Title of Project : Chemistry of Novel Naturally Occurring Super-carbon-chain Molecules

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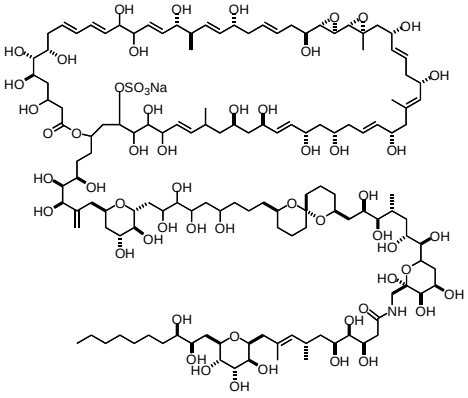
Research Area : Bioorganic Chemistry

Keyword : Natural Products Chemistry

【Purpose and Background of the Research】

Huge molecules, such as halichondrins and symbiodinolide, are some of the most unique and attractive secondary metabolites isolated from marine organisms. These compounds, which we call "super-carbon-chain compounds (SCCs)", contain a long carbon backbone that is highly functionalized by oxygen. While SCCs have been reported to show various biological activities, their functions and roles in ecosystems have not been thoroughly investigated. In this project, we aim to understand the structures, shapes, functions, and biosynthetic pathways of SCCs systematically, and to develop a new field of chemistry that involves the study of remarkable SCCs.



Symbiodinolide

【Research Methods】

By following five approaches, we aim to study SCCs generally by understanding their structures, shapes, functions, biosynthetic genes, and so on.

1. Creation of novel SCCs: We will establish an efficient method for isolating SCCs from marine organisms and construct a library of them. In addition, we will develop significant techniques for analyzing the shapes of SCCs.

2. Interaction of SCCs with cell membranes: We will try to detect the localization of SCCs in producer organisms by microscopic analyses. We will analyze the interaction of SCCs with cell membranes and study their shapes while paying attention to the microenvironment.

3. Analyses of biological activities of SCCs: The SCCs obtained will be subjected to a wide range of bioassay systems, and we will try to identify their unique characteristics. The biological activities of degraded or synthesized small fragments of SCCs will also be analyzed to specify their pharmacophores.

4. Molecular Design of SCCs: We will try to obtain information on the structures of SCCs through the synthesis of their partial structures. We will also try to develop new degradation reactions using SCCs as substrates. In addition, the shapes and movement of SCCs in solution will be clarified by computational analyses.

5. Genetic Analyses of SCCs: We will screen the biosynthetic genes of SCCs and their biosynthetic pathways will be clarified. We will also try to access SCCs or new enzymes using clones that express biosynthetic genes.

【Expected Research Achievements and Scientific Significance】

Unknown functions and roles of SCCs will be investigated from the perspectives of chemistry and biology. The discovery of novel biologically attractive SCCs with unique structures may trigger the development of novel scientific concepts and methodologies in related fields. In addition, construction of the library of SCCs will make SCCs of various kinds available to many researchers.

【Publications Relevant to the Project】

・D. Uemura, M. Kita, H. Arimoto, M. Kitamura, Recent aspects of chemical ecology: Natural toxins, coral communities, and symbiotic relationships, *Pure Appl. Chem.*, 81. 1093-1111 (2009) (*in press*)

・M. Kita, N. Ohishi, K. Konishi, M. Kondo, T. Koyama, M. Kitamura, K. Yamada, D. Uemura, Symbiodinolide, a novel polyol macrolide that activates N-type Ca^{2+} channel, from the symbiotic marine dinoflagellate *Symbiodinium* sp., *Tetrahedron*, 63, 6241-6251 (2007)

【Term of Project】 FY2009-2013

【Budget Allocation】 139,900 Thousand Yen

【 Homepage Address and Other Contact Information】

http://www.bio.keio.ac.jp/labs/uemura/kiban-s/index.html