

Dynamic Proteomics of Transcriptional Machinery and Nuclear Architecture

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【Outline of survey】

After the completion of genome sequencing, analyses of the epigenetic regulation of gene expression and the post-transcriptional processing of mRNAs as well as modifications of proteins have been highlighted for the clarification of living phenomena. To elucidate the interaction of protein complexes in regulatory mechanisms for gene transcription, the development of a method to analyze the dynamic behaviors of multiple protein molecules involved in these reactions has been needed. Identification of functional protein complexes and analysis of spatially-localized variations are important in understanding the regulatory mechanism of gene transcription. Here, we aim at establishing an analytical method for dynamic changes in these protein complexes by: i) investigating the time variation of endogenous protein complexes in transcriptional regulation with targeted proteomics; ii) performing a morphological analysis of nuclear structures using antibody probes under a confocal microscope and an ultrasoft X-ray CT microscope; and, iii) developing an integrated method for analyzing the large amount of data.

【Expected results】

For gene regulation, alterations in chromatin structure and dynamic changes in the machinery for mRNA processing may occur in a coordinated manner. An analytical tool for analyzing these changes will be obtained by producing specific monoclonal antibodies to molecules that would serve as a marker. These antibodies can be used as a tool for structural analysis and genome-wide analysis, as well as proteomics. Establishing a dynamic analytical method for endogenous protein complexes will result in elucidation of important cofactors and epigenetic factors that may play critical roles in the transcriptional regulation of nuclear receptors, and hence may lead to the search of targets for drug discovery, such as cancers and metabolic syndrome.

【References by the principal investigator】

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【Term of project】 FY2008—2012

【Budget allocation】

151,600,000 yen (direct cost)

【Homepage address】

<http://www.lsbm.org/staff/hamakubo.html/>