

Supplementary Table 1.

Primers used for amplification of HCV E2 region

Sequence (5' – 3') ¹	Use
Genotype 1a/1b/3a	
GCAACAGGGAACCTTCCTGGTTGCTC	outer fwd PCR primer, low viral load
Genotype 1a/1b	
CCGGTTCATCCAYTGC	Reverse transcription (RT), high viral load ²
GCADBTGCGCYTCBRCYCTGGT	RT, low viral load ³
ACTGTCTTCACGCAGAAAGCGTCTAGC	outer fwd PCR primer, high viral load
CTCCAGGTCRCCGACATGCA	outer rev PCR primer, high viral load
GGGGACAAGTTTGTACAAAAAAGCAGGCTTCACCATGGGTTGCTCTTTCTCTATC	inner fwd PCR primer, high viral load
Genotype 1a	
CGCCTCCGCTTGGGATATGAG	outer rev PCR primer, low viral load
GGGGACAAGTTTGTACAAAAAAGCAGGCTTCACCATGTGGGGGTCCTGGCGGGC	inner fwd PCR primer, low viral load
GGGGACCACTTTGTACAAGAAAGCTGGGTCCTACGCCTCCGCTTGGGATATGAG	inner rev PCR primer, high and low viral load
Genotype 1b	
GGCCTCRGCTYGRGCTATYAG	outer rev PCR primer, low viral load
GGGGACAAGTTTGTACAAAAAAGCAGGCTTCACCATGTGGGGAGTCCTAGCGGGC	inner fwd PCR primer, low viral load
GGGGACCACTTTGTACAAGAAAGCTGGGTCCTAGGCCTCRGCTYGRGCTATYAG	inner rev PCR primer, low viral load
Genotype 3a	
GYCTGTTTCATCCACTG	RT, high viral load
TGCTTCTGCGTGTGATATCAT	RT, low viral load
TCTGTCTTCACGCGGAAAGCGYCTAGC	outer fwd PCR primer, high viral load
TTCCAGATCRGCTGACATGCA	outer rev PCR primer, high viral load
GGGGACAAGTTTGTACAAAAAAGCAGGCTTCACCATGGGTTGCTCCTTTTCTAT	inner fwd PCR primer, high viral load
GGGGACCACTTTGTACAAGAAAGCTGGGTCCTATGCTTCTGCGTGTGATATCAT	inner rev PCR primer, high and low viral load
TGCTTCTGCGTGTGATATCAT	outer rev PCR primer, low viral load
GGGGACAAGTTTGTACAAAAAAGCAGGCTTCACCATGTGGGGGTCCTGGCGGGC	inner fwd PCR primer, low viral load

¹ Outer primers were designed to include Gateway Cloning (Invitrogen) attb1 and attb2 sequences for recombination into destination vectors, a Kozak sequence and ATG codon, and a stop codon after the last amino acid in E2 for future expression in eukaryotic cells.

² viral load of plasma sample greater than 3,000 IU/ml

³ viral load of plasma sample less than 3,000 IU/ml

Supplementary Table 2. Sequences of peptides recognized by initial and new T cell responses.

Reinfected Subjects

Reinfection outcome: Cleared

Subject 57	
Initial T cell responses	New T cell responses
KLVALGINAV	DYPYRLWHY
CINGVCWTV	DLMGYIPLV
VLSDFKTWL	AASLAGTHGLVSFLVF
RLWHYPCTV	RDAVILLMCVVHPTLV
GPRLGVRAT	GRHLIFCHSKKKCDEL
YYRGLDVSVI	NTCVTQTVDFSLDPTF
TDFAQGWGPISYANGSGL	ETTVRLRAYMNTPLG
GLIHLHQNIVDVQYLY	GENFPYLVAYQATVCA
LQYFLTRVEAQLHVWV	QWMNRLIAFASRGNHV
	WLKAKLMPQLPGIPFV
	INALSNLLRHHNLVY
	STTSRSACQRQKKVTF

Subject 133	
Initial T cell responses	New T cell responses
TPMGFSYDTRCFDSTV	ADTAACGDIINGLPV
YPPKPCGI	HPNIEEVAL
	LVAYQATVCARAQA
	EPDVAVLTSMLTDPSH
	VESENKVVILDSFDPL
	ILRKSRRFARALPVWA
	LPLAVMGSSYGFQY

Subject 180	
Initial T cell responses	New T cell responses
ALYDVVTKL	AEEYVEIRRVGDFHYV
	GKYLFNWAVRCLKL

Reinfection outcome: Persistent

Subject 18	
Initial T cell responses	New T cell responses
ALYDVVTKL	GIDPNIRTGV
QPEKGGRKPA	RDWAHNGL
RLWHYPCTV	LEDRDRSEL
CINGVCWTV	MMMNWSPTT
KLVALGINAV	WSPTAALVVAQLLRI
AVFGPLWIL	

Chronically-Infected Subjects

Same virus

Subject 17	
Initial T cell responses	New T cell responses
EPEPDVAVL	LNVRGGRDAVILLMCV
KLVALGINAV	
HPNIEEVAL	
HPTLVFDIT	
GEIPFYGKAI	
CSIYPGHITGHRMAW	
EECSQHLPYIEQGMMML	

Viral Switch

Subject 50	
Initial T cell responses	New T cell responses
RLWHYPCTV	LTPAETTVRLRAYM
ALYDVVTKL	LVAYQATVCARAQA
CINGVCWTV	
KLVALGINAV	
QGMMLAEQFKQKALGL	

Subject 51	
Initial T cell responses	New T cell responses
MMMNWSPTT	GLQDCTMLV
YPPKPCGI	ALYDVVTKL
RLIVFPDLGV	CINGVCWTV
	CSIYPGHITGHRMAW

Subject 30	
Initial T cell responses	New T cell responses
CINGVCWTV	RLIVFDLGV
DYPYRLWHY	
SPVVVGTDDRSGAPTY	
TTDRSGAPTYSWGA	

Supplementary Figure Legends

Supplementary Figure 1. Graphs demonstrating the history of viremia and plasma ALT levels in reinfected subjects. HCV genotype of primary infection and reinfection are indicated and the time over which a unique virus is detected is denoted by a horizontal black line. Black circles represent HCV RNA concentrations (IU/ml) detected in serum or plasma samples obtained at given time points from date of first detection of viremia. Dotted-line denotes the HCV RNA limit of detection. Samples below the HCV RNA limit of detection were assigned a value of 25 IU/ml. Black triangles denote ALT activity (IU/ml) detected in plasma samples obtained at given time points from date of first detection of viremia.

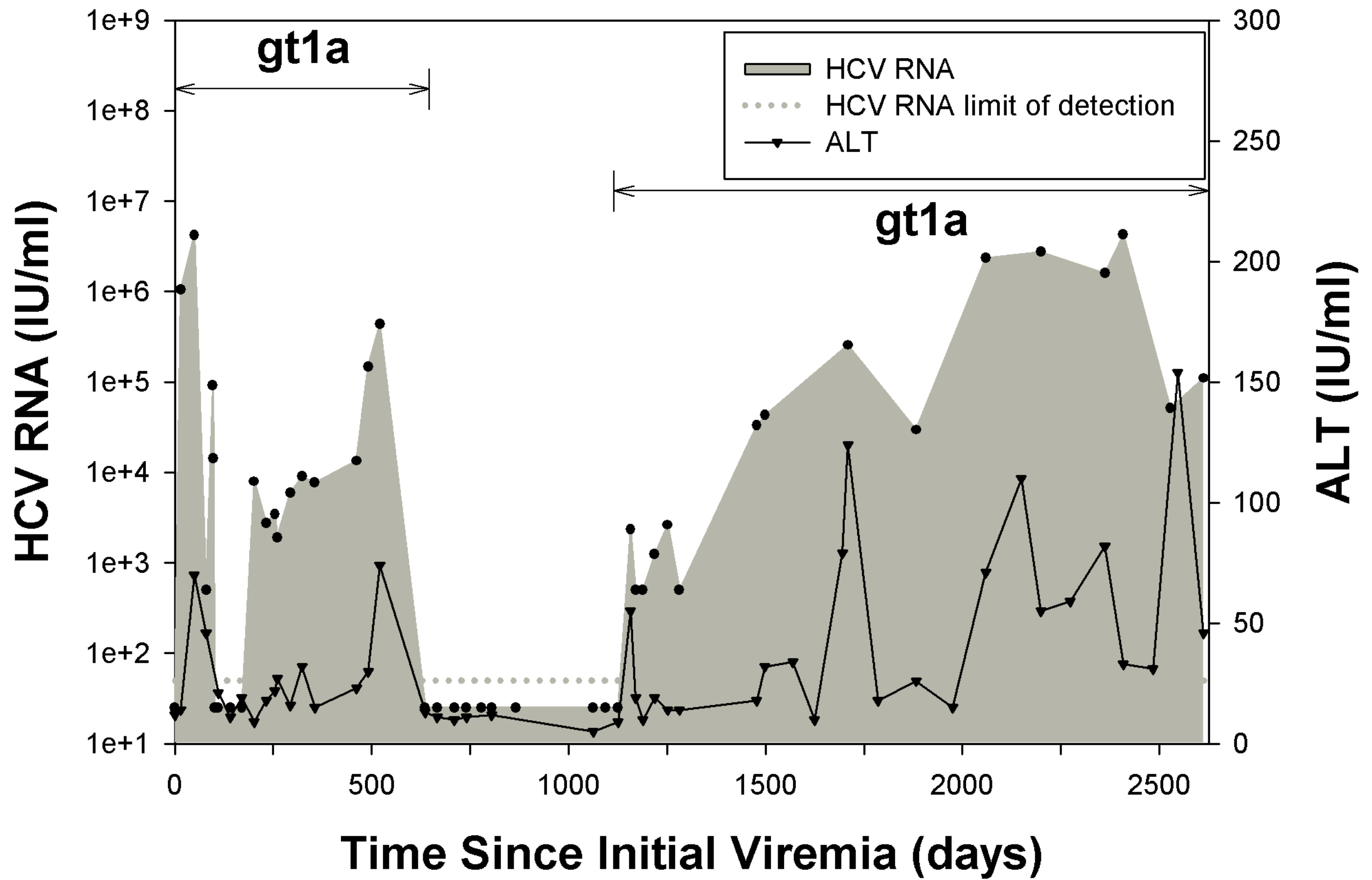
Supplementary Figure 2. Graphs demonstrating nAb titers in reinfected subjects. Solid line represents the reciprocal ID50 nAb titer against a genotype 1a HCVpp (H77). Samples with undetectable nAb titers were assigned a reciprocal titer of 25. Black circles represent HCV RNA concentrations (IU/ml) detected in serum or plasma samples obtained at given time points from date of first detection of viremia. Dotted-line denotes the HCV RNA limit of detection. Samples below the HCV RNA limit of detection were assigned a value of 25 IU/ml.

Supplementary Figure 3. A) Peptides recognized by new T cell responses in reinfected subjects are evenly distributed across the HCV polyprotein. * - the location of a peptide recognized by a reinfected subject who clears reinfection; X

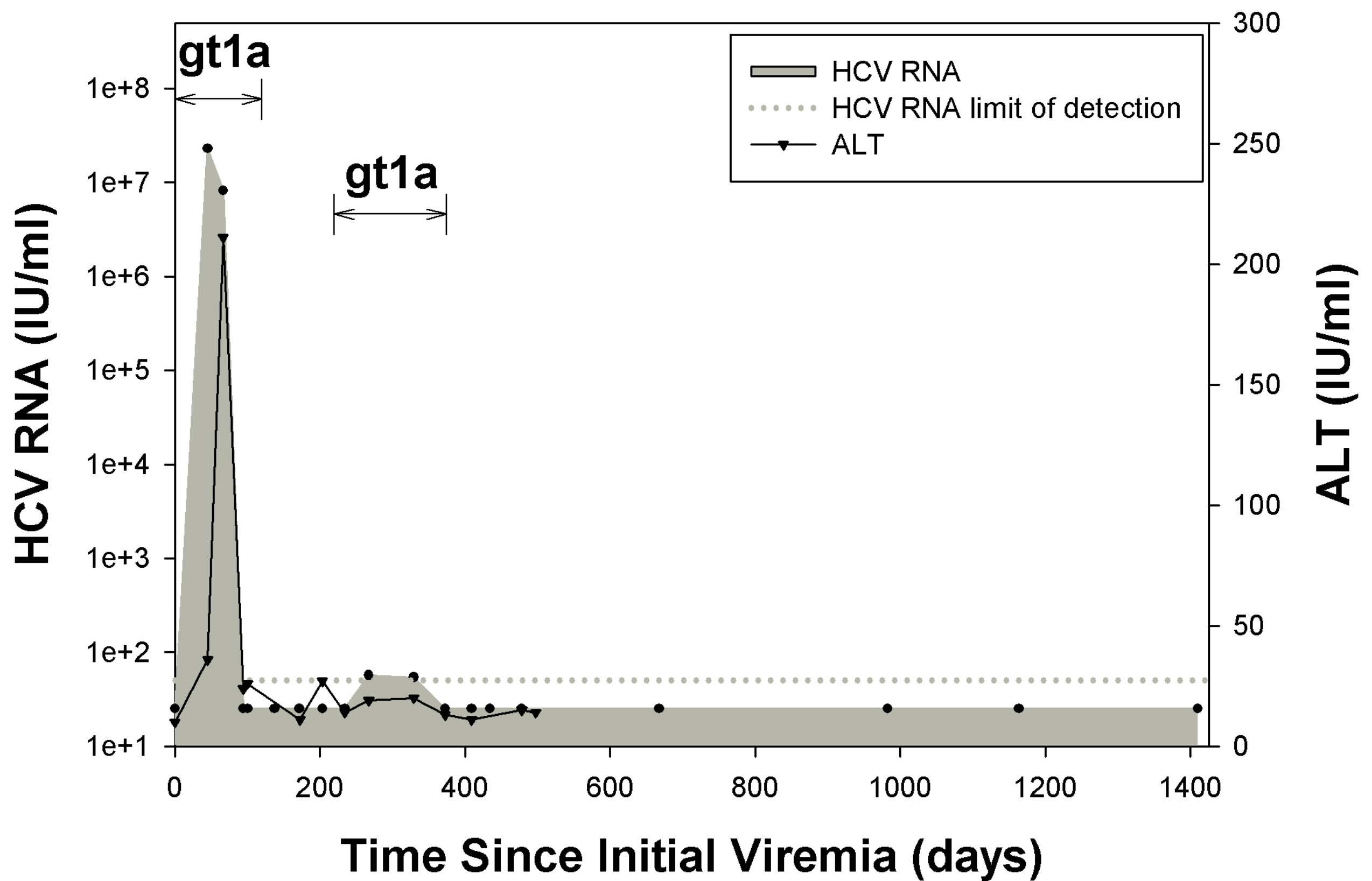
- the location of a peptide recognized by a persistently reinfected subject. Two asterisks at the same location indicate recognition of the same peptide by two subjects. B) Linear regression for reductions in maximum viremia during reinfection and the number of new T cell responses in reinfected subjects. Values represent the reduction (\log_{10} , fold-change) in maximum viremia from initial infection to reinfection. R^2 - and P -values for correlation are denoted. C) Linear regression for increases in ALT upon reinfection and the number of new T cell responses in reinfected subjects upon reinfection. Values represent the increase (fold-change) in ALT from baseline to reinfection. R^2 - and P -values for correlation are denoted.

Supplementary Figure 1 part 1

Subject 18

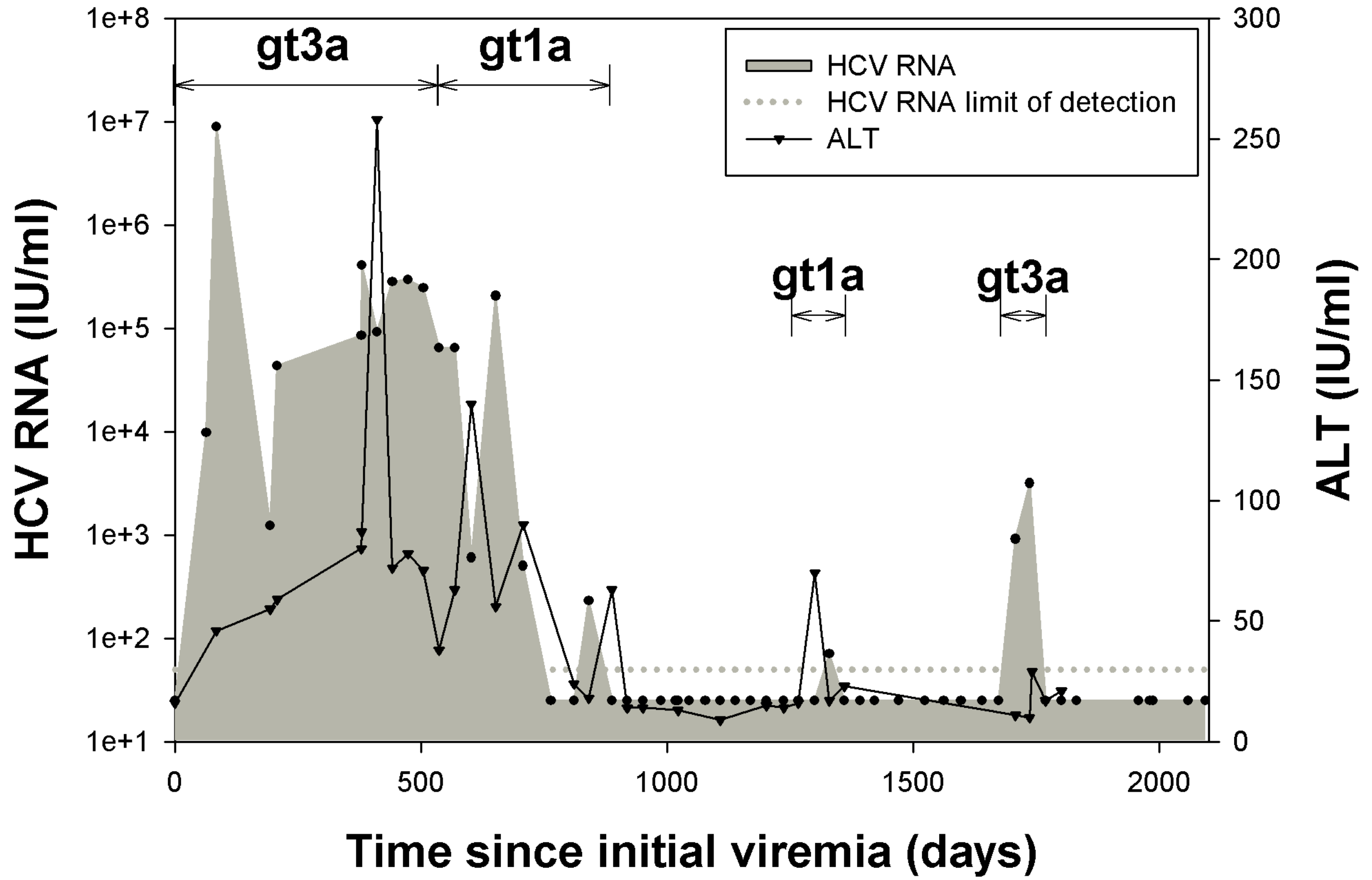


Subject 57

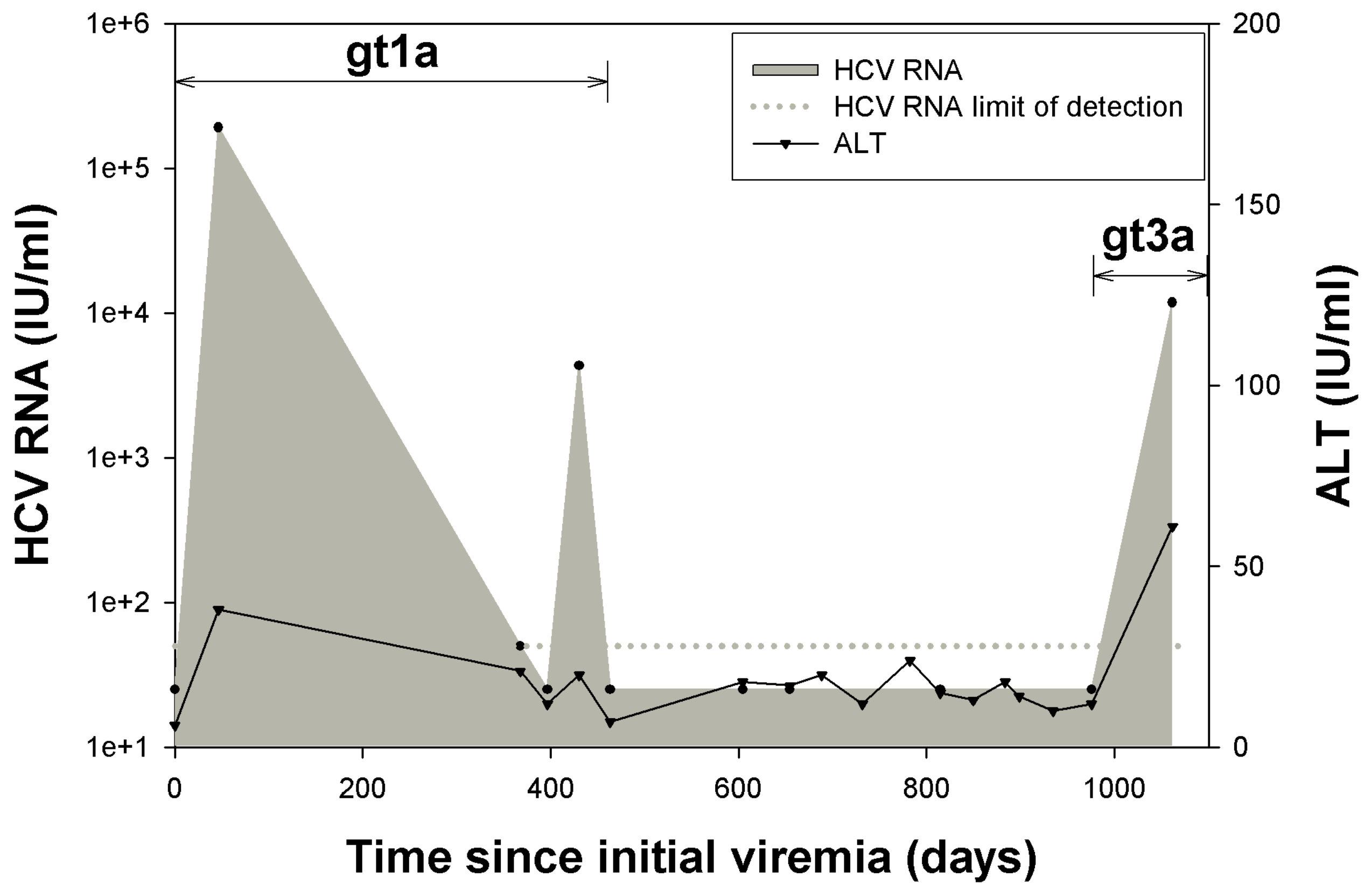


Supplementary Figure 1 part 2

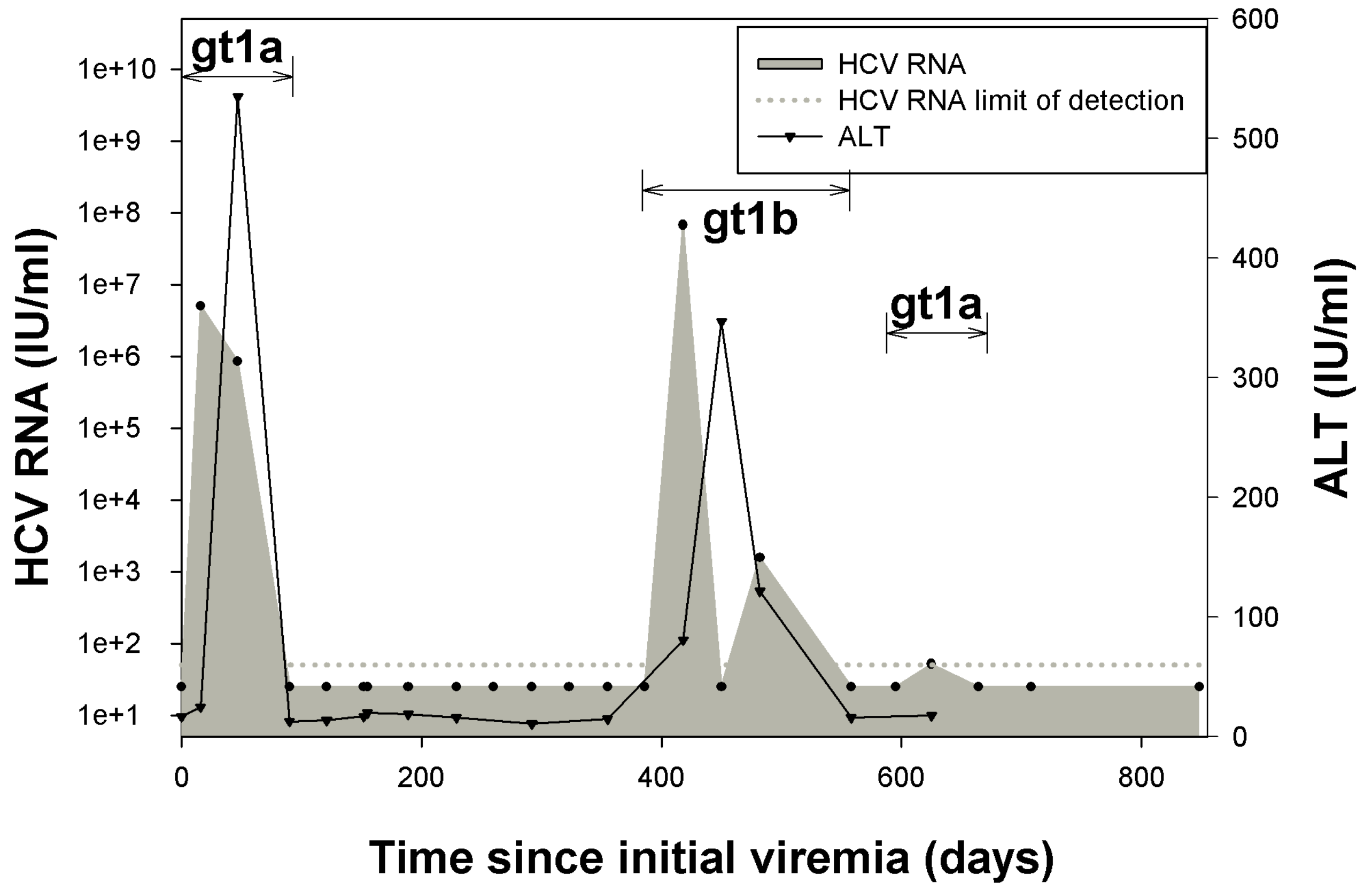
Subject 48



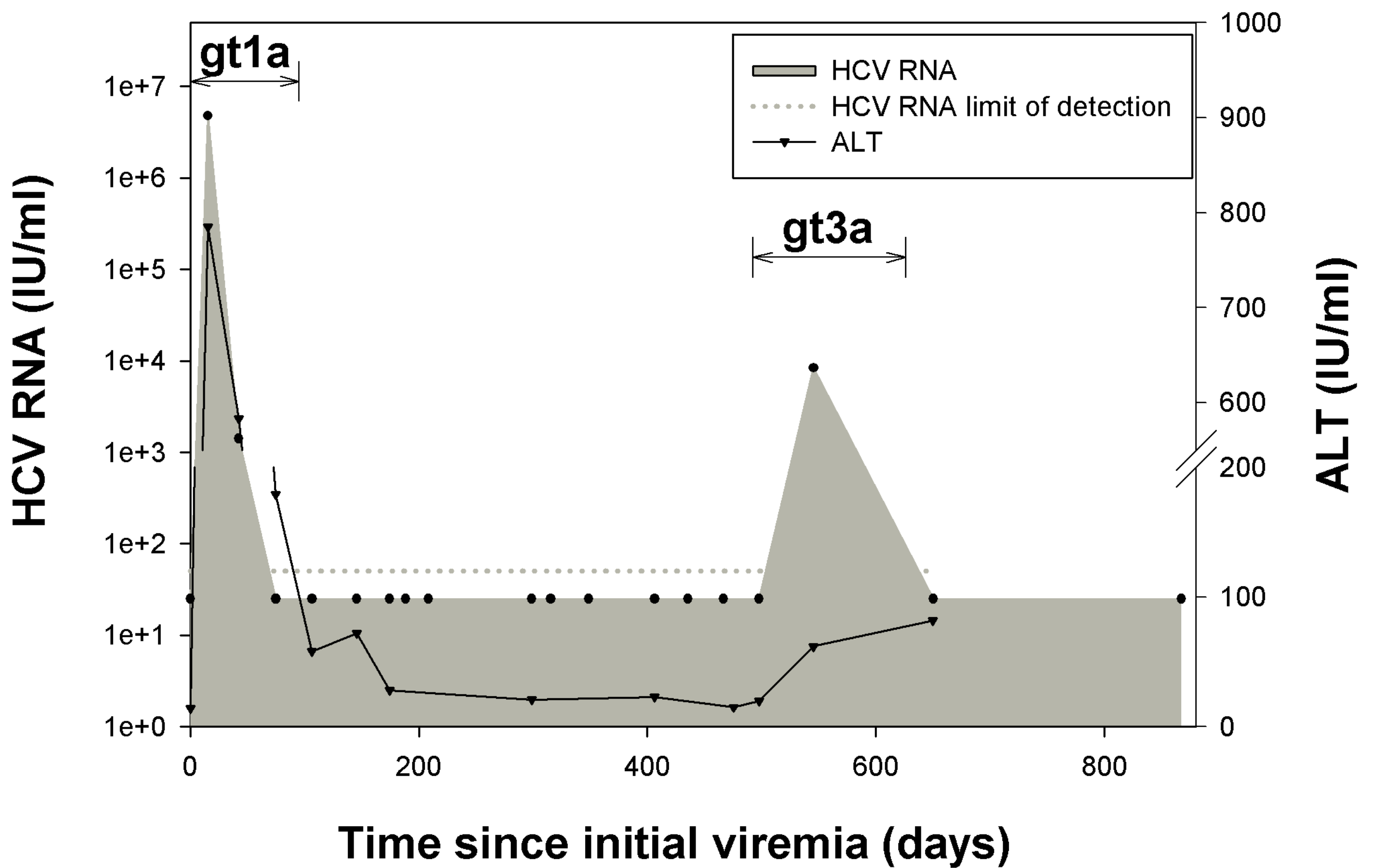
Subject 170



Subject 152

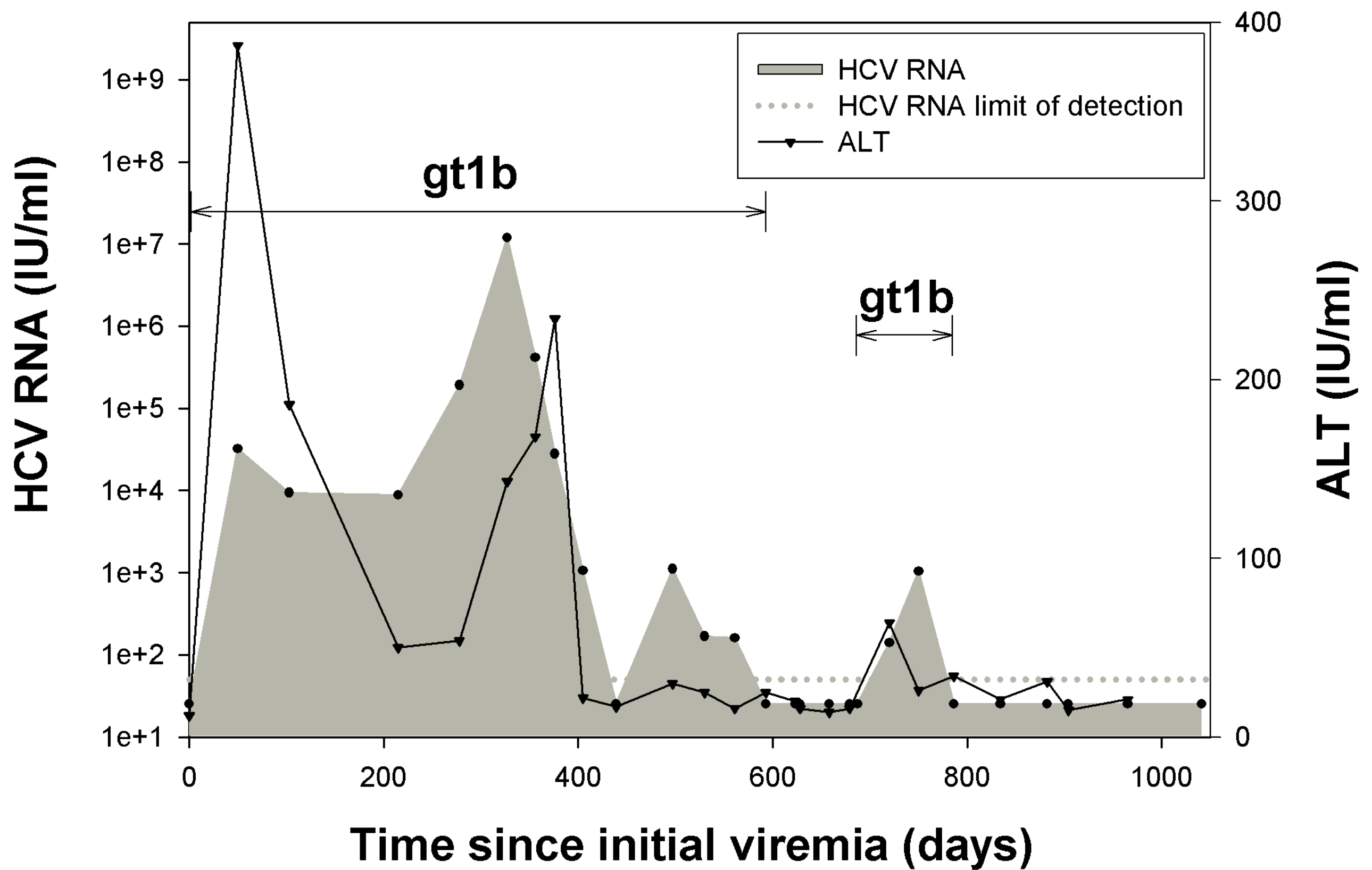


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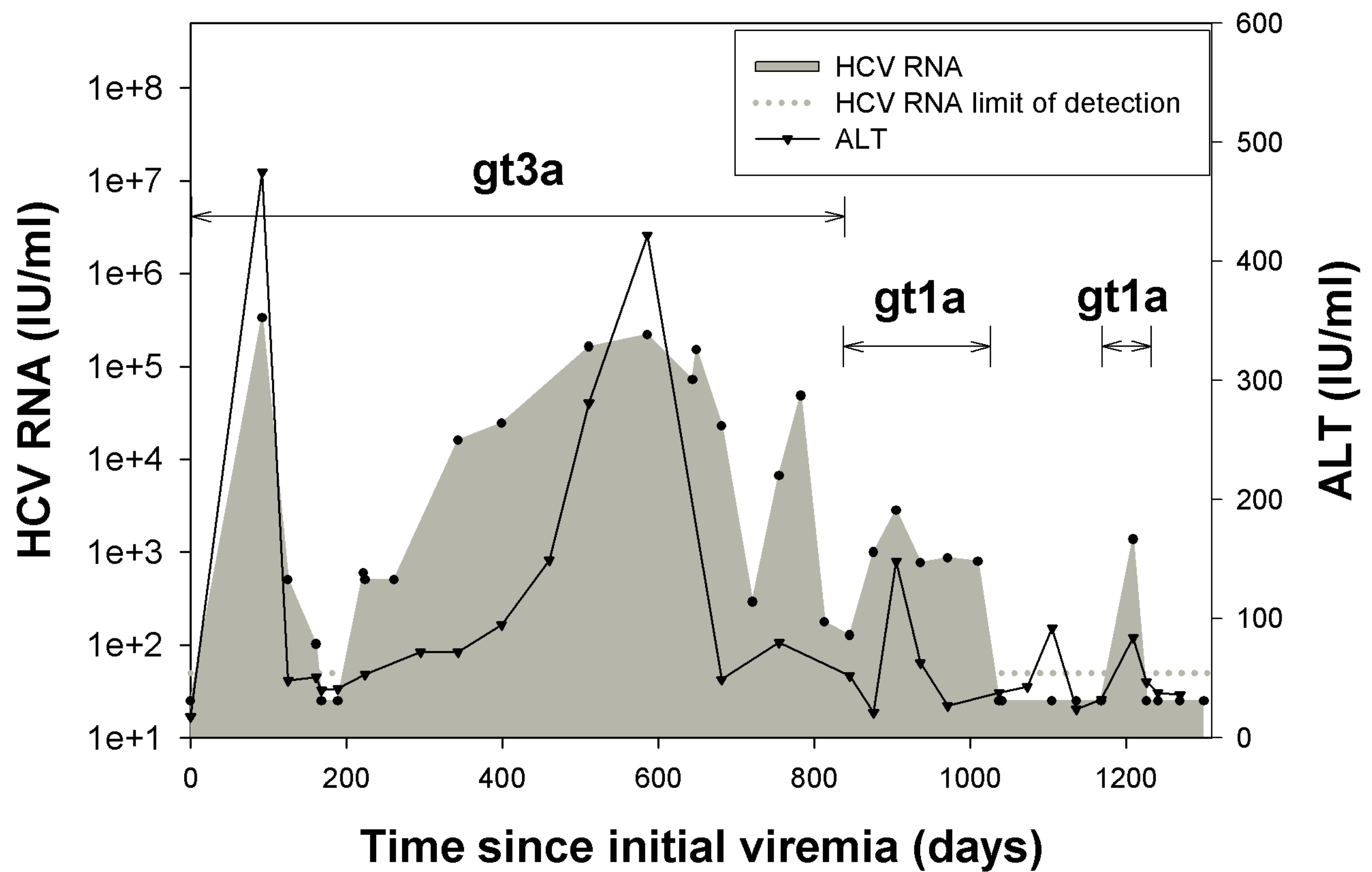


Supplementary Figure 1 part 4

Subject 172

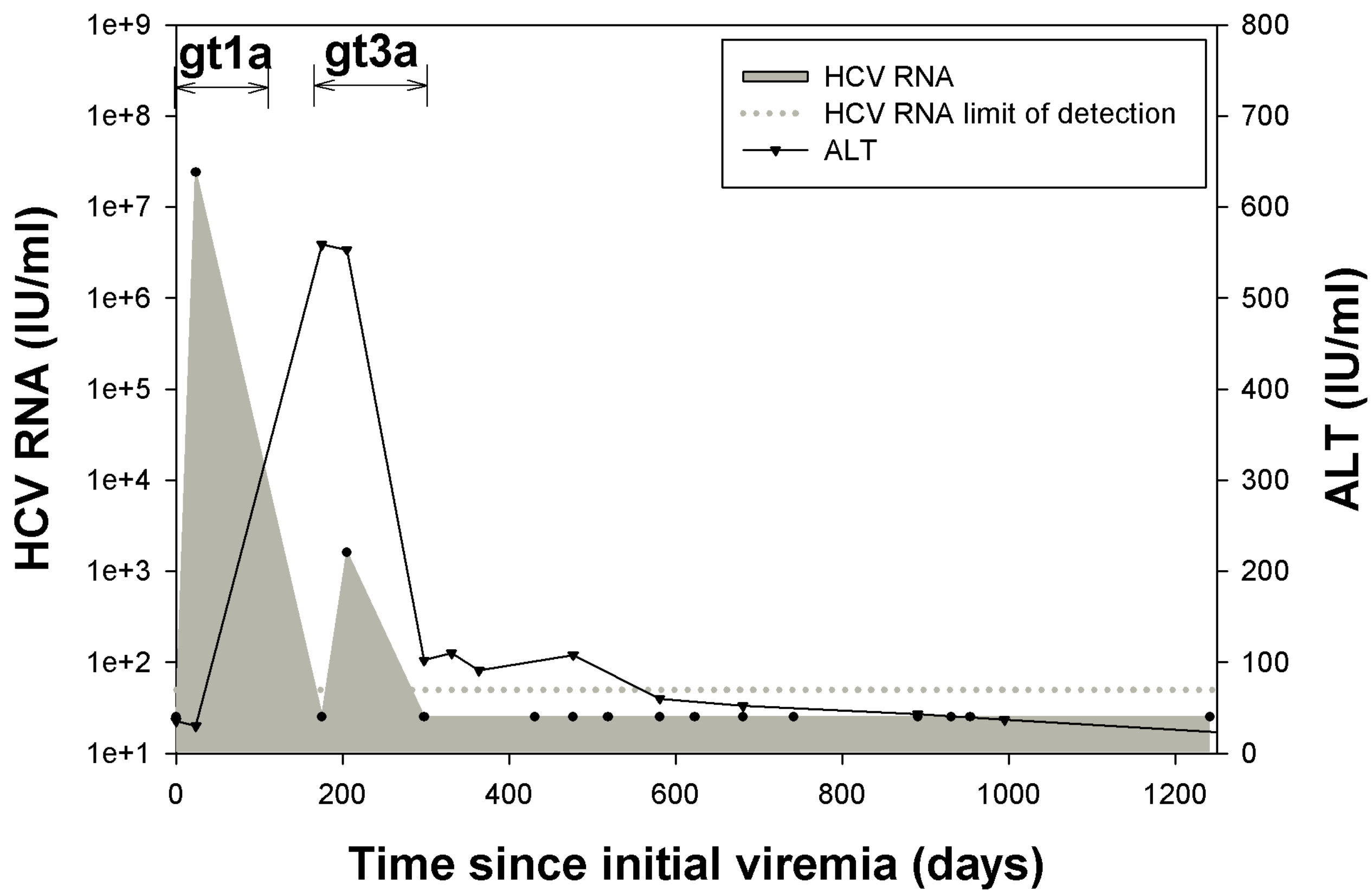


Subject 112



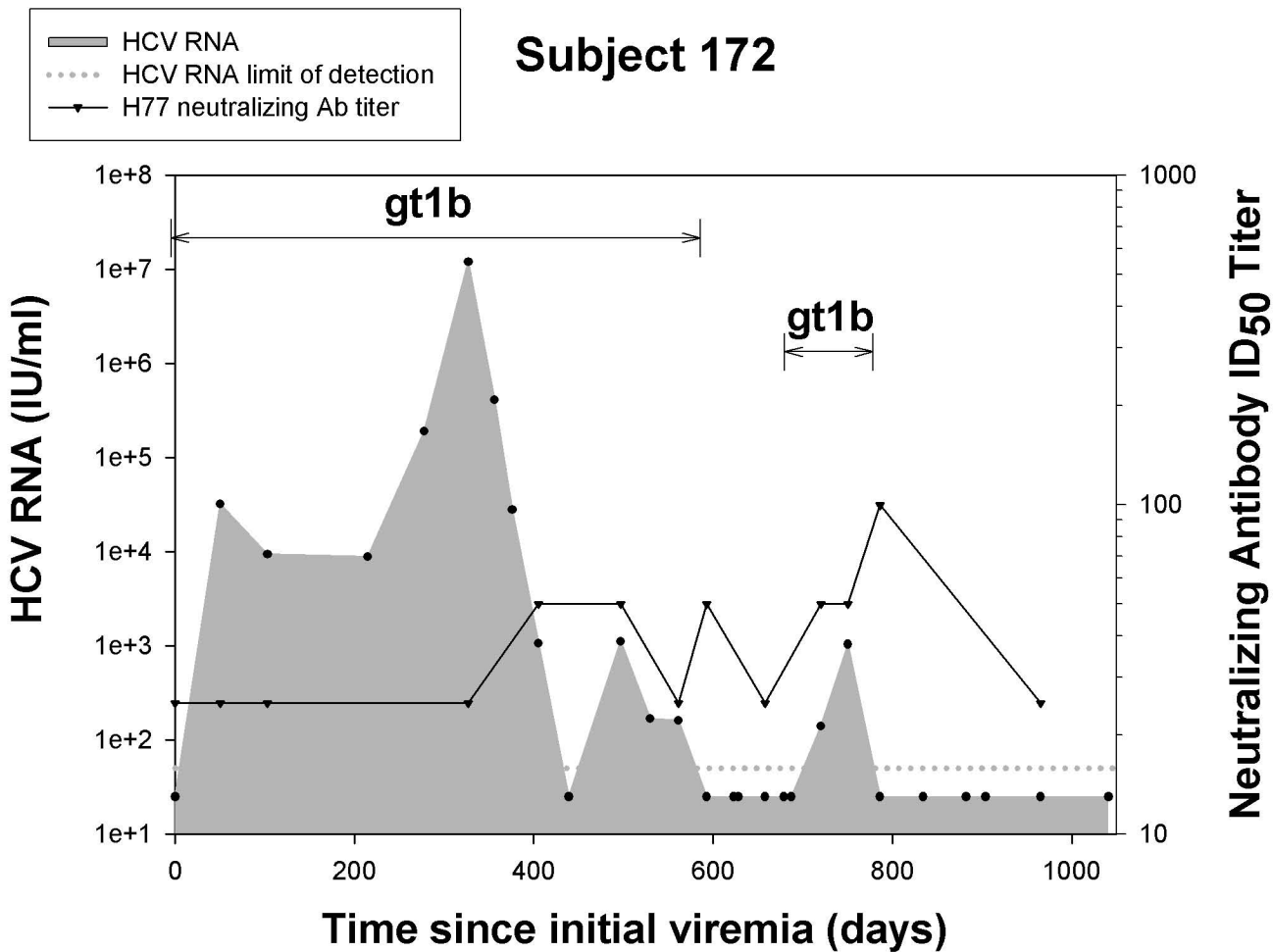
Supplementary Figure 1 part 5

Subject 27

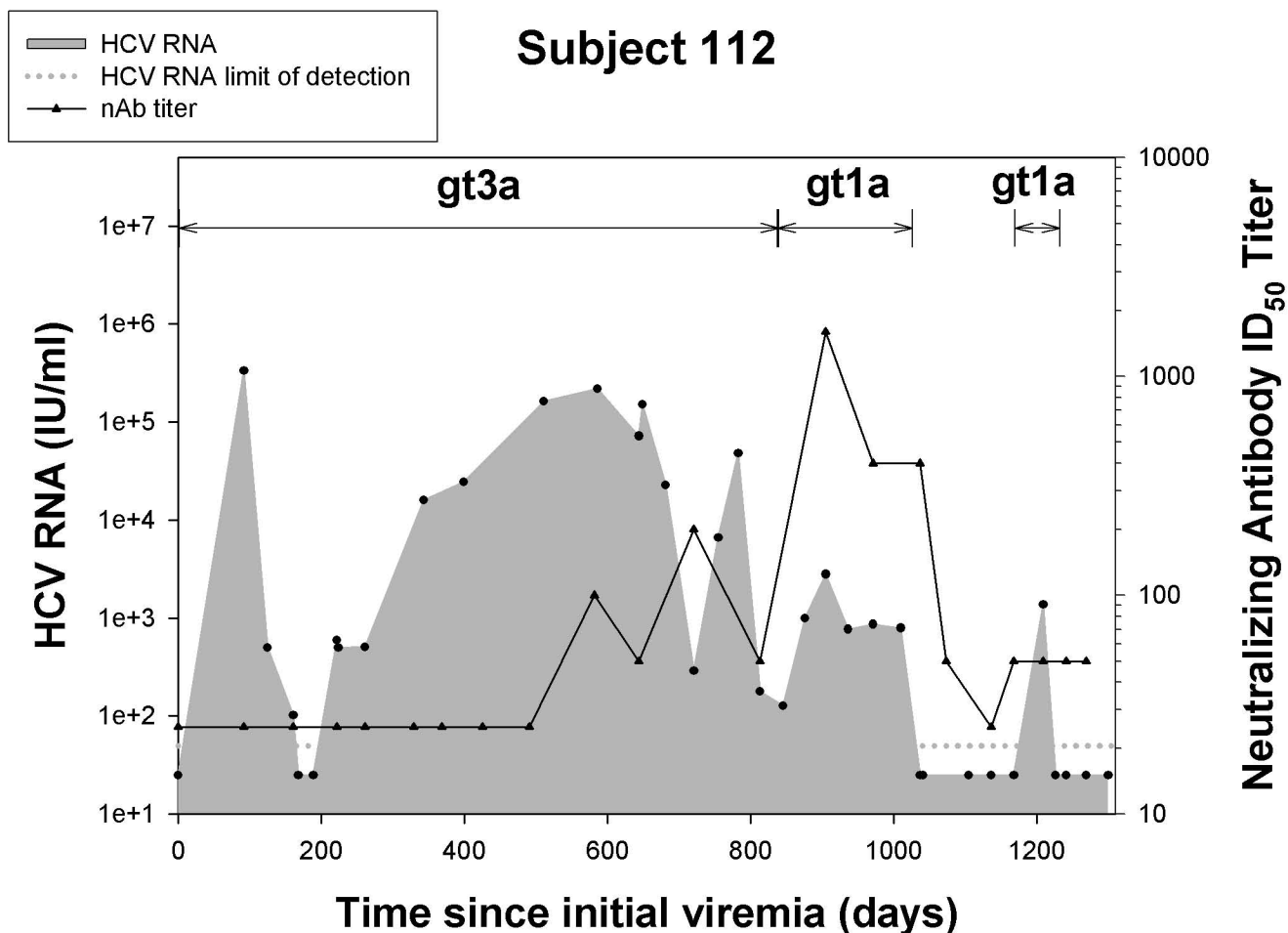


Supplementary Figure 2 part 1

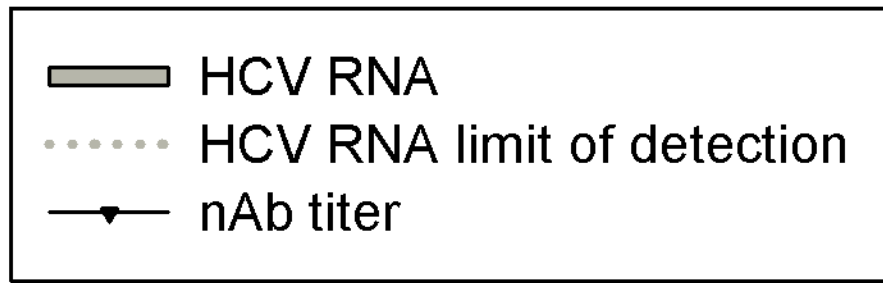
Subject 172



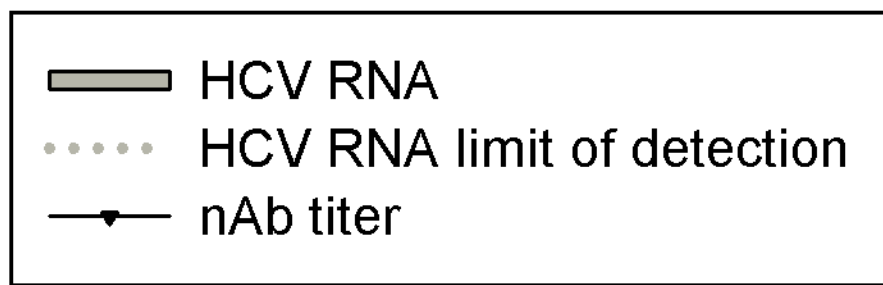
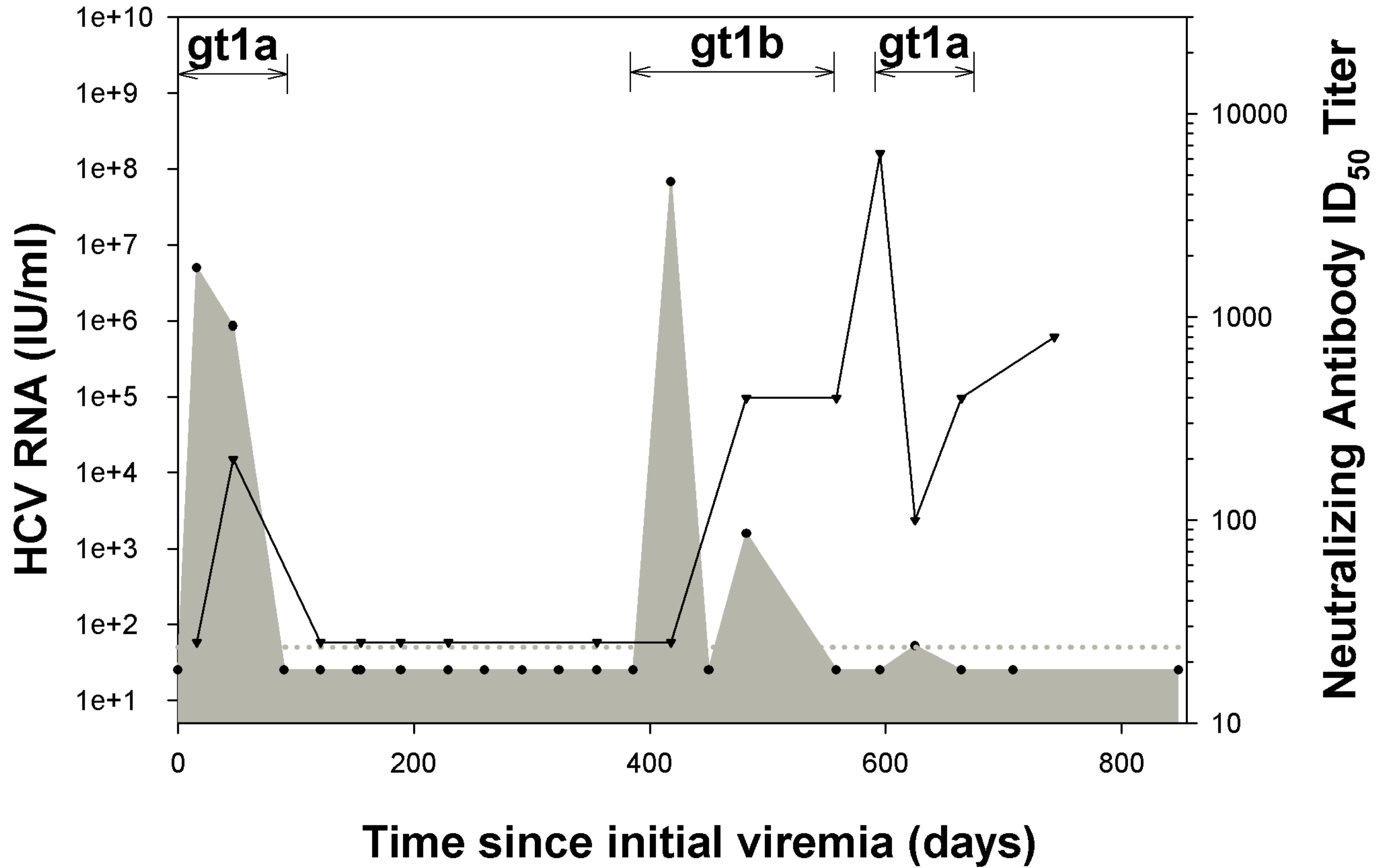
Subject 112



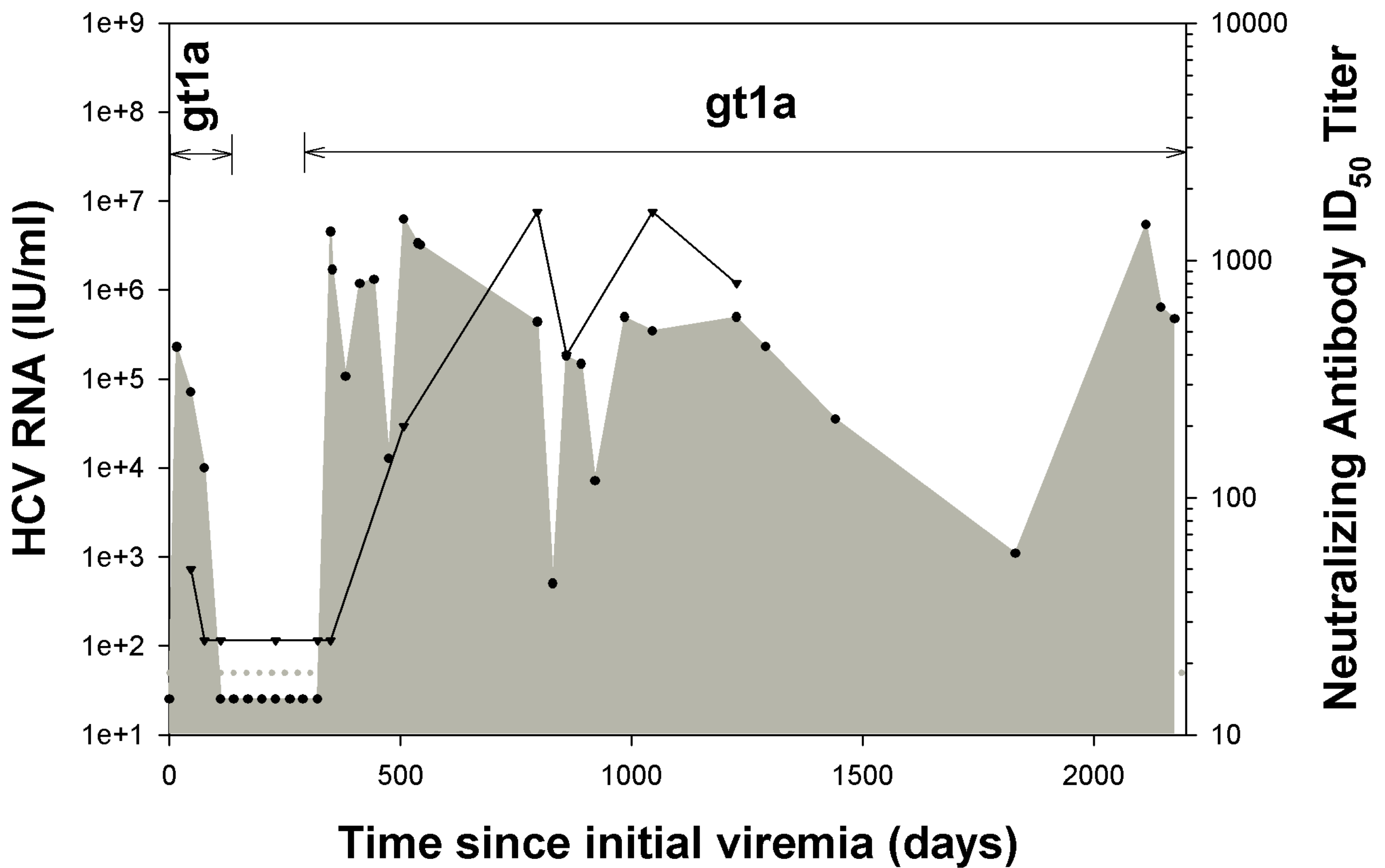
Supplementary Figure 2 part 2



Subject 152



Subject 19



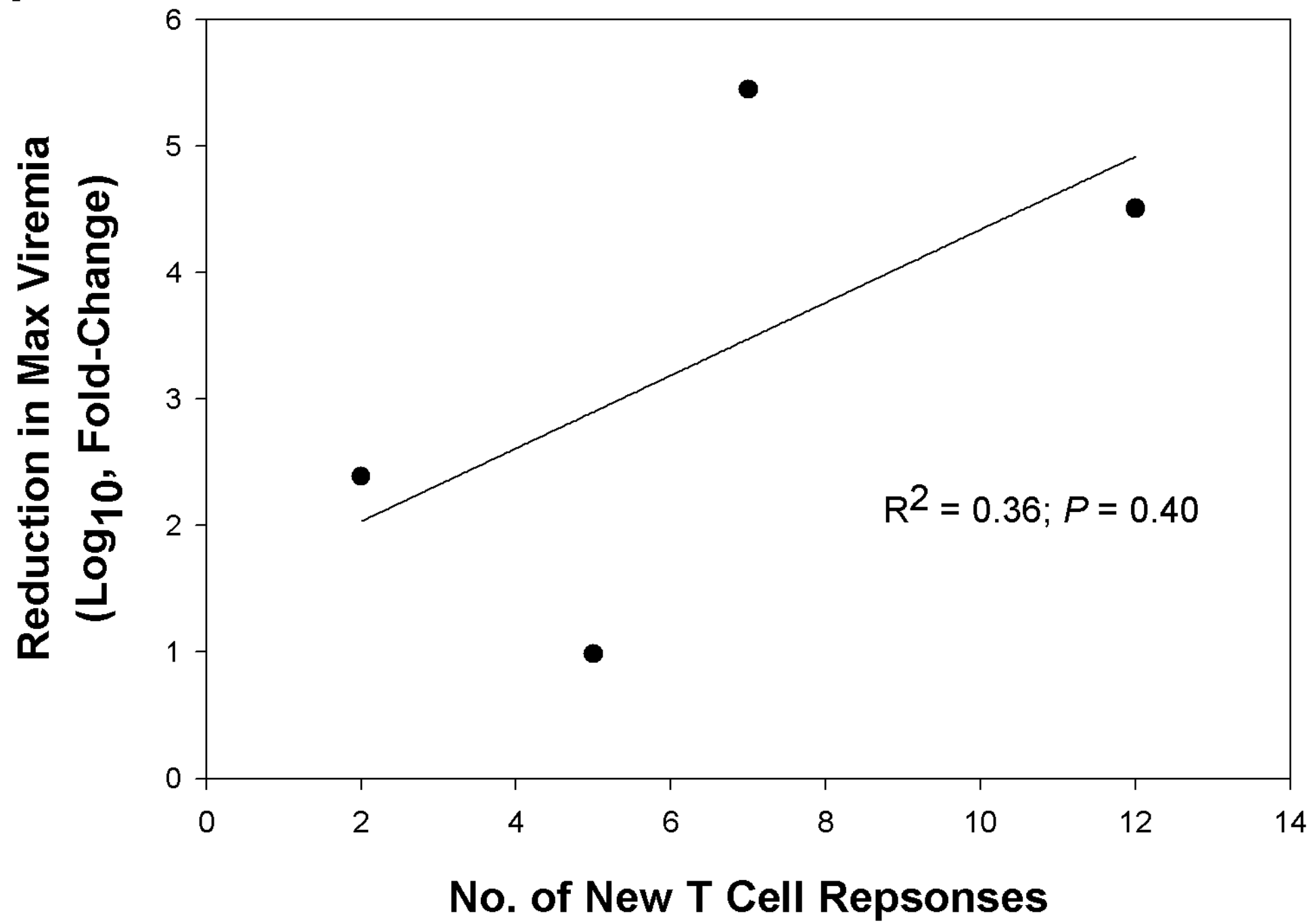
Supplementary Figure 3

A.

Core	E1	E2	P7	NS2	NS3
*	XX	* X *	X * *	X * * *	* * *
					** *

NS4A					
NS4B	NS5A	NS5B			
*	*	* *	**	*	*

B.



C.

