【Biological Sciences（Biology）】

Dynamics of intrinsically disordered proteins and their functional roles

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【Outline of survey】

In this project we will examine dynamics of intrinsically disordered proteins by using NMR and reveal their functions based on the dynamics. In eukaryotes many nuclear proteins are intrinsically disordered in their free states and upon binding to their targets, the interacting region of each protein will be folded. Especially dynamics of chromatin-related proteins, histone proteins in a nucleosome core, transcription activators, transcription repressors, and general transcription factors will be investigated in their free and target-bound states to reveal the common role of intrinsically disordered structures in transcription. For example we have already established static tertiary structures of chromodomains of chromatin remodeling factors, Chd1 and Esa1, DNA-binding domains of two telomeric proteins, hTRF1 and hTRF2 in their free and DNA-bound states, a neural restrictive silencing transcription factor, REST bound to its corepressor, mSin3, a transcription activator, ATF2, and a complex between general transcription factors, TFIIE and TFIIH by using NMR.

【Expected results】

Eukaryotic transcription factors, containing intrinsically disordered structures, regulate specific gene expression. Although classical proteins holding a specific tertiary structure interact with their targets by a simple key and lock model or an induced fit model, intrinsically disordered proteins interact with their targets by a coupled and folding mechanism. Recently some transcription factors are found to be essential for inducing iPS cell. It is very important to reveal dynamics and interacting modes of transcription factors for designing rationally iPS or ES cell. In addition histone modifications which are related to epigenetics should be revealed histone dynamics. Based on our study the basic phenomena of cell division and the maintaining mechanism of iPS or ES cell will be revealed.

【References by the principal investigator】

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- Nomura, M., Uda-Tochio, H., Murai, K., Mori, N., and Nishimura, Y. **J. Mol. Biol.**, **354,** 903-915 (2005).

【Term of project】 FY2008－2012	【Budget allocation】 **138,000,000 yen** (direct cost)

【Homepage address】 http://www.tsurumi.yokohama-cu.ac.jp/stbiol/index.html