensins I and II

Tatsuya Hirano
(RIKEN, Cluster for Pioneering Research, Chief Scientist)

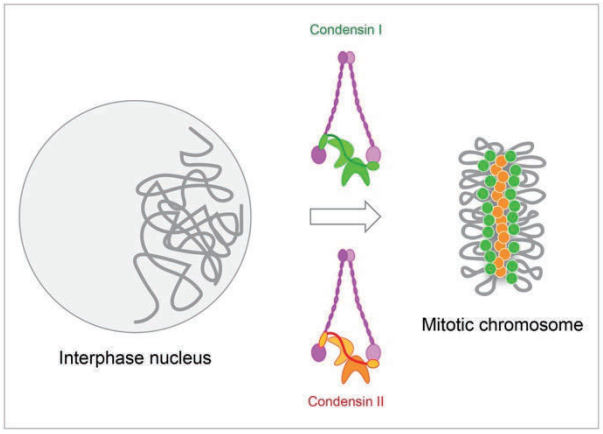
Research Project Number：18H05276　Researcher Number：50212171
Keyword：Biochemistry, Cell Biology, Mathematical Biology, Chromosomes, Cell Division

【Purpose and Background of the Research】

The assembly of mitotic chromosomes is an essential process for the faithful segregation of duplicated genetic materials into daughter cells. Our group discovered two types of protein complexes, now known as condensins I and II, that play central roles in this process, and made substantial contributions to our understanding of their cellular functions and molecular mechanisms of action. More recently, we have succeeded in reconstituting a mitotic chromosome structure with purified protein components including condensin I, and further demonstrated that a chromosome-like structure can be assembled even in the near-absence of nucleosomes in a condensin-dependent manner. The goal of this research project is to elucidate the molecular mechanisms of condensins I and II by combining two complementary approaches, namely, biochemistry and mathematical modeling (Figure below).

【Research Methods】

(1) We will reconstitute condensins I and II from their recombinant subunits, purify them, and test their ability to assemble chromosomes in *Xenopus* egg cell-free extracts. In addition to the wild-type holocomplex, holocomplexes harboring point mutations and subcomplexes lacking one or two of the regulatory subunits will be tested to understand how the two condensin complexes might work and collaborate with each other.



(2) We will establish a protocol in which the recombinant complexes can be activated in vitro by Cdk1-mediated phosphorylation, and thoroughly compare the biochemical activities of condensin I with those of condensin II.

(3) We will take an approach of mathematical modeling and computer simulation to get deeper insights into the action of condensins I and II. Such a theoretical approach will not only complement the experimental approach, but also provide us with hints about designing a new set of innovative experiments.

【Expected Research Achievements and Scientific Significance】

The question of how mitotic chromosomes might assemble is arguably one of the biggest questions left in the field of modern cell biology. It is anticipated that this research project will help uncover a whole molecular picture of how condensins I and II cooperate to assemble mitotic chromosomes at a mechanistic level. The outcome of this project will have a broad impact on our understanding of how anomalies of chromosome architecture cause human diseases including cancers and birth defects.

【Publications Relevant to the Project】

・Kinoshita, K., T. J. Kobayashi, and T. Hirano. (2015). Balancing acts of two HEAT subunits of condensin I support dynamic assembly of chromosome axes. *Dev. Cell.* 33:94-106.
・Hirano, T. (2016). Condensin-based chromosome organization from bacteria to vertebrates. *Cell.* 164:847-857.

【Term of Project】

FY2018-2022

【Budget Allocation】

148,800 Thousand Yen

【Homepage Address and Other Contact Information】

http://www.riken.jp/chromdyna/