

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

### Broad Section I



#### Title of Project : Multi Regulatory System for Gut Homeostasis and Inflammation

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Keyword : Mucosal Immunology, Organ association, Inflammatory bowel diseases

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

Intestinal mucosa senses the alteration of nutrients and commensal bacteria and modulates both maintenance of homeostasis/ induction of pathogenesis. The important effects of the intestine in the regulation of physiological function beyond the organ has been well recognized, so that it is called the “Super organ.”

Crohn's disease is a chronic inflammatory disease occurring in the intestinal mucosa. It has been reported that patients of Crohn's disease show inflammation and dysfunction in not only mucosa but surrounding tissues, such as pancreas and *Muscularis externa*. In addition, complications associated with Crohn's disease develop in the remote organs such as eyes and joints. However, the detailed mechanism of the crosstalk between surrounding tissues, or mucosa-supportive tissues, and intestinal mucosa has not been revealed yet.

With our past researches of mucosal immune system together with pioneering and accumulated profound knowledge/skills, we aim to elucidate mucosal defense mechanisms which is mediated by the gut hierarchically-organized mucosal supportive system.

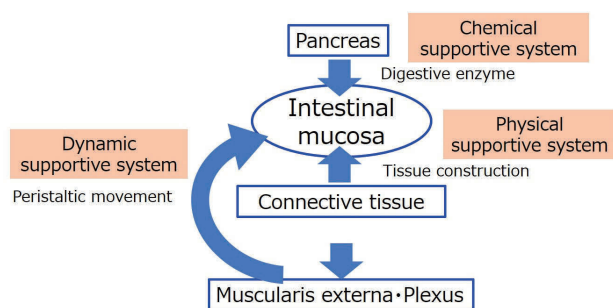


Figure 1. The gut hierarchically-organized mucosal supportive system

#### 【Research Methods】

In this study, we focus on following organ or tissue association/crosstalk.

1. pancreas-intestinal association
2. mucosal-connective tissue association
3. mucosa-muscular association

It is thought that the breakdown of association/crosstalk leads to the intestinal

pathogenesis, especially inflammatory bowel disease. By the creation of novel experimental disease models, we aim to reveal the multiple organ/tissue crosstalk systems. We also try to orchestrate these three research pieces for further understanding of gut hierarchically-organized mucosal supportive system.

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

The accomplishment of this study will provide further understanding of the contribution of mucosal system for systemic homeostasis and pathogenesis. In addition, we aim to establish the basis for therapeutic strategy of mucosal inflammation and its complications.

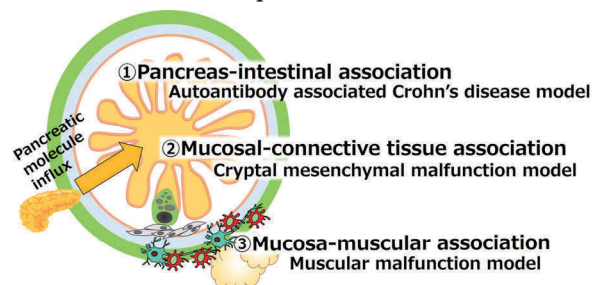


Figure 2. Understanding of mucosal supportive system and establishment of the therapeutic strategy

#### 【Publications Relevant to the Project】

1. Kurashima Y and Kiyono H. Mucosal ecological network of epithelium and immune cells for gut homeostasis and tissue healing. *Ann Rev Immunol.* 35:119-147. 2017.
2. Goto Y, Uematsu S and Kiyono H. Epithelial glycosylation is a key immunological event for gut homeostasis and inflammation. *Nature Immunol.* 17(11):1244-1251. 2016.

【Term of Project】 FY2018-2022

【Budget Allocation】 147,200 Thousand Yen

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

[http://www.ims.u-tokyo.ac.jp/enmen/index\\_j.htm](http://www.ims.u-tokyo.ac.jp/enmen/index_j.htm)  
<http://www.m.chiba-u.jp/class/innovativemed/index.html>