HBV infection-induced liver cirrhosis development in dual-humanised mice with human bone mesenchymal stem cell transplantation

With the support by the National Natural Science Foundation of China, the joint research team directed by Prof. Xia NingShao (夏宁邵) at the State Key Laboratory of Molecular Vaccinology and Molecular Diagnostics, Xiamen University, and Prof. Li Jun (李君) at the State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, Zhejiang University, recently reported the HBV infection-induced liver cirrhosis development in dual-humanised mice with robust differentiation and proliferation of human hepatocytes and multiple immune cells, which was published in *Gut* (doi: 10.1136/gutjnl-2018-316091).

Host immune and inflammatory responses are critical in HBV infection and progression to end-stage liver cirrhosis, but the mechanism remains unclear, and there is currently no cure for chronic HBV infection. Because of the narrow host range and strict hepatic tropism of HBV, few animal models can mimic the long-trem viral immune pathophysiology progression of chronic HBV infection, especially the infection-induced liver cirrhosis. Developing a small animal model that can accurately delineate the natural history of HBV infection and immunopathophysiology is important and necessary.

Based on the previous findings, their group found that the transplantation of human bone marrow mesenchymal stem cells (hBMSCs) can rescue the immunodeficient FRGS mice with fulminant hepatic failure. The transplanted mice showed robust transdifferentiation and proliferation of functional human hepatocytes and multiple immune cell lineages, including B cells, T cells, natural killer cells, dendritic cells and macrophages. The dual-humanised hBMSC-FRGS mice were sensitive to chronic HBV infection, generated specific and sustained human immune and inflammatory responses and ultimately developed liver cirrhosis at a frequency of 55% after 54 weeks.

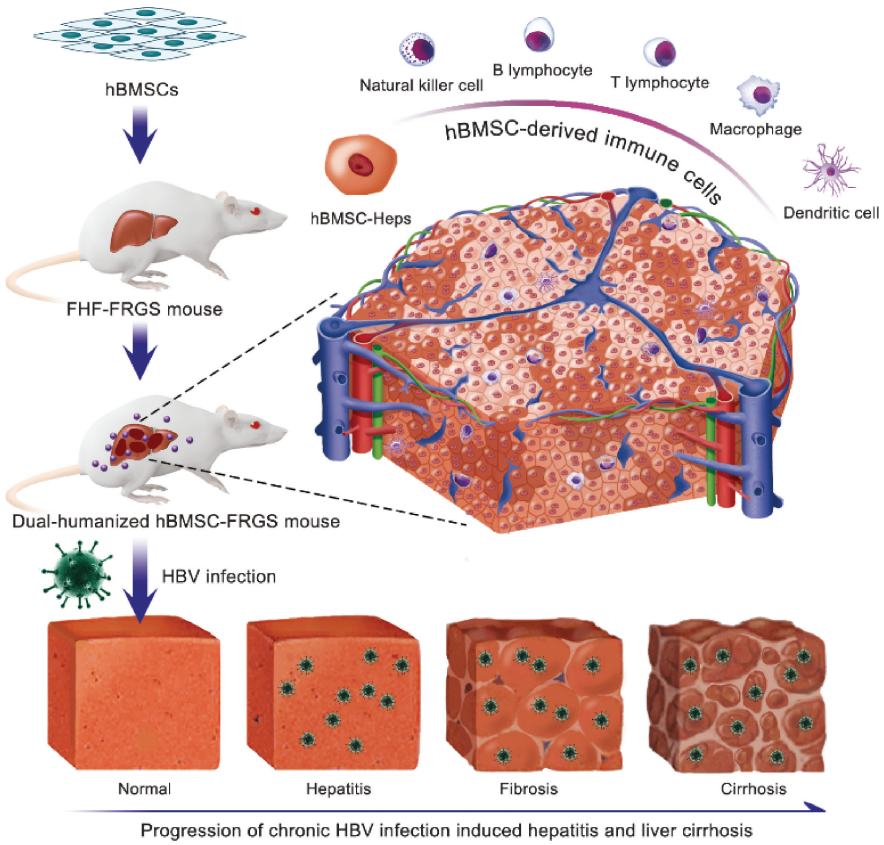

Figure Schematic presentation for hBMSC-FRGS mice generation and progression of chronic HBV infection induced hepatitis and liver cirrhosis.

The new humanised mouse model can provide a platform for observing host-virus interactions and the progression of HBV-induced hepatitis and liver cirrhosis, and also provide research opportunities for the development of novel antivirals and therapeutic strategies for HBV-related liver diseases.