International Research Center for Infectious Diseases

Department of Infectious Disease Control Division of Viral Infection

感染制御系・ウイルス学分野

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We focus on understanding how viruses are recognized by NLRP3 inflammasome and how the innate recognition receptor controls antigen-specific adaptive immune responses. We study immune responses to influenza viruses in the lung. Our recent focus also includes the study of how microbiota regulates adaptive immune responses to these pathogens. Our ultimate goal is to utilize the knowledge we gain through these areas of research in the rational design of effective vaccines for the prevention of infectious diseases.

1. High body temperature increases gut microbiota-dependent host resistance to influenza A virus and SARS-CoV-2 infection.

Nagai M, Moriyama M, Ishii C, Mori H, Watanabe H, Nitta Y, Arimitsu N, Nishimoto M, Nakahara T, Yamada T, Ishikawa D, Ishikawa T, Hirayama A, Kimura I, Nagahara A, Naito T, Fukuda S, and Ichinohe T.

Fever is a common symptom of influenza and coronavirus disease 2019 (COVID-19), yet its physiological role in host resistance to viral infection remains less clear. Here, we demonstrate that exposure of mice to the high ambient temperature of 36 °C increases host resistance to viral pathogens including influenza virus and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). High heat-exposed mice increase basal body temperature over 38 °C to enable more bile acids production in a gut microbiota-dependent manner. The gut microbiota-derived deoxycholic acid (DCA) and its plasma membrane-bound receptor Takeda G-protein-coupled receptor 5 (TGR5) signaling increase host resistance to influenza virus infection by suppressing virus replication and neutrophil-dependent tissue damage. Furthermore, the DCA and its nuclear farnesoid X receptor (FXR) agonist protect Syrian hamsters from lethal SARS-CoV-2 infection. Moreover, we demonstrate that certain bile acids are reduced in the plasma of COVID-19 patients who develop moderate I/II disease compared with the minor severity of illness group. These findings implicate a mechanism by which virus-induced high fever increases host resistance to influenza virus and SARS-CoV-2 in a gut microbiota-dependent manner.

2. Inactivation of novel coronavirus and alpha variant by photo-renewable CuxO/TiO2 nanocomposites.

Tatsuma T, Nakakido M, Ichinohe T, Kuroiwa Y, Tomioka K, Liu C, Miyamae N, Onuki T, Tsumoto K, Hashimoto K, and Wakihara T.

In order to reduce infection risk of novel coronavirus (SARS-CoV-2), we developed photocatalysts with nanoscale rutile TiO2 (4–8 nm) and CuxO (1–2 nm or less). Their extraordinarily small size leads to high dispersity and good optical transparency, besides large active surface area. Those photocatalysts can be applied to white and translucent latex paints and a

transparent varnish. Although Cu2O clusters involved in the paint coating undergo gradual aerobic oxidation in the dark, the oxidized clusters are re-reduced under >380 nm light. The paint coating inactivated novel coronavirus and its alpha (B.1.1.7) variant under irradiation with fluorescent light for 3 h. The coating also exhibited antivirus effects on influenza A virus, feline calicivirus and bacteriophage Qβ. The photocatalysts would be applied to practical coatings and lower the risk of coronavirus infection via solid surfaces.

Publications

Nagai M, Moriyama M, Ishii C, Mori H, Watanabe H, Nakahara T, Yamada T, Ishikawa D, Ishikawa T, Hirayama A, Kimura I, Nagahara A, Naito T, Fukuda S, Ichinohe T. High body temperature increases gut microbiota-dependent host resistance to influenza A virus and SARS-CoV-2 infection. ***Nat Commun.*** 14:3863. 2023

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Tatsuma T, Nakakido M, Ichinohe T, Kuroiwa Y, Tomioka K, Liu C, Miyamae N, Onuki T, Tsumoto K, Hashimoto K, Wakihara T. Inactivation and spike protein denaturation of novel coronavirus variants by CuxO/TiO2 nano-photocatalysts. ***Sci Rep.*** 13:4033. 2023

Song I, Yang J, Saito M, Hartanto T, Nakayama Y, Ichinohe T, Fukuda S. Prebiotic inulin ameliorates SARS-CoV-2 infection in hamsters by modulating the gut microbiome. ***NPJ Sci Food.*** 14;8(1):18. 2024