



Title of Project : Structural basis of cell-signaling complexes mediating signal perception, transduction and responses.

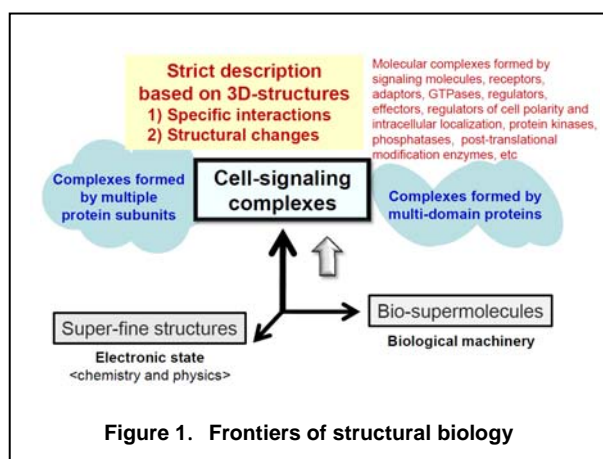
Term of Project : FY2010-2014

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【Purpose of the Research Project】

At key steps involved in cell signaling pathways, multiple proteins form molecular complexes through complexed intermolecular interactions, and these interactions control signal perception, transduction and responses. Although the primary goal of structural biology is to determine the three-dimensional (3-D) structure of these complexes, only a limited number of such complexes have been successfully determined. From our perspective, these complexes are referred to as cell-signaling complexes. Our general goal is to establish a scientific field that strictly defines the origins of the specificity of these interactions and to reveal the mechanisms by which proteins regulate their respective molecular functions. With this in mind, we are actively engaged in determining the 3-D structure of cell-signaling complexes at atomic resolution in an effort to take a snapshot of proteins in the act of performing their various functions.



【Content of the Research Project】

Structural biology continues to advance given the development of new frontiers (Fig. 1). Among these, structural investigations of cell-signaling complexes are particularly emphasized in this project. Our major interest in this area focuses on understanding the

actions of multi-domain proteins and complexes composed of multiple subunits. To overcome several difficulties inherent in the structure determination of these complexes, we integrate advanced technologies and strategies and determine the 3-D structure of the complexes at atomic resolution by means of X-ray crystallography in combination with other methods. We have set up three subprojects:

- A01. Structural biology of intracellular signal perception and transduction
- A02. Structural biology of nuclear signal recognition and responses
- A03. Structural biology of medically important cell-signaling complexes

【Expected Research Achievements】

In this project, we will define each state of the cell-signaling complexes present, which exist in a multiple-equilibrium state. This multiplicity is thought to be the origin of the pliable and elaborate regulatory circuits present in living organisms. Visualization of each state as a concrete state contributes towards a deeper understanding of the mechanisms involved. Our studies on a series of key protein complexes in a given signaling network could contribute towards delineating the complexity of the network and establish a new paradigm in the biological sciences. Our results concerning the details of the intermolecular interactions and structural changes involved should have great impact in the areas of molecular cell biology and medicine. We anticipate contributing to the so-called third wave of structural biology.

【Key Words】

Cell-signaling complex: a molecular complex formed by cell-signaling proteins in action.

The third wave of structural biology: a growing number of 3-D structures of molecular complexes since the middle of 2000.

【Homepage Address】

<http://convallaria.pharm.hokudai.ac.jp/scb>