Title of Project： **Investigation of intestinal lipid metabolism in food allergy**

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【**Purpose and Background of the Research**】

Imbalance of intestinal microbiota (dysbiosis) due to life modernization is attracting attention as a cause of food allergy. However, it is not well understood how the dysbiosis changes host's immune response and causes allergic reactions.

In the previous studies, we reported that the bioactive lipid PGD2 is an important molecule that modulates allergic reactions by strengthening the epithelial barrier of the host and by promoting IgE production against antigens. At the same time, we found that there is a correlation between changes in microbiota and changes in intestinal lipid production profile upon food allergy. There is a possibility that lipids connect intestinal microbiota to host immunity, and changes in lipid production resulting from dysbiosis may be responsible for induction of food allergy.

In this study, we will comprehensively analyze the relationship between intestinal microbiota and host's immunity focusing on bioactive lipids, and we are revealing what disturbs this relationship and increases food allergic patients. We aim to elucidate a new immunomodulatory mechanism that will provide new insight for the treatment of food allergy.

【**Research Methods**】

In this study, we will clarify how intestinal microbiota influence the production and reception of bioactive lipids in mice, humans and dogs.
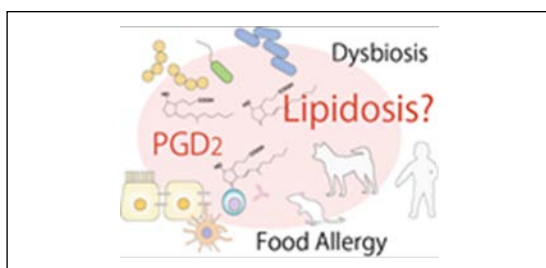

Figure 1   Analysis of the effect of dysbiosis on imunity

First, in humans, dogs, and mice suffering from food allergies, the correlation between dysbiosis and the abnormal lipid production will be clarified. We will also clarify the mechanism of how dysbiosis changes the lipid production usign murine model. Furthermore, we will explore and clarify which environmental factors and lifestyles impair the intestinal microbiota and lipid porduction. Finally, we will attempt to propose new method to improve the dysbiosis and lipid production.

【**Expected Research Achievements and Scientific Significance**】

The number of patients with food allergy has increased several times over the last decade. It is not known what has changed around us is increasing the disease.

In this study, we will clarify how the environment and lifestyles surrounding us change our immune responses focusing on the relationship between intestinal microbiota and lipid production, which have been attracting attention in recent years.

The results and concepts obtained in this study are not only for food allergies, but also for a wide range of diseases such as obesity and diabetes, enteritis and depression, in which dysbiosis may lead to the onset.
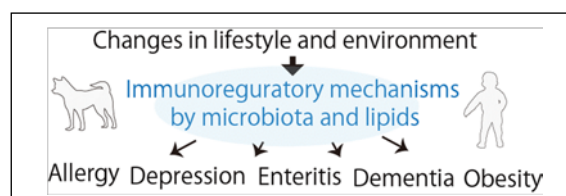

Figure 2   Scientific Significance of this study

【**Publications Relevant to the Project**】

· Therapeutic potential of D prostanoid receptor 1 signal enhancement in a murine model of food allergy. #Nakamura T and #Hirai R, Tachibana Y, Masuko S, Nagata N, *Murata T. J Allergy Clin Immunol. 143(6):2290-2293. 2019.
· 5,6-DiHETE attenuates vascular hyperpermeability by inhibiting Ca2+ elevation in endothelial cells. Hamabata T, Nakamura T, Tachibana Y, Horikami D, *Murata T. J Lipid Res. 59(10). 1864-1870. 2018.
· PGD2 deficiency exacerbates food antigen-induced mast cell hyperplasia. Nakamura T, Maeda S, Horiguchi K, Maehara T, Aritake K, Choi B, Iwakura Y, Urade Y, *Murata T. Nature Communications. 6:7514 2015.

【**Term of Project**】 FY2020- 2024

【**Budget Allocation**】 151,300 Thousand Yen

【**Homepage Address and Other Contact Information**】

http://www.vm.a.u-tokyo.ac.jp/houshasen/index.html