International Vaccine Design Center

Division of Human Immunology (Human Immune-Profiling Team)

ヒト免疫プロファイリング系 ヒト免疫学分野

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The laboratory is consisted of two groups working on vaccine and immunometabolism lead by Ken Ishii and Noriko Toyama-Sorimachi, respectively to conduct novel research on vaccine immunology and immunometabolism towards human immune-profiling to understand why and how our immune system respond to infection and other immunological disorders.

1. *Establishment of a platform for rapid development of vaccines and therapeutics in the event of an infectious disease pandemic.*

Background: After the experience of the COVID-19 pandemic, various research systems for infectious disease pandemics have been in place around the world. IMSUT is the central hub of SCARDA, and the University of Tokyo has set up UTOPIA, where researchers have begun to work together. However, much work remains to be done to overcome the various obstacles that may arise during a disaster. To address issues such as how to rapidly obtain research materials including purified proteins as antigens and antibodies as reagents to test vaccine efficacy, and how to rapidly prepare various tools and technologies for therapeutic drug discovery in parallel with vaccine development, further collaboration among researchers across disciplines, organizations, and institutions, which is unique to emergency situations, is essential. Dr. Sorimachi of the International Vaccine Design Center is the program officer in the BINDS project of AMED. BINDS is a platform consisting of a group of academic researchers with world-class analytical technologies and supports academic drug discovery research with advanced technologies ranging from structural analysis, hit discovery, protein expression analysis, and various omics analyses to in silico drug discovery.

Methods: In response to the spread of M-pox, we worked on an interproject collaboration between SCARDA and BINDS, using the SCARDA Ishii team's project to test smallpox vaccine efficacy against M-pox as a practical problem. In addition, the BINDS platform has begun to centralize plasmid information to expedite the process of applying for recombinant DNA experiments.

Conclusions: The collaboration between the SCARDA Ishii team and the BINDS researchers has enabled rapid progress in the immunological analysis of the effects of smallpox vaccine. This successful case is the first inter-project collaboration within AMED, and demonstrates that cooperation between SCARDA and BINDS can create a strong research impetus in times of emergency. We will continue to work on the establishment of a system of research collaboration to address specific issues anticipated in an emergency. Collaboration with other researchers on hu-

man immunology using human samples and cell lines are underway and some of them have resulted in the publications in 2023.

2. *Initiatives to out-license lead compounds to a company for the development of therapeutic agents for autoimmune diseases.*

We have been conducting exploratory drug discovery research to develop novel therapeutics for autoimmune diseases by targeting amino acid transporters that are preferentially expressed in immune cells, and has succeeded in obtaining lead compounds that suppress inflammatory cytokine and type I interferon production at sub-μM levels. Since a foreign pharmaceutical company have been expressing strong interest in our lead compounds, we had ongoing meetings under a confidentiality agreement regarding licensing negotiations and a third-party evaluation of the compound's potential. This was followed by discussions on the content of a term sheet for out-licensing and an agreement was reached. We are in the process of drafting an agreement. We expect to be able to out-license the compounds in 2024. In parallel, with the same pharmaceutical company, we have been preparing to enter into a broad joint research agreement.

Publication

1. Kobayashi T. and Toyama-Sorimachi N. Metabolic control from the endolysosome: lysosome-resident amino acid transporters open novel therapeutic possibilities. ***Front. Immunol.*** 2023 14: 1243104. doi:10.3389/fimmu.2023.1243104.
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10. Atsumi Y, Toriyama M, Kato H, Nakamura M, Morita A, Takaishi M, Saito K, Tanaka M, Okada F, Tominaga M, Ishii KJ, Fujita F. Anti-Inflammatory Role of TRPV4 in Human Macrophages. ***Immunohorizons.*** 2023 Jan 1;7(1):81-96. doi: 10.4049/immunohorizons.2200100.

PCT application

1. WO2023/008402 A1: THERAPEUTIC AGENT FOR PULMONARY FIBROSIS

2. WO2023/008451 A1: TREATMENT AND REHABILITATION METHOD FOR PULMONARY FIBROSIS.