

1 **Supplementary Figure S1.**

2 **Nucleotide sequence of the genotype 6a neo subgenomic replicon**

3 The replicon sequence is based on the consensus nucleotide (nt) sequence of sixteen
4 genotype 6a genomes (supplementary Table S1) available in the European HCV
5 database. This replicon contains the following 12 elements: 1) GT6a 5'-UTR: 1-342 nt;
6 2) GT6a the first 48 nucleotides of core: 343-390 nt; 3) an AscI linker: 391-399 nt; 4) the
7 neomycin phosphotransferase II (neo) gene: 400-1194 nt; 5) an FseI linker: 1195-1212 nt;
8 6) the encephalomyocarditis virus (EMCV) IRES: 1213-1815 nt; 7) GT6a NS3: 1816-
9 3711 nt; 8) GT6a NS4A: 3712-3873 nt; 9) GT6a NS4B: 3874-4656 nt; 10) GT6a NS5A:
10 4657-6009 nt; 11) GT6a NS5B: 6010-7782 nt; and 12) GT2a JFH-1 3'-UTR: 7783-8021.

11 GCCAGCCCCCTTAACGGGGCGACACTCCGCCATTATCACTCCCCTGTGAGGAACTACTGTCTTC
12 ACGCAGAAAGCGTCTAGCCATGGCGTTAGTATGAGTGTCGTACAGCCTCCAGGCCCCCCCCCTC
13 CCGGGAGAGCCATAGTGGTCTGCGGAACCGGTGAGTACACCGGAATTGCCAGGATGACCGGG
14 TCCTTTCCATTGGATCAAACCCGCTCAATGCCTGGAGATTTGGGCGTGCCCCGCAAGACTGC
15 TAGCCGAGTAGCGTTGGGTTGCGAAAGGCCTTGTGGTACTGCCTGATAGGGTGCTTGCAGAGTG
16 CCCCAGGAGGTCTCGTAGACCGTGCATCATGAGCACACTTCCAAAACCCCAAAGAAAAACCA
17 AAAGAAACACCAACGGCGCGCCAATGATTGAACAAGATGGATTGCACGCAGGTTCTCCGGCC
18 GCTTGGGTGGAGAGGCTATTCGGCTATGACTGGGCACAACAGACAATCGGCTGCTCTGATGCC
19 GCCGTGTTCCGGCTGTCAGCGCAGGGGCGCCGGTCTTTTTGTCAAGACCGACCTGTCCGGT
20 GCCCTGAATGAACTGCAGGACGAGGCAGCGCGGCTATCGTGGCTGGCCACGACGGGCGTTCC
21 TTGCGCAGCTGTGCTCGACGTTGTCACTGAAGCGGGAAGGGACTGGCTGCTATTGGGCGAAGT
22 GCCGGGGCAGGATCTCCTGTCATCTCACCTTGCTCCTGCCGAGAAAGTATCCATCATGGCTGA
23 TGCAATGCGGCGGCTGCATACGCTTGATCCGGCTACCTGCCATTCGACCACCAAGCGAAACA
24 TCGCATCGAGCGAGCACGTA CTGGATGGAAGCCGGTCTTGTCGATCAGGATGATCTGGACG
25 AAGAGCATCAGGGGCTCGCGCCAGCCGAACTGTTCCGCCAGGCTCAAGGCGCGCATGCCCGAC

26 GCGAGGATCTCGTCGTGACCCATGGCGATGCCTGCTTGCCGAATATCATGGTGGAAAATGGC
27 CGCTTTTCTGGATTCATCGACTGTGGCCGGCTGGGTGTGGCGGACCGCTATCAGGACATAGCG
28 TTGGCTACCCGTGATATTGCTGAAGAGCTTGGCGGCGAATGGGCTGACCGCTTCTCGTGCTT
29 TACGGTATCGCCGCTCCCGATTTCGACGCGCATCGCCTTCTATCGCCTTCTTGACGAGTTCTTCT
30 GAGGCCGGCCGCGGCCGCAACAGACCACAACGGTTTCCCTCTAGCGGGATCAATTCCGCCCCC
31 CCCCCCTAACGTTACTGGCCGAAGCCGCTTGAATAAGGCCGGTGTGCGTTTGTCTATATGTT
32 ATTTTCCACCATATTGCCGTCTTTTGGCAATGTGAGGGCCCGGAAACCTGGCCCTGTCTTCTTG
33 ACGAGCATTCTAGGGGTCTTCCCTCTCGCCAAAGGAATGCAAGGTCTGTTGAATGTCGTG
34 AAGGAAGCAGTTCCTCTGGAAGCTTCTTGAAGACAAACAACGTCTGTAGCGACCCTTGCAGG
35 CAGCGGAACCCCCACCTGGCGACAGGTGCCTCTGCGGCCAAAAGCCACGTGTATAAGATAC
36 ACCTGCAAAGGCGGCACAACCCAGTGCCACGTTGTGAGTTGGATAGTTGTGGAAAGAGTCA
37 AATGGCTCTCCTCAAGCGTATTCAACAAGGGGCTGAAGGATGCCAGAAGGTACCCCATTTGTA
38 TGGGATCTGATCTGGGGCCTCGGTGCACATGCTTTACATGTGTTTAGTCGAGGTTAAAAAAC
39 GTCTAGGCCCCCCGAACCACGGGGACGTGGTTTTCCCTTTGAAAAACACGATACGCGTATGGCT
40 CCCATCACCGCGTATGCGCAGCAGACGAGGGGCTAGTCGGCACCATTGTGACCAGCCTAAC
41 CGGGCGTGACAAAAATGAGGTCGAAGGGGAGGTACAGGTGGTCTCCACGGCTACCCAATCCT
42 TCCTGGCGACCTCCATTAATGGTGTGTCATGTGGACTGTTTATCATGGGGCCGGTTCAAAGACTCT
43 CGCTGGACCGAAAGGACCAGTGTGTCAAATGTACACCAATGTGGACAAGGACCTAGTAGGAT
44 GGCCATCTCCCCGGGAGCAAGGTCGCTACCCCATGTACTTGTGGCTCTAGTGACCTCTATCT
45 GGTCACGAGGGAGGCCGACGTTATCCCCGCAAGGCGCAGGGGTGACAACCGTGCTGCCCTCC
46 TCTCTCCTAGGCCATAAGCACCTTGAAAGGCTCCTCGGGAGGCCCCATTATGTGTCCCTCGG
47 GGCACGTTGTGGGACTCTTCCGAGCTGCCGTATGCACAAGGGGTGTAGCAAAATCCTTAGATT
48 TTATCCCAGTGGAAAACATGGAGACGACTATGCGCTCTCCCTCATTACAGACAACCTCCACGC
49 CGCCTGCGGTGCCCCAGACCTATCAGGTAGGGTATCTGCACGCACCAACAGGCAGCGGAAAG
50 AGCACCCGTGTTCCGGCGGCGTACGCTAGCCAGGGCTACAAGGTGTTGGTCTTGAACCCATCG
51 GTGGCGGCAACGCTTAGCTTTGGCTCTTATATGAGGCAAGCTTACGGCGTGGAGCCGAATGTC
52 CGGACCGGGGTCAGGACTGTAACCACAGGGGGCGCTATCACGTA CTCCACATATGGGAAATT
53 CTTGGCCGATGGGGGATGTTCCGGAGGAGCGTACGACATCATCATCTGTGATGAGTGCCACTC

54 CACAGACCCTACGACGGTGTGGGCATTGGCACGGTTCTCGACCAGGCTGAGACTGCCGGGGT
55 TCGCCTTACTGTGCTCGCAACAGCAACGCCGCCGGGTTCTGTCACTGTCCCCATCCTAACATA
56 ACAGAGACAGCCCTCCCGACTACGGGAGAAATACCATTTTATGGAAAGGCCATCCCCCTGA
57 GTACATCAAAGGGGGAAGACATCTCATATTCTGTCACTCAAAGAAGAAGTGCGATGAGCTGG
58 CCGGGAAACTGAAATCACTCGGCTTAAACGCCGTGCGATTCTACAGAGGTGTCGATGTGTCCG
59 TCATCCCCACCTCGGGCGATGTCGTGCTGCGCAACAGACGCCCTTATGACCGGCTACACAG
60 GCGATTTTCGATTCCGTCATCGACTGTAACGTAGCCGTGACACAGGTGGTGGATTTAGCTTGG
61 ACCCAACATTTTCCATAGAGACTACCACCGTCCCTCAGGATGCGGTATCACGGAGCCAACGAC
62 GAGGCCGCACGGGGCGGGGTAAACCGGGGGTGTACAGATTTGTCTCCCAAGGGGAGAGGCCT
63 TCGGGTATGTTTCGACACCGTCGTCCTGTGTGAGGCTTATGACACGGGATGCGCGTGGTACGAA
64 CTAACCCCTTCTGAAACAACCTGTCAGGTTGAGGGCCTATATGAACACTCCTGGCCTTCCCGTA
65 TGCCAAGACCACCTGGAATTTTGGGAAGGCGTGTTTACTGGCTTGACTCACATAGACGCCAC
66 TTTCTGTCTCAGACGAAGCAGGGGGTGAAGACTTCGCGTACCTCGTGGCATAACCAGGCTACA
67 GTGTGCGCCAGGGCCAAAGCCCCCGCCTTCTTGGGATACGATGTGGAAGTGTCTCATCAGA
68 CTCAAACCCACCCTTACCGGCCCACTCCACTTTTGTATCGGCTGGGGGCCGTCCAAAATGAG
69 ATAATAACAACCCATCCAATAACCAAATACATCATGACCTGTATGTCTGCGGATTTGGAGGTT
70 ATCACCAGCACATGGGTCCTCGTGGGTGGAGTCCTAGCCGCGCTCGCAGCCTACTGCTTGTC
71 GTGGGCTGTGTTGTCATCTGTGGCAGGATAACTTTGACTGGCAAGCCTGCTGTTGTCCCTGATC
72 GCGAGATCTTATACCAGCAATTTGACGAGATGGAGGAGTGCTCTAGGCACATCCCCTACCTCG
73 CTGAGGGCCAGCAGATCGCCGAACAGTTCAGACAAAAGGTGTTGGGACTCCTCCAAGCGAGC
74 GCTAAGCAGGCAGAAGAAGCTGAAGCCTGCTGTCCATTCCGCGTGGCCTAGGGTGGAGGAGTT
75 TTGGAGGAAACACATGTGGAACCTTGTGTCAGCGGGATTTCAGTACTTGGCGGGCTTATCCACTCT
76 GCCCGGCAACCCAGCCGTGGCATCATTGATGTCATTTACAGCGTCGCTGACCAGTCCTCTGAG
77 GACTTCTCAGACCCTGCTCCTCAACATACTCGGCGGCTGGATAGCCACCCAAGTGGCTCCCC
78 CCCC GCGTCTACAGCTTTTGTGCTGAGCGGTCTAGCAGGAGCCACGGTTGGAAGCATCGGGCT
79 CGGGAGGGTGTGGTTGATGTGCTCGCCGATACGGAGCCGGTGTGTCGGGTGCTCTAGTCGC
80 TTTCAAGATCATGAGCGGCGAGTGCCCGACCACGGAAGACATGGTCAATCTGCTACCCGCGCT
81 GTTGTGCGCCAGGGGCTCTCGTGGTGGGGTTCGTGTGTGCTGCCATCTTAAGACGCCACGTTGG

82 CCCTGCTGAGGGTGCTAACCAGTGGATGAACAGGCTAATAGCCTTTGCATCAAGAGGCAACC
83 ACGTGTCCCCGACGCACTACGTGCCTGAGACTGACGCATCAAAAAATGTGACTCAGATACTCA
84 CTTCTCTTACCATCACCAGCCTACTCCGTAGATTACATCAGTGGGTCAATGAAGACACGGCCA
85 CCCCTTGCGCTACCTCATGGTTACGCGACGTGTGGGACTGGGTGTGTACAGTGTTATCTGATTT
86 TAAAGTATGGCTGCAAGCCAAACTTCTCCCTCGCCTGCCGGGGATCCCCTTCCTCTCGTGCCA
87 AACGGGATATAGGGGAGTCTGGGCAGGGGACGGGGTGTGCCACACCACTTGTACCTGTGGGG
88 CCGTGATAGCTGGACACGTCAAAAATGGCACCATGAAAATCACAGGGCCCAAGACATGCAGT
89 AACACTTGGCACGGGACTTTTCCAATCAACGCCACCACTACCGGCCCCAGCACACCACGACCA
90 GCCCCAACTATCAGCGCGCTCTTTGGCGGGTATCTGCCGAGGACTACGTTGAGGTACGGAGG
91 TTGGGCGACTGCCACTATGTGGTAGGGGTCACTGCTGAAGGGTTGAAGTGCCCTTGCCAGGTG
92 CCTGCGCCTGAATTCTTCACTGAGGTGATGGCGTGAGGATACACCGTTACGCGCCACCTTGC
93 AAGCCCTTGCTCAGGGACGAAGTGACTTTCTCTGTGGGTCTTTCAAATATGCCATAGGGTCG
94 CAGCTCCCTTGCGAGCCAGAGCCTGACGTGACCGTAGTCACCTCAATGCTCACAGACCCACG
95 CACATCACCGCAGAGACGGCAGCACGGCGGTTGAAGAGGGGGTCCCCCCCCTCCTTAGCCAG
96 CTCTTCGGCCATCCAGCTGTCTGCACCGTCCCTCAAGGCTACTTGCACAACCTTCCAAAGACCA
97 CCCGGACATGGAACCTCATCGAGGCCAACCTCCTTTGGAGGCAGGAGATGGGAGGCAACATCA
98 CTCGAGTCGAGTCAGAGAACAAAGTTGTAGTACTTGACTCCTTTGAGCCTCTAACCGCTGAGT
99 ATGACGAGAGGGAAATCTCAGTATCAGCTGAGTGCCATAGGCCACCCAGGCACAAATTCCT
100 CCAGCTCTCCAATATGGGCCAGGCCTGACTACAATCCACCTCTCCTACAAGCATGGCAAATG
101 CCCGGATACGAGCCTCCAGTCGTGTCTGGGTGTGCCGTGCCCCACCTAAACCGGCACCAATT
102 CCCCCGCCGAGGCGGAAGAGGCTAGTGCACTTGGATGAGTCCACGGTCTCGCACGCCTTGGC
103 GCAGCTCGCCGACAAGGTATTTGTGGAGAGTAGTAGTGACCCAGGACCTAGTTCAGACTCGG
104 GACTATCAATAACCAGTCCCGTTCCACCTGCCCAACAACACCGGACGACGCCTGCTCAGAAG
105 CAGAGTCCTATAGCTCAATGCCCCCTTTGAGGGGGAGCCTGGTGACCCTGACCTAAGCTCAG
106 GCTCTTGGTCCACTGTGAGCGATCAGGACGACGTCGTGTGTTGTTCCATGTCCTATTCCTGGAC
107 GGGGGCTCTAATAACACCATGTGCTGCGGAGGAGGAGAAGCTTCCAATAAATCCCCTGAGCA
108 ACTCCCTCATAAGACACCATAACATGGTGTATTCCACCACATCACGCAGCGCCAGCCTCCGCC
109 AGAAGAAGGTACATTTGACAGAGTGCAAGTGTTGACCAACATTATCAGGATGTACTAAAG

110 GAGATTAAGCTTCGAGCGTCCACGGTGCAGGCGAAGCTCCTATCCATAGAGGAAGCCTGCGA
111 CCTCACACCATCGCACTCAGCCCGGTCCAAATATGGGTATGGTGCACAGGACGTTAGAAGCCA
112 TGCTAGCAAGGCCGTTGACCACATCCGCTCCGTGTGGGAGGACTTGCTAGAAGACTCTGATAC
113 CCCAATTCCCACGACCATCATGGCTAAGAATGAAGTCTTCTGCGTAGATCCGTCGAAGGGTGG
114 ACGCAAGCCGGCACGCCTAATAGTTTACCCAGACTTGGGCGTGCGGGTCTGCGAGAAGATGG
115 CCCTATACGACGTGACGCGGAAGTTACCACAGGCCGTGATGGGTTTACGCATACGGATTCCAGT
116 ACTCCCCTAACCAGAGGGTTGAGTACTTGCTCAAAATGTGGCGGTCAAAGAAGGTGCCCATG
117 GGCTTTTCTTACGACACCAGGTGTTTTGATTCAACCGTCACCGAGCGGGATATCCGGACTGAG
118 AACGACATCTATCAGTCTTGCCAGCTGGATCCCGTGGCAAGGAAGGCAGTATCATCCCTAACA
119 GAACGGCTCTACGTAGGCGGCCCCATGGTAAACTCCAAGGGACAGTCATGTGGCTACCGTAG
120 ATGCCGCGCCAGTGGGGTGCTGCCACGAGCATGGGAAACACCCTCACATGCTATCTGAAGG
121 CACAGGCCCGCTGCAGGGCGGCCAACATCAAGGACTGTGACATGTTGGTGTGCGGAGATGAC
122 TTAGTGGTCATTTGTGAGAGTGCTGGCGTCCAGGAGGACACTGCGTCACTGCGAGCATTACG
123 GATGCTATGACCAGGTACTCAGCTCCCCCTGGAGACGCCCCGCAACCTACGTATGACCTTGAG
124 CTCATAACATCGTGCTCATCCAATGTCTCCGTCGCCCACGACGGCAATGGGAAGAGATATTAC
125 TACCTCACACGTGACTGTACCACTCCACTTGCGCGGGCCGCTGGGAGACAGCCCGCCACACT
126 CCAGTCAATTCGTGGTTGGGCAACATCATTATGTTTGGCCCCACGATATGGGTGCGTATGGTTC
127 TGATGACCCATTTTTTCTCCATCCTCCAGTCGCAAGAACAATTGGAGAAAGCACTCGACTTTG
128 ACATCTACGGAGTGACCTATTCCGTCTCTCACTTGATCTCCAGCAATCATTCAACGACTCCA
129 TGGCATGGCAGCATTTTCACTCCACGGATACTCTCCAGTTGAGCTCAATAGGGTAGGGGCTTG
130 CCTCAGGAAACTTGGGGTACCTCCCTTGCGAGCCTGGAGACATCGAGCCAGAGCTGTCAGAG
131 CCAAACCTCATTGCCCAAGGGGGGAAAGCGGCTATATGCGGTAAGTACCTCTTCAACTGGGCG
132 GTGAAGACCAAACATAAACTCACTCCATTGGTCTCCGCGAGCAAGCTTGACTTATCAGGCTGG
133 TTCGTGGCAGGCTACGACGGGGGGGACATTTATCACAGCGTGTCCAGGCTCGACCCCGTCTC
134 TTA CTCTTGGCCTACTCCTACTCACCGTAGGGGTAGGCATCTTTTTGCTCCCCGCTCGGTAGA
135 GCGGCACACACTAGGTACACTCCATAGCTAACTGTTCTTTTTTTTTTTTTTTTTTTTTTTTTTT
136 TTTTTTTTTTTTTTTCTTTTTTTTTTTTTTCCCTCTTCTCCCTTCTCATCTTATTCTACTTTCTTT

137 CTTGGTGGCTCCATCTTAGCCCTAGTCACGGCTAGCTGTGAAAGGTCCGTGAGCCGCATGACT

138 GCAGAGAGTGCCGTAACGGTCTCTCTGCAGATCATGT

139

140

141

142

143

144

145

146

147

148

149

150

151

152

153

154

155

156

157

158 **Supplementary Table S1.**

159 **The list of sixteen genotype 6a genomes in the European HCV database**

160 **used to generate consensus for the genotype 6a subgenomic replicon**

Accession #	Virus Isolate	Sequence Length	Note
AY859526	6a33	9355	Complete coding sequence; no 3'-UTR
DQ480512	6a77	9358	Complete coding sequence; no 3'-UTR
DQ480513	6a35	9358	Complete coding sequence; no 3'-UTR
DQ480514	6a63	9358	Complete coding sequence; no 3'-UTR
DQ480515	6a64	9358	Complete coding sequence; no 3'-UTR
DQ480516	6a61	9358	Complete coding sequence; no 3'-UTR
DQ480517	6a73	9358	Complete coding sequence; no 3'-UTR
DQ480518	6a65	9358	Complete coding sequence; no 3'-UTR
DQ480519	6a66	9358	Complete coding sequence; no 3'-UTR
DQ480520	6a67	9358	Complete coding sequence; no 3'-UTR
DQ480521	6a69	9358	Complete coding sequence; no 3'-UTR
DQ480522	6a72	9358	Complete coding sequence; no 3'-UTR
DQ480523	6a62	9358	Complete coding sequence; no 3'-UTR
DQ480524	6a74	9361	Complete coding sequence; no 3'-UTR
EU246930	D9	9376	Complete coding sequence; no 3'-UTR
Y12083	EUHK2	9340	Complete coding sequence; no 3'-UTR

161 The consensus sequence shown in supplementary Figure S1 was generated using Vector

162 NTi software (Invitrogen)

163

164

165

166

167 **Supplementary Table S2.**

168 **Mutations identified in stable GT6a replicon colonies**

Cells	Replicon Clone#	NS3	NS4A	NS5A	NS5B
1C	1	K272R			
	2		K34R		
	3	K272R			
	4	D405Y		L361P	
	5	K272R			
	6	E30V(E)			
	7	P89L			
	8	K272R			
	9	E110V			
	10	Q195P			
	11	K272R			
Lunet	1	T580A/T621A(T)			
	2				I11V
	3	T621A			
	4	T261P			
	5	T312P			
	6		E52V		
	7		K34R		
	8	T76I			
	9		K34R		
	10	E30V(E)			
	11		L31V		
	12	K272R			

169 The selected GT6a replicon clones were expanded and subjected to genotypic analysis.

170 Only amino acid changes were indicated in the table.