

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

### Broad Section H



#### Title of Project : Studies on the regulation of infection and immunity via paired receptors

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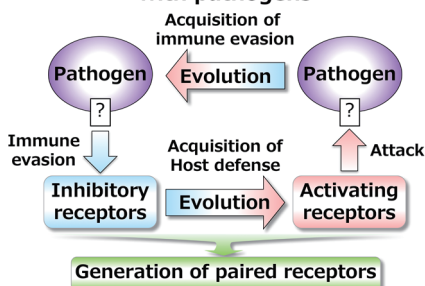
Research Project Number : 18H05279 Researcher Number : 10261900

Keyword : Paired receptors, Host-pathogen interaction, Immune evasion

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

Immune system express a series of paired receptors that consist of inhibitory and activating receptors. We have elucidated the function of various paired receptors based on our original hypothesis that the paired receptors have evolved with viruses (*Cell* 2008; *Nat. Immunol.* 2012). Furthermore, we have shown that paired receptors are involved in not only virus infection but also in bacterial and malaria infection (*Nat. Microbiol.* 2016, *Nature* 2017 Fig. 1). In this study, we would like to elucidate how pathogens are using inhibitory paired receptors for immune evasion. In addition, we will elucidate the function of paired receptors in host defense mechanism. Based on the studies on host-pathogen interaction, function of paired receptors in autoimmune diseases and allergic diseases will be elucidated.

Fig. 1 Coevolution of paired receptors with pathogens



#### 【Research Methods】

We will perform the following studies. 1. We will identify the pathogen ligands for paired receptors. 2. We will study the role of paired receptors in severe infection, persistent infection or latent infection. 3. We will study the contribution of in paired receptors in autoimmunity or allergic diseases.

##### ● Studies on the function of paired receptors in infectious diseases.

We will elucidate the interactions of various paired receptors with malaria molecules like FIRINs. Furthermore, association of RIFIN expression and severe malaria will be elucidated. Furthermore, function of paired receptors in persistent and latent infection of virus as well as viral reactivation will be analyzed.

##### ● Studies on relationship between polymorphisms of paired receptors and diseases.

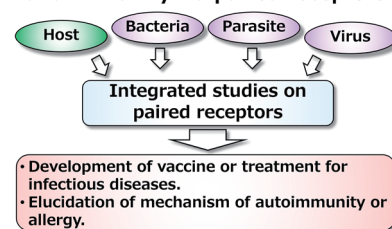
By analyzing polymorphism of paired receptors from

both host and pathogen side, we will elucidate the mechanism of autoimmunity or allergy.

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

Total function of paired receptors in host-pathogen interaction will be elucidated in this study. In addition, involvement of paired receptors

Fig. 2 Studies on regulation of infection and immunity via paired receptors



in immune homeostasis will be elucidated. This study will be important to develop a method for prevention or treatment of infectious and immune diseases as well as vaccines (Fig. 2).

#### 【Publications Relevant to the Project】

- Saito F, 17 others, Arase H. Immune evasion of *Plasmodium falciparum* by RIFIN via inhibitory receptors. *Nature* 552: 101-105, 2017.
- Hirayasu K, 14 others, Arase H. Microbially cleaved immunoglobulins are sensed by the innate immune receptor LILRA2. *Nature Microbiology* 25: 16054, 2016.
- Wang J, 3 others, Arase H. Neutrophil infiltration during inflammation is regulated by PILRA via modulation of integrin activation. *Nature Immunology* 14: 34-40, 2013.

【Term of Project】 FY2018-2022

【Budget Allocation】 148,800 Thousand Yen

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

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