Chemistry

# Chemical compounds with antiviral activities against positive-sense single-stranded RNA viruses

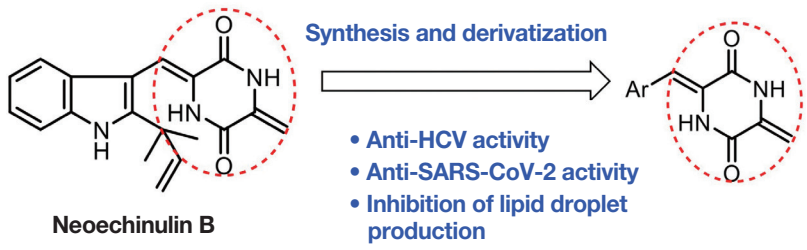
Kouji KURAMOCHI (Professor, Department of Applied Biological Science, Tokyo University of Science)

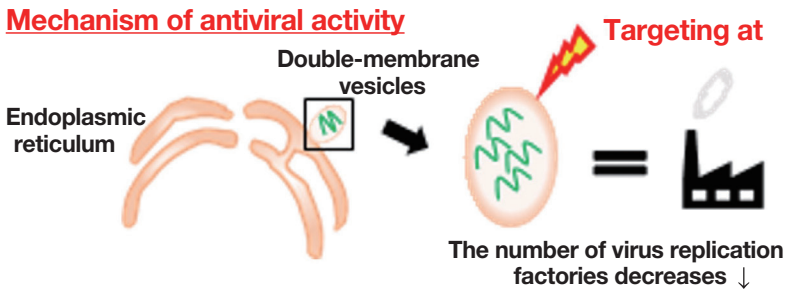
## Summary of Research

We have discovered a group of compounds with antiviral activities against positive-sense single-stranded RNA viruses such as SARS-CoV-2, hepatitis C virus (HCV), and poliovirus. The most significant characteristics of the compounds are that their molecular targets are host-cell derived instead of virus-derived. This means that the compounds can change the expression levels of host cell genes thereby inhibiting the virus from growing in cells. The uses of conventional antiviral drugs are limited to treatment of infections caused by specific viruses. In contrast, these compounds, which have antiviral activities against viruses, can be used as an all-purpose anti-multiviral drug for the treatment of variety of infections.

## Research Results

A natural product neoechinulin B (Neo B) was identified as a compound that inhibits replication of HCV. Our study revealed that this compound acts as an antagonist of liver X receptor (LXR) and reduces the expression levels of LXR downstream genes, thereby disrupting the formation of lipid droplets and double-membrane vesicles and inhibiting HCV particles formation and genome replication. We have also found that Neo B has antiviral activities against positive-sense single-stranded RNA viruses such as SARS-CoV-2 and poliovirus. Furthermore, we established a method of synthesis of a series of Neo B derivatives, with which we successfully obtained derivatives with a higher activity.




### Comparison with Conventional or Competitive Technology

- We have developed an antiviral drug against positive-sense single-stranded RNA viruses such as HCV and SARS-CoV-2
- In addition to its antiviral activities, the antiviral drug can also inhibit production of lipid droplets
- The drug may be used for the treatment of not only viral hepatitis, but also nonalcoholic steatohepatitis

### Expected Applications

- Treatment of infections
- Treatment of nonalcoholic steatohepatitis
- Prevention of liver cancer, arteriosclerosis, myocardial infarction, and strokes

### Challenges in Implementation/ Expectations for Business and Other Research Partners

- Joint research for nonclinical studies
- Conducting a clinical study jointly if safety and pharmacological activity are demonstrated

**Points**

- **This technology can be used to develop anti-multiviral drugs targeting positive-sense single-stranded RNA viruses. In addition to the application for antiviral drugs, the compound's capability to inhibit lipid droplet production can be utilized for the development of drugs for nonalcoholic steatohepatitis**

## Future Developments

By March 2023: Obtaining compounds with a higher activity
April 2023: Start of nonclinical studies
April 2025: Start of preparation for clinical studies

Keywords
Positive-sense single-stranded RNA virus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), hepatitis C virus (HCV), nonalcoholic steatohepatitis (NASH)

■ Intellectual Property:
Novel compound, agent against positive-sense single-stranded RNA, inhibitor of lipid droplet formation (Japanese Patent Application No. 2020-198970)
■ Public Funding Programs Used:
FY2018–2021: Research Program on Hepatitis from the Japan Agency for Medical Research and Development (AMED)
FY2021: Research Program on Emerging and Re-emerging Infectious Diseases from the AMED