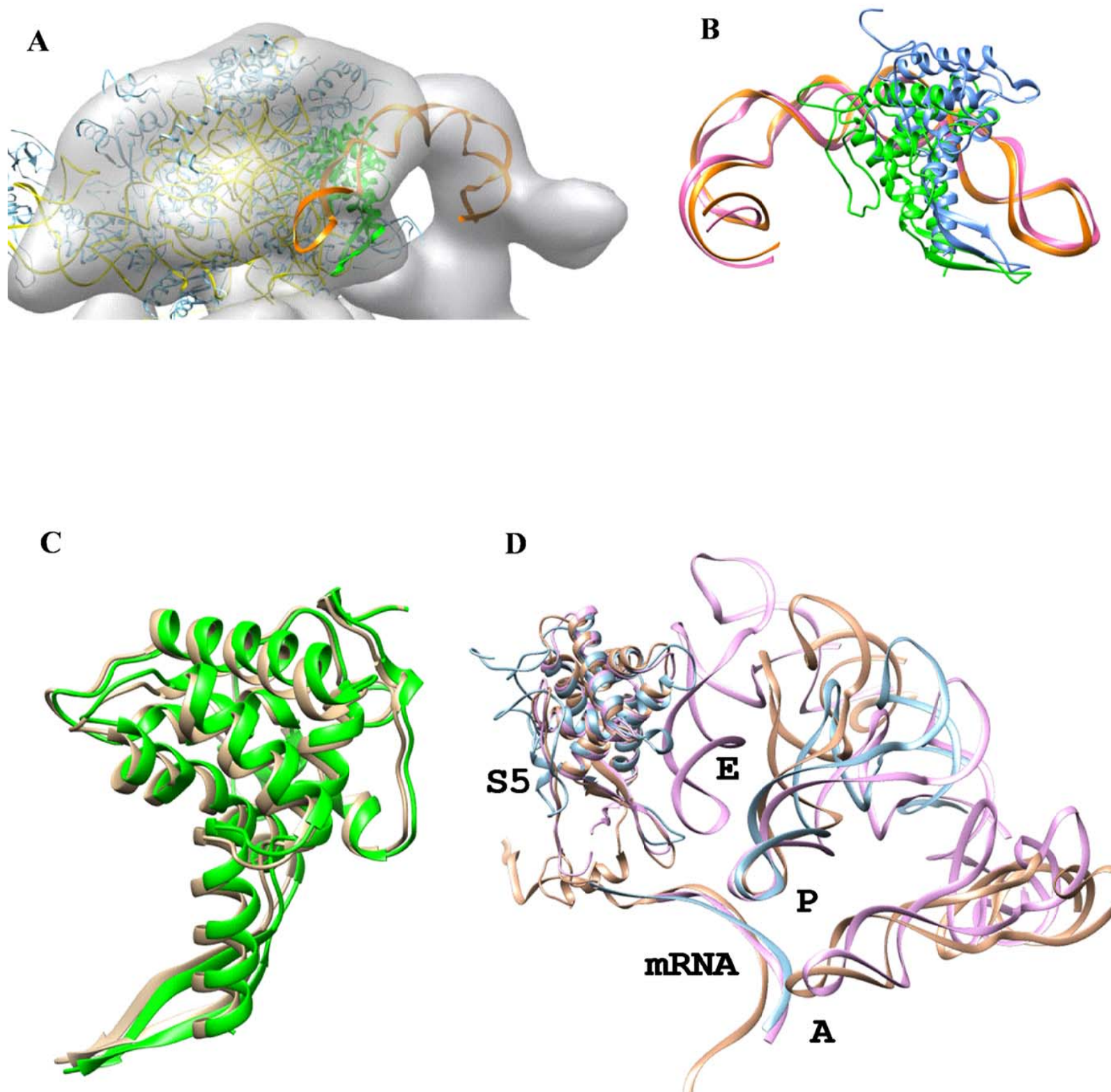


## Supplementary Figure S1



**Computational modeling of HCV IRES-RPS5 interactions.** (A) CryoEM derived model of RPS5 and domain II interaction. The figure highlights the Exit site region of 40S at the 80S interface. The relative orientation of RPS5 (green) and domain II (brown) obtained by optimizing the fit of human 40S ribosomal head (rRNA in yellow and proteins in blue) (39) and NMR model of domain II (PDB ID: 1P5O) (17), is shown. (B) Comparison of the cryoEM derived model (domain II in magenta and RPS5 in blue) with the docking based model (domain II in brown and RPS5 in green). (C) Comparison of S5 models obtained by fitting crystal structure of Tetrahymena 40S ribosomal subunit (orange) (45) and human 40S subunit (green) (39), in the IRES-80S complex cryoEM density (16). (D) Structural interactions between ribosomal protein S5 (prokaryotic S7), mRNA and E (magenta) site tRNA. The figure shows the superposition of ribosomal protein S7 from two crystals structures with PDB IDs 3J10 (20) (orange) and 2WDM (21) (magenta) and 4KZZ (44) (blue). The associated mRNA and tRNA coordinates (A, P and E site) are shown.

## Supplementary Table 1.

<b>Aminoacid:Nucleotide</b>	<b>Aminoacid:Nucleotide</b>	<b>Aminoacid:Nucleotide</b>
<b>R130: U340</b>	<b>R164: U91</b>	<b>Y188: A72,A73</b>
<b>A131: C341</b>	<b>N165: G71</b>	<b>K191: A73</b>
<b>T133: G87</b>	<b>I166: A70</b>	<b>K192: A73</b>
<b>V134: U86</b>	<b>K167: A70</b>	<b>R198: A74</b>
<b>R136: C84</b>	<b>K182: A99</b>	
<b>L103: G100</b>	<b>N186: U97</b>	

**List of amino acids of RPS5 and nucleotides of HCV IRES involved in HCV IRES-RPS5 interaction.**