HCV induces the expression of Rubicon and UVRAG to temporally regulate the maturation of autophagosomes and viral replication

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Hepatitis C virus (HCV) induces autophagy to enhance its replication. However, how HCV regulates the autophagic pathway remains largely unclear. In this report, we demonstrated that HCV infection could induce the expression of Rubicon and UVRAG, which inhibited and stimulated the maturation of autophagosomes, respectively. The induction of Rubicon by HCV was prompt whereas the induction of UVRAG was delayed, resulting in the accumulation of autophagosomes in the early time points of viral infection. The role of Rubicon in inhibiting the maturation of autophagosomes in HCV-infected cells was confirmed by siRNA knockdown and the over-expression of Rubicon, which enhanced and suppressed the maturation of autophagosomes, respectively. Rubicon played a positive role in HCV replication, as the suppression of its expression reduced HCV replication and its over-expression enhanced HCV replication. In contrast, the over-expression of UVRAG facilitated the maturation of autophagosomes and suppressed HCV replication. The HCV subgenomic RNA replicon, which expressed only the nonstructural proteins, could also induce the expression of Rubicon and the accumulation of autophagosomes. Further analysis indicated that the HCV NS4B protein was sufficient to induce Rubicon and autophagosomes. Our results thus indicated that HCV, by differentially

inducing the expression of Rubicon and UVRAG, temporally regulated the autophagic flux to enhance its replication.