MicroRNA-122 (miR-122) is the most abundant liver-specific miRNA and plays a role in the regulation of hepatocyte differentiation and liver development. In addition, miR-122 controls hepatitis C virus (HCV) infection. HCV infection is a major cause of chronic liver diseases, often progressing to liver cirrhosis and hepatocellular carcinoma. HCV is an enveloped RNA virus and has a single stranded, positive polarity RNA genome, which consists of one long open reading frame flanked by untranslated regions (UTRs) at both the 5’ and 3’ ends of the genome. Mir-122 binds to two closely spaced target sites within the 5’-UTR, resulting in up-regulation of viral RNA levels by stimulation of replication and translation of HCV. HCV core protein is the viral nucleocapsid protein that binds and packages the viral RNA genome. Besides its function as a viral structural protein, the core protein is implicated in HCV chronic infection-associated liver diseases by induction of reactive oxygen species and modulation of apoptosis.

Here, we show that HCV core protein regulates the abundance of miR-122. Expression of the core protein transiently or in a stable cell line derived from the hepatocellular carcinoma cell line Huh7 led to reduction of the miR-122 abundance, as assessed by Northern blot analysis and real-time quantitative RT-PCR. Our results suggest that down-regulation of intracellular and extracellular miR-122 abundance by core protein dampens the stimulatory role of miR-122 in controlling HCV infection.