International Vaccine Design Center

Division of Immunology and Genomics (New Dimensional Vaccine Design Team)

新次元ワクチンデザイン系・ゲノム免疫学分野

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Summary of Activity

This division has been collaborating with Pasteur Institute in Paris, France via Prof. James Di Santo and Prof. Anavaj Sakuntabhai based on MOU between IMSUT and Pasteur Institute. In FY 2024, Pasteur International Unit on Mucosal Immunomics led by Ken Ishii and James Di Santo together with Prof Sakuntabhai conducted the research and development on immunology and genomics on infectious diseases and cancer. The team also contributed to the establishment of Institute Pasteur Japon (IPJ).

1. Supporting research in response to Public Health Emergency Declaration for Mpox

Two researchers from the Pasteur Institute have already been sent to IMSUT, and both institutions are deepening their research through close collaboration. In particular, the integrated systems immunological analysis technology using nasal swabs developed by Professor James Di Santo and colleagues is gaining attention as an innovative method capable of evaluating mucosal immunity in healthy individuals and patients with respiratory diseases at a high level. By integrating this with the "immunological analysis technology for exhaled breath particles" independently developed by Professor Ishii's team, they are pioneering a new field of "mucosal immunomics" that comprehensively captures the immune state of respiratory mucosa in a way previously unattainable.

2. Identification of a protective factor to dengue infection

Dengue virus (DENV) is a global health threat, causing approximately 390 million infections annually, ranging from mild dengue fever to severe dengue hemorrhagic fever and shock syndrome. MicroRNAs (miRNAs) are key post-transcriptional regulators that may influence host resistance to DENV infection. This study aimed to identify miRNAs associated with natural resistance to DENV. Individuals from a dengue-endemic area were classified as susceptible (SD) or resistant (RD) based on anti-DENV antibody status, with RD individuals remaining seronegative despite high exposure. Monocyte susceptibility to DENV was assessed in vitro, and miRNome profiles from 7 individuals per group were analyzed following mock or DENV-2 infection. The antiviral effects of differentially expressed miRNAs were evaluated using miRNA mimics in HeLa cells infected with DENV-1 to DENV-4. RNA-seq was performed to identify miRNA-targeted genes interacting with DENV proteins. Monocytes from RD individuals showed reduced DENV-2 production and overexpression of miR-155, miR-132-3p, and miR-576-5p upon infection. Notably, miR-155-5p mimic reduced viral infection and production, regulating 18 genes involved in interferon response, TP53 regulation, apoptosis, and vesicle trafficking (e.g., HSD17B12,

ANXA2). These findings indicate that RD monocytes display a distinct miRNA profile and reduced viral replication, highlighting miR-155-5p as a potential therapeutic target against dengue (Casadémont I. *et al*., ***Med Microbiol Immunol***, 2025).

Publications

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