



Title of Project : Chemical Biology using bioactive natural products as specific ligands: identification of molecular targets and regulation of bioactivity

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【Purpose of the Research Project】

A naturally occurring ligand is a bioactive molecule isolated from the creature. This is the molecule is committed as a key which controls a biofunction of living body. Though research on naturally occurring ligands was traditionally popular in our country, interest concerning an organic chemistry of their complex structure has been placed in center for a long time. This new scientific research on innovative area will emphasize the charm of the bioactivity of the naturally occurring ligands and aim at the establishment of "chemical biology of naturally occurring ligand" which involves chemical biology, biochemistry, molecule biology and bioinformatics unite in the good structure organic chemical base.

【Content of the Research Project】

It is widely known that naturally occurring ligands combines with the target protein in the living body to develop a bioactivity. This relationship is compared to the relations between "the key and the keyhole". But, as for naturally occurring ligands, it is recently found that it works as "a bunch of keys" to combine with plural target protein more than "a key" to combine with one target protein. The bioactivity which naturally occurring ligands shows is the total peace of the bioactivity which more than one "key" brings, and we have been discussing the "most conspicuous" one. This complexity of the bioactivity has been one of the great obstacles for the foundation research which naturally occurring ligands are used for as well as its application. Recently, it was revealed that disassembly of "the bunch of keys" into individual key or modification of the structure of "the master key" can enable the dramatic change of molecular target and bioactivity of a naturally occurring ligand.

This innovative area research aims at the establishment of novel theory of science that target identification and the analysis of ligand-target complex structure brings rational identification of the "key" structure which can be used as a scaffold of the molecular tool for the rational control of biofunction. The

disassembly of "the bunch of keys" realizes the simplification of structure of the naturally occurring ligands. Additionally, modification of "the key" structure by organic synthesis will create a new functional tools for the control of biofunction.

【Expected Research Achievements and Scientific Significance】

During this innovative area research, we will establish a protocol of the target identification which can be applied to any naturally occurring ligand as well. The analysis of ligand-target complex structure leads to the logical molecule design of "the key structure analog " of desired bioactivity.

This innovative area research goes through from naturally occurring ligands (chemistry), via target identification (biology), reaches the development of the key structure analog (chemistry). This spiral structure of research organization should be called chem-bio-chemistry. It will also bring an innovation in a philosophy of natural products chemistry "from structure to the bioactivity".

【Key Words】

Naturally occurring ligand: bioactive molecule isolated from the creature (natural product).
Molecular target: Target of the naturally occurring ligand in a living system.

【Term of Project】 FY2011-2015

【Budget Allocation】 1,030,500Thousand Yen

【Homepage Address and Other Contact Information】

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