Jun Nakabayashi
Graduate University for Advanced Studies (SOKENDAI)
e-mail: nakabayashi_jun@soken.ac.jp

Mathematical models of the intracellular replication and within host evolution of HBV and HCV

Hepatitis virus type B (HBV) is a major causative agent of acute and chronic hepatitis. Especially, chronic hepatitis is a major risk factor of liver cirrhosis and hepatocellular carcinoma. During the long time course of chronic hepatitis, severity of hepatitis varies depending on the viral load. It is important to estimate the viral kinetics of HBV for the prediction of the outcome of hepatitis. Though the detailed mechanism of HBV replication is revealed according to the development of molecular biological technique, how reproduction rate of HBV is determined in single cell level had not been clear yet. To investigate the intracellular replication dynamics of HBV, a mathematical model of HBV replication process is constructed. And how the long time course of hepatitis is affected by within host evolution of HBV was investigated by using an evolutionary simulation [1]. From the analysis of our model, the condition for the exacerbation of hepatitis during the chronic hepatitis is obtained. It is shown by our model that the waiting time for release of newly produced virion from infected cell plays critical roles for determining the clinical course of hepatitis. Now, a mathematical model of HCV is additionally constructed to compare with HBV.

In the intracellular replication of virus, the viral genome should play several distinguished roles, as a template of the genome replication, as a component of the viral particle and as a template for the viral gene expression. Because it is impossible to simultaneously play many roles, it is necessary to optimally distribute the viral genome to these roles for the efficient replication. The optimum distribution of genome is common problem for many viruses. HBV is DNA virus, on the other hand, HCV is the positive strand RNA virus, and their replication patterns are quite different. HBV and HCV respectively achieve the optimum distribution of genome by different regulatory mechanism. The intracellular replication dynamics of HBV and HCV are drastically changed by the distribution of genome. I would like to show how the replication dynamics of HBV and HCV is affected by the distribution of their genome. And I would like to discuss how the long time course of chronic hepatitis is affected by the intracellular dynamics and within host evolution of HBV and HCV in this mini-symposium.

References

[1] Nakabayashi J. and Sasaki A, *A mathematical model of the intracellular replication and within host evolution of hepatitis type B virus: Understanding the long time course of chronic hepatitis.* J Theor Biol. 2011 **269** 318-329.