Abstract:
A mouse model for persistent HBV infection is essential for the development of a therapeutic vaccine against HBV. Because HBV cannot infect mouse hepatocytes, even if the HBV receptor is introduced, surrogate models are used. A suitable model needs to establish persistent HBV replication and must allow the establishment of HBV-specific adaptive cellular and humoral immune responses. Therefore, an immunocompetent mouse model is needed in which one can break HBV-specific tolerance and ideally eliminate the HBV transcription template. The most widely used model for chronic HBV infection is the HBV transgenic mouse. Although HBV replicates from an integrated transgene, HBV-specific immune tolerance can be broken upon adequate immune stimulation because antigen expression only starts shortly before birth. Alternative mouse models of chronic HBV infection are generated by introducing HBV genomes either using viral vectors or using hydrodynamic injection. In these alternative models, the HBV transcription template is introduced into a proportion of hepatocytes and stays extra-chromosomal. It thus mimics the natural HBV transcription template, the HBV cccDNA in humans. Unlike an HBV transgene, however, it can be cleared upon appropriate treatment or immune stimulation. Human hepatocyte chimeric mice in which murine hepatocytes are widely replaced by human hepatocytes represent another important mouse model for persistent
HBV infection. These mice are susceptible for HBV infection, but need to be severely immune
deficient to accept human hepatocytes. In conclusion, a variety of mouse models for persistent HBV
infection are available suitable for preclinical efficacy evaluations of therapeutic vaccination strategies
against HBV.