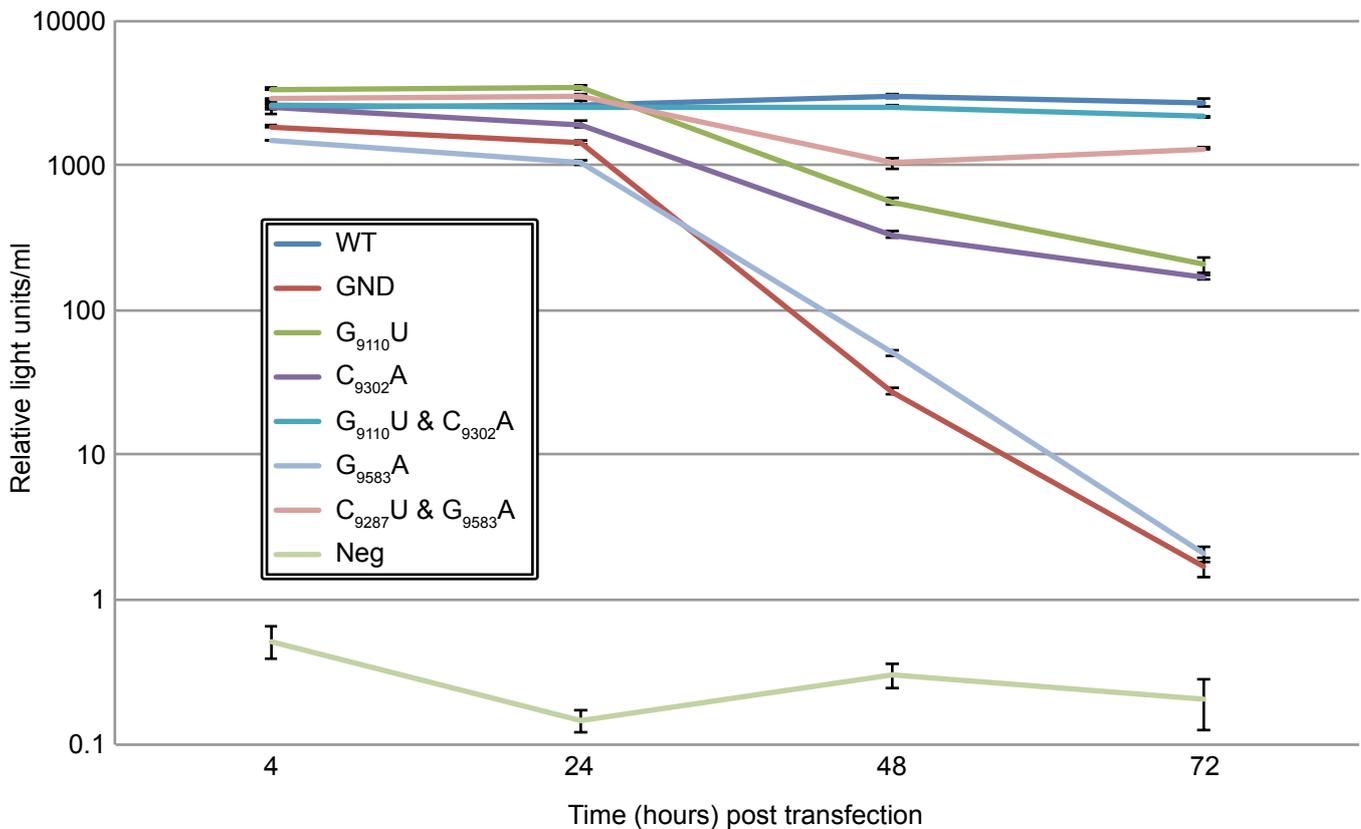


Supplementary figure S1

SHAPE mapping of J6/JFH-1

Schematic diagram of the genome of HCV J6/JFH-1 showing the short and long transcripts used for SHAPE mapping above representative SHAPE gels generated from short (top) and full-length (bottom) J6/JFH-1 templates. In each case a conventional Sanger sequencing reaction is adjacent and below primer extension reactions of templates treated (+) or untreated (-) with NMIA. Open block arrows indicate the bioinformatically-predicted duplexed regions with filled rectangles (terminal loop = black, sub-terminal bulge loop = grey) representing unpaired regions.



Supplementary figure S2

Luciferase activity of Con1b-luc-rep sub-genomic replicons

Replication phenotypes of Con1b-luc-rep sub-genomic replicons bearing substitutions of G₉₁₁₀U, C₉₃₀₂A, G₉₁₁₀U and C₉₃₀₂A, G₉₅₈₃A, C₉₂₈₇U and G₉₅₈₃A. *In vitro* generated RNA was transfected into Huh 7.5 cells and luciferase activity determined at the time points indicated. The assay was conducted three times independently and the average luciferase activity was plotted with the standard error indicated. WT indicates an unmodified Con1b-luc-rep template, GND indicates a template bearing a GDD to GND substitution in the active site of the NS5B polymerase and Neg indicates an untransfected control.