

**S2 Table.** Mutations, corresponding amino acid substitutions and point accepted mutation (PAM) of the NS5A-coding region in the mutant spectra HCV p0 subjected to three passages in the absence of drug analyzed by ultra deep pyrosequencing<sup>a</sup>.

Amplicon A1			Amplicon A2			Amplicon A4		
Mutation <sup>b</sup>	Amino acid substitution <sup>c</sup>	PAM 250	Mutation <sup>b</sup>	Amino acid Substitution <sup>c</sup>	PAM 250	Mutation <sup>b</sup>	Amino acid Substitution <sup>c</sup>	PAM 250
A6260G <sup>d</sup>	I259V <sup>d</sup>	4	A6452G	N62D	2	G6959U	V231L	2
G6391A	-	-	A6491G	T75A	1	U7016C	Y250H	0
G6394A	-	-	A6578G	T104A	1	A7020G	D251G	1
A6452G	N62D	2	A6636G	Q123R	1	A7026G	D253G	1
A6453C	N62T	0	U6716C	F150L	2	A7074G	E269G	0
C6454A	N62K	1	C6753U	A162V	0	U7095C	V276A	0
			A6763U	-	-	G7117A	M283I	2
			G6766A	-	-	U7137C	L290P	-3
			C6767U	P167S	1	C7142U	P292S	1
			C6767G	P167A	1	A7148G	I294V	4
						U7149C	I294T	0
						A7150G	I294M	2
						C7152U	P295L	-3
						C7155U	S296L	-3
						A7158G	E297G	0
						G7159C	E297D	3
						U7160C	C298R	-4
						A7163G	M299V	2
						U7164C	M299T	-1
						U7167C	L300P	-3
						G7178A	G304R	-3
						A7207G	-	-
						A7215G	D316G	1
						G7240C	-	-
<b>Different mutations<sup>e</sup></b>	<b>6</b>		<b>Different mutations<sup>e</sup></b>	<b>10</b>		<b>Different mutations<sup>e</sup></b>	<b>24</b>	
Synonymous (%) <sup>f</sup>	2 (33.3)		Synonymous (%) <sup>f</sup>	2 (20)		Synonymous (%) <sup>f</sup>	2 (8.3)	
Non-synonymous (%) <sup>f</sup>	4 (66.6)		Non-synonymous (%) <sup>f</sup>	8 (80)		Non-synonymous (%) <sup>f</sup>	22 (91.6)	

<sup>a</sup>The population analyzed correspond to passage 3 of the infections described in Fig. 1 and Table 1 of the main text.

<sup>b</sup>The HCV genome residue numbering corresponds to the Jc1-1 genome (accession number #AB047639).

<sup>c</sup>Amino acid residues (single letter code) are numbered from N- to the C-terminus of NS5A.

<sup>d</sup>Mutations (and deduced amino acid substitutions) at the NS4B-coding region.

<sup>e</sup>Number of different mutations found comparing the sequence of each individual clone with the consensus sequence.

<sup>f</sup>Number of different synonymous and non-synonymous mutations; their percentage is indicated in parenthesis.