Project Leader **Fumihiko Yasui** Viral Infectious Diseases Project

Control of viral infectious diseases: Virology, immunology, vaccinology and therapy

Our project studies the virology, immunology, vaccinology and therapy of incurable viral diseases. We currently focus on liver diseases, influenza and dengue fever. However, the lack of suitable infection models in in vitro and in vivo has hampered the clarification of pathogenesis by these virus infections. To overcome the problems, we have been developing various animal models including transgenic mice, humanized mice with human liver cells, monkeys and tree shews. We also investigate the precise mechanisms by which host factors regulate viral growth.

"We are studying to clarify the mechanisms underlying development of severe acute inflammation and establishment of chronic infection by viruses through the development of suitable animal models that are capable of infecting viruses."

Hepatitis

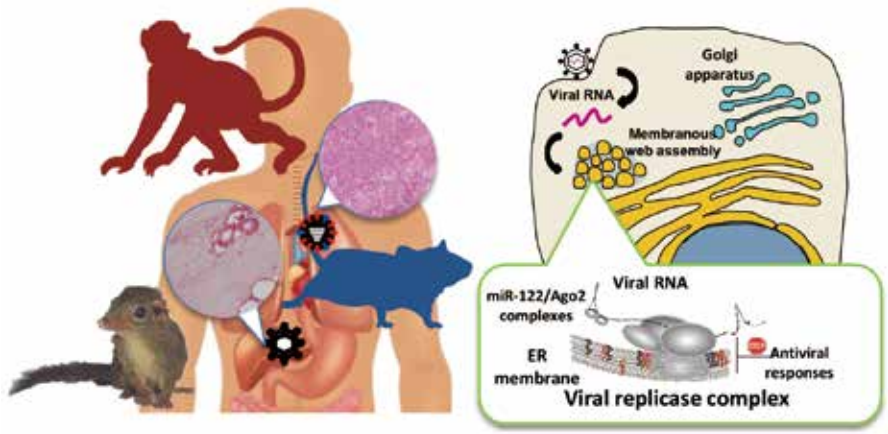
- Identification of host factors regulating virus growth.
- Elucidation of the mechanisms underlying pathogenesis caused by hepatitis virus infection.
- Development of therapeutic vaccine and drug for chronic HBV/HCV infection and other liver diseases.

Influenza

- Elucidation of the mechanisms by which highly pathogenic Flu causes severe pneumonia.
- Development of novel vaccine and therapeutic drug against highly pathogenic Flu and seasonal Flu.

Dengue fever

- Development of suitable animal models to study vaccine efficacy and pathogenesis of dengue fever.
- Development of novel vaccine for all serotypes of DENV.



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Viral Infectious Diseases

Topics of our research

Selective inhibitor of Wnt/β-catenin/CBP signaling ameliorates hepatitis C virus-induced liver fibrosis in mouse model

Chronic hepatitis C virus (HCV) infection is one of the major causes of serious liver diseases, including liver cirrhosis. We investigated the effects of a β-catenin/CBP inhibitor on liver fibrosis. PRI-724, a selective inhibitor of β-catenin/CBP, reduced liver fibrosis in HCV-Tg mice while attenuating αSMA induction. PRI-724 led to increased levels of matrix metalloproteinase (MMP)-8 mRNA in the liver, along with elevated levels of intrahepatic neutrophils and macrophages/monocytes. These results suggest that inhibition of hepatic stellate cells activation and induction of fibrolytic cells expressing MMP-8 contribute to the anti-fibrotic effects of PRI-724.

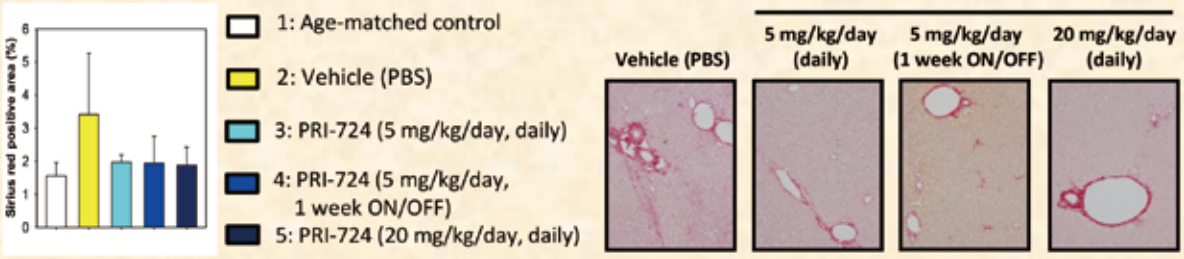
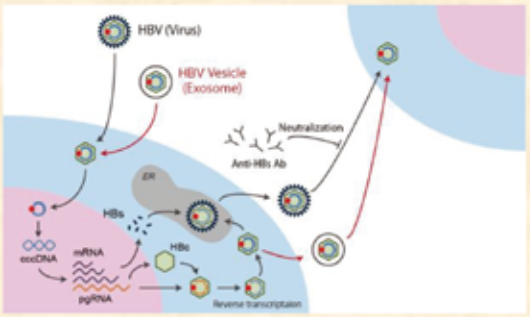


Figure. PRI-724ameliorates hepatitis C virus-induced liver fibrosis.

Transmission of HBV DNA Mediated by Ceramide-Triggered Extracellular Vesicles

Extracellular vesicle is a nanovesicle that shuttles proteins, nucleic acids, and lipids, thereby influencing cell behavior. We showed that ceramide-triggered extracellular vesicles work as DNA cargo for hepatitis B virus-DNA and are capable of trasmitting to naive hepatocytes. Further, we demonstrated that the transmission of hepatitis B virus-DNA via these extracellular vesicles is resistant to antibody neutralization.



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