Structures and Functions of Membrane-bound Biomolecules

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【Outline of survey】

Biomembranes have recently been regarded as the final frontier of biosciences. However, the conformation and interaction of biomolecules specifically occurring in biomembranes, which are a key for understanding the biomembrane functions, remain largely unknown. Sluggish progress in this area is mainly due to difficulties in applying X-ray crystallography to membrane systems. To solve this problem, we should treat biomembranes as molecular assemblies rather than two dimensional fluid. Besides spectroscopic techniques such as CD, ESR and NMR, organic synthesis should be crucial for selectively labeling membrane lipids and bound compounds. In this project, we are going to elucidate the structure and functions of molecular assemblies formed in biomembranes using isotope-labeled lipids and membrane-active agents for solid-state NMR measurements.

【Expected results】

Since molecular interactions occurring in biomembranes are largely based on weak VDW and electrostatic forces, introduction of a large labeling moiety such as fluorogenic and photoaffinity groups often hamper these delicate interactions. Therefore, isotope labeling with NMR nuclei without touching the structure should provide the best method to explore molecular conformation and recognition in membrane. If a robust and versatile method of analysis is established by this project, it will potentially applicable to biomedical and pharmaceutical researches; e.g., membrane-targeting antibiotics, which are often necessary for treatment of AIDS and transplant surgeries, are known to hardly engender drug-resistant mutants.

【References by the principal researcher】

- Amphotericin B-ergosterol covalent conjugate with powerful membrane permeabilizing activity. Matsumori, N., Eiraku, N., Matsuoka, S., Oishi, T., Murata, M., Aoki, T. and Ide, T. *Chem. Biol.* **11,** 673-679 (2004).
- Mycosamine orientation of amphotericin B controlling interaction with ergosterol: sterol-dependent activity of conformation-restricted derivatives with an amino-carbonyl bridge. Matsumori, N., Sawada, Y. and Murata, M. *J. Am. Chem. Soc.***127**, 10667-10675 (2005).

【Term of project】 FY2006－2010	【Budget allocation】29,200,000 yen

【Homepage address】 http://www.ch.wani.osaka-u.ac.jp/lab/murata/welcome-english.htm