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

Associate Professor　Takeshi Ichinohe, Ph.D.

准教授　博士（工学）　一　戸　猛　志

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. SARS-CoV-2 infection primes cross-protective respiratory IgA in a MyD88- and MAVS-dependent manner.

Kobayashi M, Kobayashi N, Deguchi K, Omori S, Ichinohe T.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is constantly evolving mutations in the Spike protein to evade humoral immunity. Respiratory tract antiviral IgA antibodies are superior to circulating IgG antibodies in preventing SARS-CoV-2 infection. However, the role of innate immune signals required for the induction of mucosal IgA against SARS-CoV-2 infection is unknown. Here we show that hamsters recovered from ancestral SARS-CoV-2 infection are cross-protected against heterologous SARS-CoV-2 alpha, gamma, delta, and omicron BA.1 variants. Intranasal vaccination with an inactivated whole virus vaccine completely protects hamsters against heterologous SARS-CoV-2 infection. In addition, we show that intranasal boost vaccination of mice recovered from SARS-CoV-2 infection with unadjuvanted Spike protein induces robust levels of respiratory anti-Spike IgA and protects the mice from a heterologous SARS-CoV-2 infection. Furthermore, our findings suggest that MyD88 and MAVS play a role in the induction of the memory IgA response following an intranasal booster with unadjuvanted Spike protein in mice recovered from the SARS-CoV-2 infection. These findings provide a useful basis for the development of cross-protective mucosal vaccines against heterologous SARS-CoV-2 infection.

2. Partially hydrolyzed guar gum attenuates symptoms and modulates the gut microbiota in a model of SARS-CoV-2 infection.

Yang J, Song I, Saito M, Hartanto T, Ichinohe T, Fukuda S.

The coronavirus disease 2019 (COVID-19) pandemic has caused health issues worldwide. Studies have suggested that modulation of the gut microbiota could attenuate the severity of COVID-19 symptoms. In light of this, we explored the effects of the prebiotic dietary fibre partially hydrolyzed guar gum (PHGG) on SARS-CoV-2 infection in a Syrian hamster model, hypothesizing that modulation of the gut microbiome and intestinal metabolites through PHGG administration would improve COVID-19 disease outcomes. Eight hamsters each were assigned to the PHGG ad-

ministration and control groups. The PHGG group was given a diet supplemented with 5% PHGG for two weeks. Consequently, PHGG improved the host survival rate to 100% compared to 25% of the control group (P = 0.003) and attenuated morbid weight loss. Another non-infected set of hamsters was used for the analysis of the gut microbiome composition with 16S rRNA amplicon sequencing, serum, and faecal metabolites with GC-MS and LC-MS. PHGG altered the gut microbiome composition and increased the relative abundances of Ileibacterium, Bifidobacterium, and Prevotella. Furthermore, it elevated the concentrations of faecal valeric acid, propionic acid, ursodeoxycholic acid, and serum deoxycholic acid. Taken together, our data suggest that the prebiotic PHGG modulates gut metabolites and has the potential to reduce COVID-19 morbidity.

3. Antiviral potential of proton-type zeolite.

Kimura Y, Takemoto M, Nakamura N, Ichinohe T, Nakakido M, Iyoki K, Ohta S, Miyamae N, Egami Y, Sato K, Okubo T, Tsumoto K, Wakihara T.

This study reports the potent antiviral ability of proton-type zeolites without the aid of any metal cations. Antiviral activities of zeolites with different topologies and chemical compositions are investigated using M13 phage and influenza virus. Proton-type zeolites exhibit excellent antiviral activity, equivalent to 99% inactivated. Antiviral tests using a centricon device suggest that direct contact of viruses on the external surface of zeolites is required to inactivate the viruses. This discovery is of importance in an interdisciplinary research field covering both zeolite science and virological science and shed light on the possibility of the development of low-cost and environmentally friendly antiviral zeolites.

Publications

Kobayashi M, Kobayashi N, Deguchi K, Omori S, Ichinohe T. SARS-CoV-2 infection primes cross-protective respiratory IgA in a MyD88- and MAVS-dependent manner. ***NPJ Vaccines.*** 10(1):40. 2025

Yang J, Song I, Saito M, Hartanto T, Ichinohe T, Fukuda S. Partially hydrolyzed guar gum attenuates symptoms and modulates the gut microbiota in a model of SARS-CoV-2 infection. ***Gut Microbiome (Camb).*** 6:e1. 2025

Kimura Y, Takemoto M, Nakamura N, Ichinohe T, Nakakido M, Iyoki K, Ohta S, Miyamae N, Egami Y, Sato K, Okubo T, Tsumoto K, Wakihara T. Antiviral potential of proton-type zeolite. ***PLoS One.*** 20(5): e0324484. 2025

Yano S, Asami N, Kishi Y, Takeda I, Kubotani H, Hattori Y, Kitazawa A, Hayashi K, Kubo KI, Saeki M, Maeda C, Hiraki C, Teruya RI, Taketomi T, Akiyama K, Okajima-Takahashi T, Sato B, Wake H, Gotoh Y, Nakajima K, Ichinohe T, Nagata T, Chiba T, Tsuruta F. Propagation of neuronal micronuclei regulates microglial characteristics. ***Nat Neurosci.*** 28(3):487-498. 2025