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Mediator lipidomics approach to understand the roles of fatty acid metabolism in controlling inflammation and tissue homeostasis

Makoto Arita[1, 2, 3]

[1]Laboratory for Metabolomics, RIKEN Center for Integrative Medical Sciences (IMS),
[2]Graduate School of Medical Life Science, Yokohama City University, [3]PRESTO, JST

Lipids are recognized as extremely diversified molecules, with nearly 10^4 different structures of lipids currently being stored in the lipid structure database. Precise determination of molecular lipid species becomes a prerequisite not only to understand their biological functions in physiology and disease, but also to discover the novel link between lipid metabolisms and biological phenotypes.

In healthy conditions, inflammatory processes are self-limiting and self-resolving, suggesting the existence of endogenous mechanisms for the control of inflammation and resolution. A comprehensive understanding of the cellular and molecular events of a well-orchestrated inflammatory response is required. Polyunsaturated fatty acids (PUFAs) exhibit a range of biological effects, many of which are mediated through the formation and actions of lipid mediators such as prostaglandins, leukotrienes, lipoxins, resolvins, and protectins. These lipid mediators are potent endogenous regulators of inflammation and related diseases. To better understand the molecular and cellular mechanisms underlying the coordinated processes of inflammation and resolution, it's important to know when, where, and how much of those lipid mediators are formed in the inflammatory sites. To this end, we developed LC-ESI-MS/MS-based lipidomics, which is designed to simultaneously analyze and measure lipid mediators. Using this system, we uncovered a coordinated class switching of PUFA metabolites expressed in the course of acute inflammation and resolution, and their functional roles in regulating inflammatory responses.

Several lines of evidence have revealed the involvement of dietary fatty acids in the regulation of inflammation and tissue homeostasis. We demonstrated a differential display and identified several unique omega-3 PUFA metabolites with potent anti-inflammatory properties. These metabolites may underlie some of the beneficial actions of omega-3 PUFAs in controlling inflammation and tissue homeostasis. Dietary fatty acids are metabolized not only by the host enzymes but also by microbes in the intestinal tract. We identified novel structures of a series of fatty acid metabolites by gut bacterium that include hydroxy, oxo, conjugated, and partially saturated trans fatty acids. These microbial products in host tissues are enriched in specific pathogen-free mice as compared to germ-free mice, suggesting that fatty acid metabolism by gastrointestinal microbes might affect the tissue homeostasis of the host by modifying fatty acid composition.

In this symposium, I'll present recent advances in understanding the formation and action of these fatty acid-derived mediators, especially focusing on the LC-MS/MS-based lipidomics approach, and the emerging roles of lipid mediators in controlling inflammation and tissue homeostasis.

【References】

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