

【Grant-in-Aid for Scientific Research(S)】

Biological Sciences (Medicine, dentistry, and pharmacy I)



Title of Project : Biology of diversity and asymmetry of membrane lipids

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Research Area : Medicine

Keyword : Lipidomics, metabolomics, phospholipids

【Purpose and Background of the Research】

Glycerophospholipids are a major constituent of biological membrane using their amphipathic properties (soluble both in water and lipids).

The glycerophospholipids have diverse and asymmetrical characters; *sn*-1 position of glycerol backbone contains only saturated or mono-unsaturated fatty acids, while *sn*-2 position attaches polyunsaturated fatty acids such as arachidonic acid or eicosapentaenoic acid. However, the molecular mechanisms and biological consequence of the diversity remains to be clarified. We and other group recently identified a gene family of phospholipase A2 and lysophospholipid acyltransferases.

In this research grant, it is our goal to reveal the biological significance of lipid diversity, by the combination of cell and molecular biology and lipid biochemistry (LC-MS).

【Research Methods】

Heterologous overexpression and /or knockdown of phospholipase A2s and acyltransferases in cultured cells. We identify the detail composition of glycerophospholipids by LC-MS (lipidomics

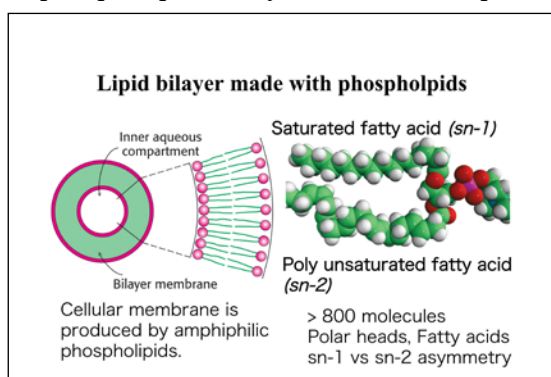


Figure 1

approach) and analyze phenotypes of thus treated cells. We will establish genetic engineered mice which either overexpress or lack these genes involved in phospholipid metabolism. Analyses of membrane phospholipids by LC-MS and various phenotypes of the mice will be done. We will

develop and improve lipidomics studies with high sensitivity, accuracy and highthroughput.

【Expected Research Achievements and Scientific Significance】

We will expect following future outcome with the present research project. (1)Identification of molecular mechanism and biological output of diversity and asymmetry of membrane phospholipids. (2)Development of drug screening systems and potential lead compounds which affects membrane biogenesis and diversity. (3)Development of lipidomics procedures and LC-MS instruments. (4) The nurture of young scientists with high quality background of lipid biochemistry and MS analyses.

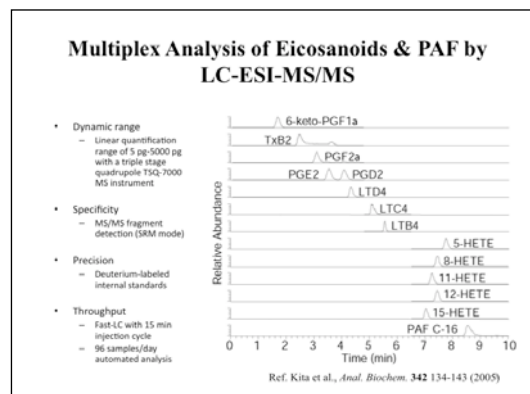


Figure 2

【Publications Relevant to the Project】

- Shimizu, T. (2009) Lipid mediators in health and disease. *Ann. Rev. Pharmacol. Toxicol.* 49, 123-150.
- Jonson, F, Marcardi, DA, Kita, Y. et al. Mouse and human neutrophils induce anaphylaxis. *J. Clin. Invest.* 121, 1484-1496

【Term of Project】 FY2012-2016

【Budget Allocation】 167,800 Thousand Yen

【Homepage Address and Other Contact Information】

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