Abstract

Hepatitis B virus (HBV) represents one of the hot topics of current basic and pharmaceutical research. Although an effective vaccine against HBV exists since 1982, the world prevalence of chronic infection is still alarming. The infection can lead to significant liver damage, often resulting in hepatocellular carcinoma. Chronic HBV infection cannot be cured due to the fact that the viral genome persists in the infected hepatocyte hidden from the host immune response as well as from the antiviral treatment. One of the novel approaches aiming for HBV cure suggests that this cccDNA pool could be destroyed using gene editing tools such as CRISPR/Cas9 system. In order to shift this gene editing system to possible medicinal application, CRISPR/Cas9 has to be specifically delivered into the target cell in order to minimize its putative off-target activity. This thesis focuses at first on the design and efficacy testing of new sgRNAs targeting HBV cccDNA and secondly, it describes modular lipid nanoparticles developed specially for delivery of the CRISPR/Cas9 system in the form of RNA.

Keywords: hepatitis B virus, CRISPR/Cas9, gene editing, lipid nanoparticles, mRNA delivery, targeted delivery