

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

Broad Section F



Title of Project : Integrated understanding of food functional responsible factors and their functional interactions

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Keyword : food functional responsible factors, miRNA, food factor sensing, epigenome, functional food pairing

【Purpose and Background of the Research】

Accurate understanding of "food intake", which is the most basic life activity in the maintenance and development of living organisms, is important both academically and socially. Applicants have aimed to elucidate the mechanism of bioregulatory action of food factors by considering food factors as bioregulatory signal factors and clarifying their sensing mechanism. We demonstrated that cell surface 67 kDa laminin receptor confers EGCG responsiveness to various type of cells at physiological concentrations (direct action pathway) (Fig. 1). On the other hand, the mechanism of functional expression of food factors, which are poorly absorbed and difficult to act directly on peripheral tissues and cells, is still largely unknown. In order to understand these, not only the molecules contained in food, but also the metabolites produced through living organisms and microorganisms, and the food-derived molecules that act on living organisms are regarded as " food functional responsible factors ". It is necessary to comprehensively understand the interrelationship (functional food pairing) (Fig. 2).

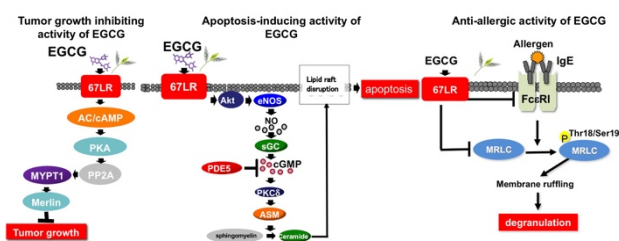


Figure 1 67LR is a critical sensor molecule to respond to EGCG and mediates the biological activities

【Research Methods】

We use liquid biopsy that captures changes in exosomes, functional RNAs, metabolites, DNA methylation, etc. in human blood. By analyzing the biological response that occurs before and after ingestion of food, we will elucidate the molecular mechanism that leads to the biological response from the food functional responsible factors. We will understand the function of food by analyzing the functional interaction between food factors. By conducting the following research items, we will elucidate the whole picture of food functional responsible factors.

- 1) Micro RNAs as food functional responsible factors
- 2) Circular RNAs as food functional responsible factors
- 3) Dietary plant-derived miRNA as food factors

- 4) Metabolites as food functional responsible factors
- 5) Epigenomic regulation by food factors
- 6) Identification of sensory molecules for hard-absorbing polyphenols
- 7) Elucidating of functional interactions between food functional responsible factors

【Expected Research Achievements and Scientific Significance】

It is positioned as a frontier study of "Precision Functional Food Science" that elucidates the actual state of dietary function-executive molecules and their mechanism of action, and presents scientific evidence on food intake that should be practiced for maintaining and improving health.

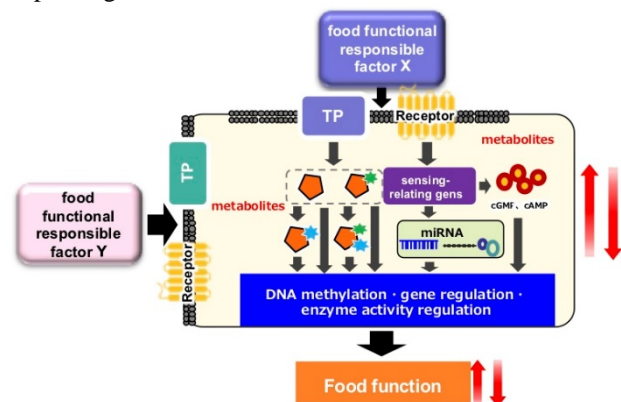


Figure 2 Concept of functional interactions between food functional responsible factors

【Publications Relevant to the Project】

- Kumazoe, M., *et al.* 67-kDa laminin receptor increases cGMP to induce cancer-selective apoptosis. *J. Clin. Invest.*, 123, 787-799 (2013)
- Yamada, S., *et al.* Epigallocatechin-3-O-gallate up-regulates microRNA-let-7b expression by activating 67-kDa laminin receptor signaling in melanoma cells. *Sci. Rep.*, 6, 19225 (2016)
- Bae, J., *et al.* Procyanidin C1 inhibits melanoma cell growth by activating 67-kDa laminin receptor signaling. *Mol. Nutr. Food Res.*, 64, 1900986 (2020)

【Term of Project】 FY2020- 2024

【Budget Allocation】 148,800 Thousand Yen

【Homepage Address and Other Contact Information】

<http://www.agr.kyushu-u.ac.jp/lab/syokuryo/>