

【Grant-in-Aid for Specially Promoted Research】
Biological Science



Title of Project : Molecular dissection of epigenetic regulations supporting gene regulations

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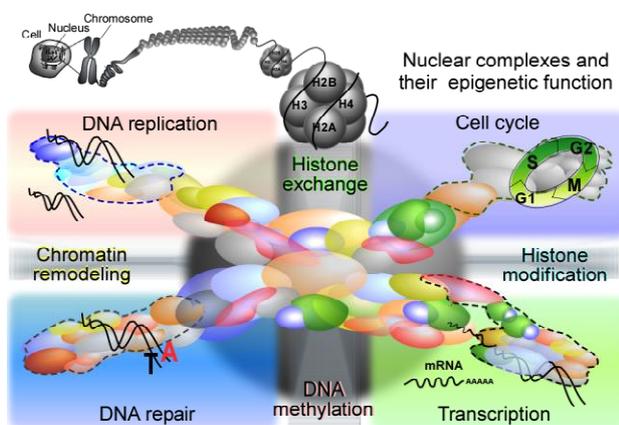
Research Area : Biology

Keyword : Genomic function and expression, Molecular genetics

【Purpose and Background of the Research】

Gene expression is in general suppressed by contacting with histone octamers in eukaryotic chromatin. Hence, chromatin reorganization is indispensable for gene regulations. Recently, certain combinations of histone chemical modifications have been shown to direct chromatin state, and these combinations are hypnotized as “histone code”. Histone code is supposed to play a central role in epigenetic controls.

We have studied the molecular basis of transcriptional controls by means of nuclear steroid hormone receptors, and have shown that transcriptional co-regulators mediate ligand-dependent transcriptional controls by nuclear receptors. Further characterization of such transcriptional co-regulators have uncovered that the prime function of identified co-regulators is associated with chromatin reorganization as histone modifying enzymes and chromatin remodelers, and they often form multisubunit complexes. However, the species of such complexes and their complex components largely remain to be studied. In the present study, to clarify the molecular basis of transcriptional controls at chromatin levels, we try to identify novel complexes supporting transcriptional controls through chromatin reorganization, and uncover their roles in chromatin reorganization.



【Research Methods】

Co-regulators/co-regulator complexes are tried to be identified by biochemical purification using DNA binding transcription factors as purification bait. Besides of nuclear receptors, several transcription factors primarily controlling cell fate decisions are also the targets. Prepared nuclear extracts from cultured cells endogenously expressing given transcription factors are used for biochemical purification, and the factors will be identified by mass-spectrometric finger printing. Genetic screening will be performed in transgenic flies expressing transcription factors. The physiological impact of identified factors will be verified by fly and mouse genetics.

【Expected Research Achievements and Scientific Significance】

This study will uncover the molecular basis of transcriptional controls with chromatin reorganization in terms of epigenomic regulations.

【Publications Relevant to the Project】

- Kim, M., Kondo, T., Takada, I., Youn, M., Yamamoto, Y., Takahashi, S., Matsumoto, T., Fujiyama, S., Shirode, Y., Yamaoka, I., Kitagawa H., Takeyama, K., Shibuya, H., Ohtake, F., **Kato, S.**: DNA demethylation in hormone-induced transcriptional derepression. *Nature*, 461, 1007-1012, 2009.
- Fujiki, R., Chikanishi, T., Hashiba, W., Ito, H., Takada, I., Roeder, R. G., Kitagawa, H., **Kato, S.**: GlcNAcylation of a histone methyltransferase in retinoic-acid-induced granulopoiesis. *Nature*, 459, 455-459, 2009.

【Term of Project】 FY2010-2014

【Budget Allocation】 605, 300 Thousand Yen

【Homepage Address and Other Contact Information】

<http://www.iam.u-tokyo.ac.jp/bnsikato/index.html>