

# MicroRNA let-7b Negatively Regulated Hepatitis C Virus Infection

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## Background/Objective

MicroRNAs are small RNAs that participate in regulation of the virus life cycle and pathogenesis. Previously, we demonstrated that microRNA let-7b is induced by HCV infection and targets on the HCV viral genome. However, the role of let-7b-target host factors involved in HCV replication is still unclear.

## Method

To understand if let-7b-target host factors involved in HCV replication, microarray and bioinformatic analyses were performed to define the host genes that are down-regulated by let-7b in HCV infection. Following, the candidate let-7b target gene was verified by reporter assay. The signaling affected by the let-7b target gene was also examined by various cell-based assays.

## Result

Among these genes, the suppressor of cytokine signaling 1 (SOCS1) was identified as a let-7b-target gene by luciferase reporter assay. Accordingly, transfection of Huh7 cells with the wild-type of let-7b decreased SOCS1 expression but not seed region mutant, and concomitant with an increase in STAT1 phosphorylation at Y701. Consistent with the role of SOCS1 in the regulation of interferon (IFN) response, the IFN-stimulated response element (ISRE) promoter activity and IFN-stimulated gene MX1 were all increased.

## Conclusion

Our data reveal that let-7b elicits dual anti-HCV effects by direct target of HCV genome and by target SOCS1 with subsequent activation of JAK/STAT signaling and increased MX1 expression. Regulation of let-7b expression is thereby crucial in the intervention of HCV infection and may explore a novel anti-HCV therapeutic approach.