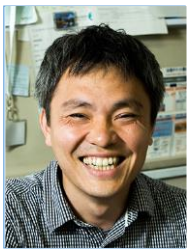
【Grant-in-Aid for Transformative Research Areas（B）】

Parasitomimetics: Identification and application of highly functional factors of parasites



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Research Area Information	Number of Research Area : 22B301　Project Period (FY) : 2022-2024 Keywords : Parasite, immune regulation, bioresource

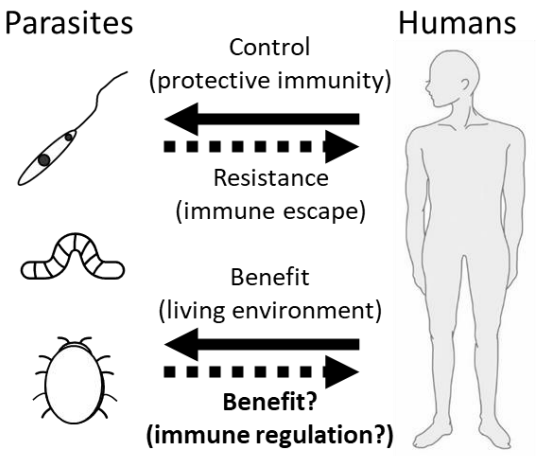
Purpose and Background of the Research

●Outline of the Research

In world of increasing immune-mediated diseases such as cancer, allergies, and autoimmune diseases, technologies that can control the enhancement or suppression of immune responses to specific antigens are key to disease control. To identify new immunoregulators, it is effective to utilize diverse organisms as resources. However, although there have been many attempts to search for useful natural substances from various organisms such as soil bacteria, algae, and plants, these organisms have not necessarily established close contact/relationship with mammals. Are there any suitable organisms as biological resources that possess a number of substances that could affect human immune system? We therefore give our attention to parasites.

Parasites have adaptation skills as a prerequisite for survival in humans. Human beings also have formed various immune mechanisms through the selective pressure by parasite infection. Together, we and parasites are kind of co-evolution partners. In other words, parasites do not unilaterally benefit from the host, but the host could also benefit from the parasites. In fact, many papers have supported the "hygiene hypothesis" that the decrease in parasitic infections has led to the increase in allergies and autoimmune diseases. Therefore, it is reasonable to think that 'if we reproduce the "parasite-infected state" in modern society, we may be able to successfully regulate the immune balance. However, artificial infection with parasites aimed at modifying immune balance is not realistic from a risk-benefit perspective.

This research aims to **develop the academic field of "parasitomimetics: mimicry of parasites" in which parasites with high immune manipulation skills are considered as biological resources, and parasite-derived molecules rather than the parasites themselves are utilized to develop novel medical interventions**. This unique concept that we utilized 'harmful' resources in a safe way is expected to have tremendous potential in both academic and industrial perspective.



Parasitomimetics

Identification and application of highly functional factors of parasites

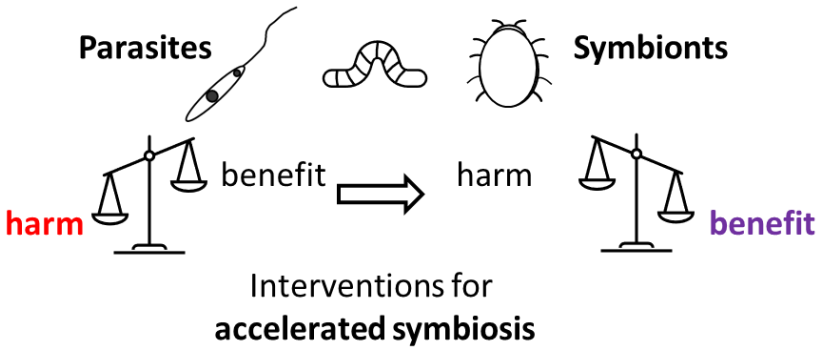
Depending on their mode of parasitism, parasites have different targets (cell/tissue types, biological processes etc.) to manipulate and penetrate.

→As a proof-of-concept, we aim at identifying unique molecules from different types of parasites, i.e.,

- **Protozoan**
- **Helminth**
- **Ectoparasite**

Figure 1. Concept and structure of the project

If we understand how parasites manipulate host immunity, the knowledge can be used not only for applications to many immunological disorders but also for appropriate control of the parasitic diseases caused by the target parasites. By achieving both, we don't need to call them as 'parasites' as they are now 'symbionts'.



Increase Benefit

- Know and utilize beneficial parasite molecules for our lives

Decrease Harm

- Know and interfere harmful parasite molecules to achieve better health conditions rather than killing the parasites

Figure 2. Long-term goal of the project

Expected Research Achievements

●Goals for Project Area and Planned Projects

The project area aims to identify and utilize highly functional immune mediators of parasites, and the goal of the Area is to show successful applications of parasitic factors to immunological disorders other than parasitic diseases in each planned study. As parasites can be broadly classified into three categories: protozoa (single-celled endoparasites), helminths (multicellular endoparasites), and ectoparasites, and one planned study is allocated for each category.

Planned project A01
Elucidation of mechanisms for macrophage manipulation by *Leishmania*

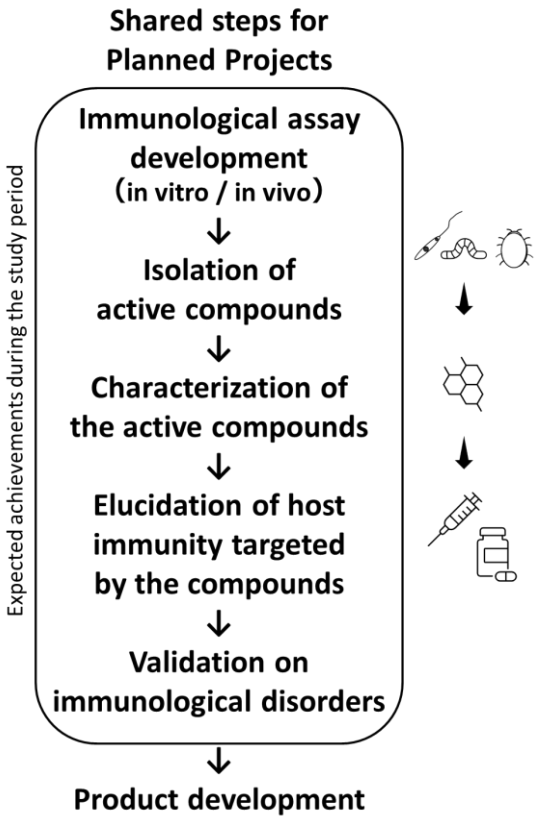
1) Identification of immune accelerators possessing anti-tumor effects
2) Identification of immune regulators for sepsis and endotoxin shock
3) Identification of adjuvant molecules for carbohydrate antigen-based vaccines

Planned project A02
Elucidation of host-gut microbiome interaction influenced by parasite-derived substances

1) Identification of regulatory molecules on the onset of autoimmune diseases
2) Identification of anti-obesity molecules
3) Identification of molecules preventing disease progression in viral infections

Planned project A03
Saliva of hematophagous arthropods -Pharmacological analysis for the drug discovery-

1) Identification of anti-allergy molecules
2) Identification of anticoagulant molecules
3) Identification of molecules inhibiting angiogenesis



Homepage Address, etc.	Project Area Website is under construction. Website of the PI's group: http://www.vm.a.u-tokyo.ac.jp/immune/index_en.html