# Molecular mechanism and regulation of assembly and remodeling of proteins

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## 【Outline of survey】

Most biological reactions occur when many factors assemble on a specific region at a specific time period and express their functions. In chromosomal DNA replication, many proteins including DNA polymerases assemble on replication origins and then they are remodeled to start DNA synthesis for elongating DNA strands in a cell-cycle dependent manner. However, the molecular mechanism governing this process has not been well elucidated. In this project, we analyze chromosomal DNA replication in budding yeast as a model system, focusing on cell-cycle dependent protein assembly on replication origins and subsequent remodeling of these proteins. We purify the proteins assembling on replication origins and reconstitute an assembly in vitro. We further characterize how assembled proteins are remodeled for transition from the initiation step to the elongation step by in vivo analyses as well as reconstituted in vitro assays.

## 【Expected results】

We expect a break-through achievement for DNA replication research; the molecular mechanism of initiation in eukaryotic DNA replication will be revealed in this project. This is a big advancement and an epoch-making hallmark in molecular biology. We characterize protein-assembly on replication origins, which is regulated by a cell-cycle main-engine, CDK. Thus, the result leads to understanding of the cell-cycle regulation, which is often disordered in cancers and diseases. We hope that the results we will obtain in this project give clues to future characterization of cancers and genetic diseases.

## 【References by the principal researcher】

- Tanaka, S., Umemori, T., Hirai, K., Muramatsu, S., Kamimura, Y. and Araki, H. (2007) CDK-dependent phosphorylation of Sld2 and Sld3 initiates DNA replication in budding yeast. **Nature** 445, 328-332.
- Walter, J. C. and Araki, H. (2006). Activation of pre-replication complexes. In **DNA Replication and Human Disease** (ed. DePamphilis, M. L.), pp. 89-104, Cold Spring Harbor Laboratory Press, NY.

| 【Term of project】 FY2008− 2012 | 【Budget allocation】 **153,700,000 yen** (direct cost) |
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【Homepage address】 http://www.nig.ac.jp/section/araki/araki-e.html