

P009 Regulation of hepatitis C virus by microRNA-122

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Most cellular microRNAs bind to sites in the 3' untranslated regions (UTRs) of mRNA targets and negatively regulate protein synthesis. The liver-specific microRNA -122 (miR-122), however, exerts a positive effect on hepatitis C virus (HCV) RNA levels by binding directly to a site in the 5' UTR of the viral RNA. HCV translation and RNA stability are unaffected, and therefore miR-122 is likely to act at the level of viral replication.

We have examined the miR-122 binding site in HCV RNA to determine whether the nature of the site is responsible for the unusual mode of action for a microRNA. We found that when the site was placed in the 3' UTR of a reporter mRNA, miR-122 repressed gene expression, and therefore the effect on HCV replication is likely to be position dependent.

We have also identified a second binding site for miR-122 in the HCV 5' UTR show that miR-122 binding to both sites in the same viral RNA is necessary for viral replication. The two sites are adjacent and are separated by a short spacer, and the role of the sites and spacer region will be discussed. The binding site requirements for miR-122 to mediate HCV replication provide an insight into this unusual mode of microRNA action.