Supplemental Material

Plasma deconvolution identifies broadly neutralizing antibodies associated with hepatitis C virus clearance

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Figure S1 (part 1). Example calculation, Subject C117 plasma deconvolution quality of fit.

subject C117 combined mAb neutralization profile =
*(HC-1 proportion * HC-1 neutralization profile)*
*+ (AR3A proportion * AR3A neutralization profile)*
*+ (AR4A proportion * AR4A neutralization profile)*
*+ (HEPC74 proportion * HEPC74 neutralization profile)*
*+ (HEPC98 proportion * HEPC98 neutralization profile)*

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strain	HC-1 proportion	*	HC-1 neutralization profile	+	AR3A proportion	*	AR3A neutralization profile	+	AR4A proportion	*	AR4A neutralization profile	+	HEPC74 proportion	*	HEPC74 neutralization profile	+	HEPC98 proportion	*	HEPC98 neutralization profile	=	Subject C117 combined mAb neutralization profile
1b34	0.08		3.8		0.06		6.4		0.34		7.4		0.40		5.6		0.12		16.0		7.38
1a53	0.08		11.0		0.06		2.6		0.34		2.8		0.40		2.2		0.12		4.2		3.41
1a31	0.08		1.2		0.06		2.2		0.34		8.4		0.40		14		0.12		12.2		10.15
1b38	0.08		17.2		0.06		5.0		0.34		10.6		0.40		4		0.12		9.0		8.02
1a154	0.08		4.0		0.06		6.2		0.34		4.4		0.40		7.2		0.12		1.2		5.19
1b09	0.08		9.2		0.06		1.4		0.34		3.8		0.40		1.4		0.12		13.2		4.31
1a123	0.08		13.8		0.06		16.2		0.34		2.6		0.40		11.2		0.12		14.0		9.11
1a80	0.08		7.0		0.06		11.2		0.34		11.0		0.40		12.2		0.12		3.2		10.20
1a157	0.08		5.6		0.06		8.8		0.34		15.2		0.40		11.2		0.12		1.8		10.81
1b21	0.08		5.0		0.06		15.0		0.34		2.6		0.40		2.8		0.12		11.8		4.70
1a09	0.08		8.2		0.06		11.8		0.34		16.2		0.40		12.6		0.12		15.4		13.76
1b58	0.08		15.2		0.06		17.2		0.34		15.0		0.40		14.2		0.12		11.0		14.33
1a72	0.08		15.2		0.06		10.2		0.34		9.0		0.40		13		0.12		12.0		11.54
1a38	0.08		12.8		0.06		11.2		0.34		17.4		0.40		12.4		0.12		6.2		13.31
1a116	0.08		3.4		0.06		16.8		0.34		13.4		0.40		19		0.12		4.6		13.90
1a142	0.08		14.8		0.06		12.8		0.34		6.8		0.40		12.4		0.12		12.2		10.69
1b52	0.08		15.2		0.06		10.0		0.34		15.2		0.40		9		0.12		14.0		12.30
1b14	0.08		14.2		0.06		8.8		0.34		10.8		0.40		7.8		0.12		13.8		10.15
1a129	0.08		13.2		0.06		16.2		0.34		17.4		0.40		17.8		0.12		14.2		16.75

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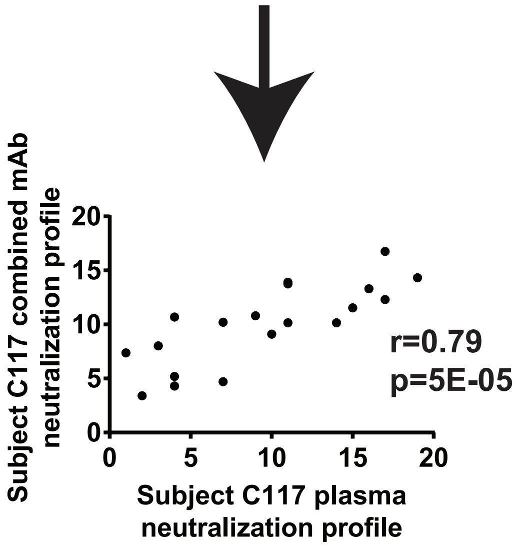
Figure S1 (part 2). Example calculation, Subject C117 plasma deconvolution quality of fit.

strain	HC-1 scaled neutralization profile	+	AR3A scaled neutralization profile	+	AR4A scaled neutralization profile	+	HEPC74 scaled neutralization profile	+	HEPC98 scaled neutralization profile	=	Subject C117 combined mAb neutralization profile
1b34	0.32		0.36		2.52		2.23		1.96		7.38
1a53	0.92		0.14		0.95		0.87		0.52		3.41
1a31	0.10		0.12		2.86		5.57		1.50		10.15
1b38	1.43		0.28		3.61		1.59		1.10		8.02
1a154	0.33		0.35		1.50		2.86		0.15		5.19
1b09	0.77		0.08		1.29		0.56		1.62		4.31
1a123	1.15		0.90		0.89		4.45		1.72		9.11
1a80	0.58		0.62		3.75		4.85		0.39		10.20
1a157	0.47		0.49		5.18		4.45		0.22		10.81
1b21	0.42		0.84		0.89		1.11		1.45		4.70
1a09	0.68		0.66		5.52		5.01		1.89		13.76
1b58	1.27		0.96		5.11		5.65		1.35		14.33
1a72	1.27		0.57		3.07		5.17		1.47		11.54
1a38	1.07		0.62		5.93		4.93		0.76		13.31
1a116	0.28		0.94		4.56		7.56		0.56		13.90
1a142	1.23		0.71		2.32		4.93		1.50		10.69
1b52	1.27		0.56		5.18		3.58		1.72		12.30
1b14	1.18		0.49		3.68		3.10		1.69		10.15
1a129	1.10		0.90		5.93		7.08		1.74		16.75



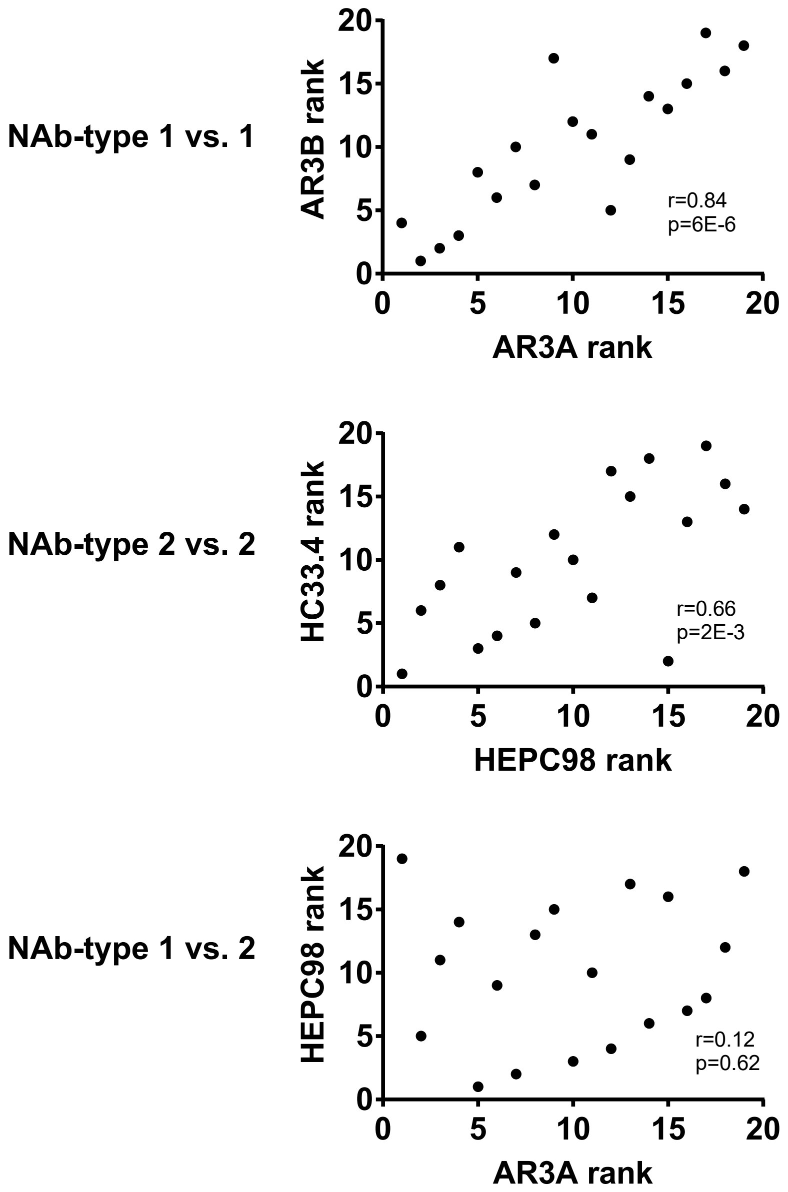


Figure S2. Correlations between reference mAb neutralization profiles. Examples of correlations between neutralization profiles of reference mAbs falling in the same NAb-type (AR3A vs. AR3B; HEPC98 vs. HC33.4) or reference mAbs falling in different NAb-types (AR3A vs. HEPC98). Points on each graph represent the ranking of relative neutralization sensitivity of each of 19 HCVpp by one mAb on the x-axis and a different mAb on the y-axis. R and p-values are for Pearson correlations. Neutralization profiles shown here were determined in a single experiment, with neutralization of each HCVpp measured in duplicate. Neutralization profiles of the eight reference mAbs representative of each NAb-type were subsequently tested in four additional independent experiments.

Reference mAbs

mAb added	[NAb] (μg/mL)	AR1A	HC-1	HEPC98	CBH-2	AR3A	HEPC74	HC84.26	AR4A	breadth	p value
AR1A	50	0.85	0.13	0.00	0.00	0.00	0.00	0.00	0.02	1	<1E-06
	10	1.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0	2E-06
HC-1	10	0.00	0.91	0.00	0.00	0.09	0.00	0.00	0.00	2	<1E-06
	2	0.00	0.87	0.00	0.08	0.03	0.02	0.00	0.00	1	7E-05
HEPC98	10	0.10	0.00	0.89	0.00	0.00	0.00	0.01	0.00	6	<1E-06
	2	0.07	0.04	0.78	0.11	0.00	0.00	0.00	0.00	5	1E-03
CBH-2	10	0.13	0.00	0.07	0.80	0.00	0.00	0.00	0.00	1	1E-02
	2	0.14	0.00	0.06	0.52	0.09	0.19	0.00	0.00	1	4E-02
AR3A	10	0.00	0.00	0.00	0.10	0.84	0.00	0.05	0.00	13	<1E-06
	2	0.00	0.00	0.00	0.07	0.93	0.00	0.00	0.00	5	<1E-06
HEPC74	10	0.00	0.00	0.00	0.00	0.00	0.73	0.27	0.00	16	<1E-06
	2	0.00	0.02	0.00	0.00	0.00	0.94	0.04	0.00	10	<1E-06
HC84.26	10	0.00	0.00	0.00	0.00	0.11	0.00	0.89	0.00	15	<1E-06
	2	0.07	0.00	0.00	0.00	0.02	0.07	0.80	0.03	11	<1E-06
AR4A	10	0.00	0.04	0.00	0.00	0.00	0.00	0.08	0.88	16	<1E-06
	2	0.00	0.20	0.00	0.00	0.00	0.00	0.00	0.80	6	<1E-06

Figure S3. Deconvolution of samples containing known mAbs at two different concentrations. Neutralization profiles were determined in a single experiment, with neutralization of each HCVpp measured in duplicate. Reference mAb profiles were averaged from five independent experiments. Values are proportion of the neutralization activity of the sample attributed to each reference mAb by the deconvolution analysis. The highest proportion for each experiment is highlighted in gray. Breadth is the number out of 19 HCVpp neutralized by >50%. P values indicate the Pearson correlation of the neutralization profiles of spiked-in mAbs with a combined reference mAb neutralization profile comprising the indicated proportion of each reference mAb (**see Materials and Methods and Fig. S1**).

		Reference mAbs									
		narrow-breadth				bNAbs					
	Subject ID	**AR1A**	**HC-1**	**HEPC98**	**CBH-2**	**AR3A**	**HEPC74**	**HC84.26**	**AR4A**	**breadth**	**p-value**
Persistence Plasma	**P150**	0.00	0.35	0.00	0.20	0.00	0.00	0.00	0.44	7	7E-02
	P51	0.11	0.00	0.50	0.16	0.00	0.23	0.00	0.00	0	2E-01
	P175	0.00	0.00	0.39	0.39	0.00	0.22	0.00	0.00	0	1E-01
	P111	0.00	0.34	0.25	0.21	0.00	0.00	0.00	0.20	0	4E-01
	P113	0.00	0.38	0.03	0.28	0.00	0.30	0.00	0.00	0	2E-01
	P13	0.46	0.00	0.19	0.31	0.00	0.00	0.00	0.03	0	9E-02
	P16	0.00	0.00	0.26	0.40	0.00	0.34	0.00	0.00	0	5E-02
	P17	0.06	0.00	0.64	0.06	0.00	0.24	0.00	0.00	0	1E-01
	P21	0.23	0.25	0.00	0.52	0.00	0.00	0.00	0.00	0	9E-01
	P22	0.00	0.31	0.25	0.35	0.00	0.00	0.09	0.00	0	2E-01
	P28	0.00	0.27	0.10	0.08	0.19	0.00	0.00	0.35	3	5E-02
	P29	0.00	0.02	0.21	0.45	0.00	0.00	0.00	0.32	0	8E-02
	P30	0.09	0.11	0.17	0.21	0.00	0.00	0.00	0.42	1	1E-01
Clearance Plasma	**C112**	0.15	0.02	0.28	0.31	0.00	0.24	0.00	0.00	0	2E-01
	C176	0.00	0.11	0.09	0.29	0.00	0.38	0.00	0.13	0	5E-02
	C180	0.00	0.00	0.53	0.28	0.00	0.00	0.00	0.19	0	5E-01
	C181	0.00	0.00	0.53	0.15	0.00	0.27	0.00	0.05	1	2E-01
	C403	0.08	0.00	0.31	0.06	0.00	0.09	0.00	0.44	3	1E-01
	C27	0.04	0.04	0.11	0.47	0.00	0.00	0.09	0.24	4	4E-01

Figure S4. Plasma samples with poor fit of deconvolution analysis. Reference mAbs are on the x-axis with plasma samples on the y-axis. Each plasma sample is from a different subject. Plasma neutralization profiles each were averaged from two independent experiments. Reference mAb profiles were averaged from five independent experiments. Values shown are the proportion of each plasma neutralizing response attributed to each reference mAb, with higher values shaded darker. Plasma samples are grouped by subject outcome. Neutralizing breadth was calculated as the # out of 19 HCVpp neutralized > 50% by a 1:100 dilution of plasma. P values are for the Pearson correlation between the plasma sample neutralization profile and the best fit combined reference mAb neutralization profile.

Table S1. Neutralization profiles of reference NAbs. The neutralization profile of each reference NAb is the average of five independent experiments. Neutralization of each HCVpp in each experiment was measured in duplicate. Values are the rank order of sensitivity of each HCVpp to each reference NAb.

strain	**HC84.26**	**HC-1**	**CBH-2**	**AR1A**	**AR3A**	**AR4A**	**HEPC74**	**HEPC98**
1b34	2	3.8	4	15.6	6.4	7.4	5.6	16
1a53	6.2	11	10.2	5.4	2.6	2.8	2.2	4.2
1a31	11.4	1.2	14	1.6	2.2	8.4	14	12.2
1b38	8.8	17.2	2.8	16	5	10.6	4	9
1a154	3.8	4	15.2	3.6	6.2	4.4	7.2	1.2
1b09	2	9.2	1.2	16.2	1.4	3.8	1.4	13.2
1a123	4.4	13.8	16.6	4.4	16.2	2.6	11.2	14
1a80	17.4	7	13.8	9	11.2	11	12.2	3.2
1a157	14.8	5.6	7.4	10.6	8.8	15.2	11.2	1.8
1b21	7.2	5	15.4	8	15	2.6	2.8	11.8
1a09	16.2	8.2	14.8	5.8	11.8	16.2	12.6	15.4
1b58	12	15.2	9.4	14.8	17.2	15	14.2	11
1a72	15	15.2	8.8	6.6	10.2	9	13	12
1a38	8.8	12.8	6.4	13	11.2	17.4	12.4	6.2
1a116	16	3.4	13.8	10.2	16.8	13.4	19	4.6
1a142	19	14.8	16	7.4	12.8	6.8	12.4	12.2
1b52	7.2	15.2	5.4	16.2	10	15.2	9	14
1b14	4.6	14.2	5	12.4	8.8	10.8	7.8	13.8
1a129	13.2	13.2	9.8	13.2	16.2	17.4	17.8	14.2

Table S2. Neutralization profiles of plasma samples. The neutralization profile of each plasma sample is the average of two independent experiments, with plasma at 1:100 or 1:20 dilution. Neutralization of each HCVpp in each experiment was measured in duplicate. Values are the rank order of sensitivity of each HCVpp to each plasma sample. Rank order for each sample has been reversed to satisfy input requirements of the deconvolution code.

strain	**P138**	**P142**	**P150**	**P151**	**P154**	**P49**	**P155**	**P51**	**P52**	**P156**	**P157**	**P158**
1b34	15	12	15	16	15	1	10	3	17	17	12	16
1a53	3	9	3	6	13	16	9	10	12	8	15	17
1a31	10.5	11.5	12	12	12.5	6	8.5	1	12	11.5	6	8.5
1b38	17	16	12	14	12	17	12	4	15	13	11	12
1a154	10.5	6.5	12	10	11.5	7.5	7	8	10.5	11.5	7	6.5
1b09	12.5	13.5	10	11.5	13	11	10.5	8.5	11.5	9	10.5	9.5
1a123	7	11	10	10	9	13	17	7	10	5	14	3
1a80	2	5	5	8	5	15	11	13	4	15	7	10
1a157	8	10	6	9	8	5.5	6	12.5	8	7.5	6.5	10
1b21	10	5	11	11	11	10	11	10	11	10	11	9
1a09	6.5	6	5.5	8	7	3	6	9.5	4.5	8	5	7
1b58	12	10	14	4	2	12	8	12	1	6	9	2
1a72	5	3.5	4.5	3.5	4.5	4.5	3	3.5	3	2.5	10.5	9.5
1a38	3	2	5	2.5	6	7	9	7	4.5	2.5	2	3.5
1a116	11	11	10	10	7	11	7	7	9	11	10	10
1a142	1	7	13	5	4	8	2	6	9	11	16	14
1b52	7	8	2.5	5.5	2	6	8.5	7	5.5	2.5	3.5	1.5
1b14	6	3	9	1	1	9	1	17	6	7	1	7
1a129	4.5	4	1	5	5.5	3	7	8	3	3	5.5	3.5
strain	**P53**	**P54**	**P161**	**P164**	**P56**	**P168**	**P31**	**P173**	**P175**	**P111**	**P115**	**P113**
1b34	12	17	14	15	10	17	8	15	7	12	13	16
1a53	15	8	4	11	14	15	17	11	16	2	10	8
1a31	12.5	10.5	8	9.5	4.5	7	10	7	2	2	10.5	2
1b38	2	15	8	14	9	14	12	14	13	6	15	5
1a154	9	8.5	7.5	11	7.5	6	9	5	6	12	9	7
1b09	4	13.5	10	12.5	11.5	12.5	7.5	12.5	9	9	14	11.5
1a123	7	7	1	3	4	5	9	7	1	5	6	3
1a80	14	4	13	7	6	9	16	12	12	16	7	13
1a157	7	9	9.5	10	6	7	7	11	6	10	6	7.5
1b21	10	10	11	11	11	11	9	10	11	10	9	11
1a09	10.5	3.5	7	3	9.5	4.5	6	5	8	7.5	10	9
1b58	10	6	7	5	11	13	6	5	15	9	3	12
1a72	2.5	2	3	5.5	2.5	8.5	3.5	4.5	7.5	4	8.5	4.5
1a38	3.5	1.5	4.5	3.5	9.5	4	2.5	4	7.5	4.5	2	6.5

1a116	11	9	9	9	9	10	6	11	8	11	10	9
1a142	11	11	11	2	1	7	10	3	4	17	12	10
1b52	4	7.5	8.5	6	10	2.5	2.5	3.5	4.5	5	3.5	11
1b14	5	13	17	4	17	2	15	13	8	13	5	7
1a129	8	3.5	4	8	2.5	6	7.5	6.5	11.5	5	1	3.5
strain	**P461**	**P551**	**P13**	**P14**	**P15**	**P42**	**P126**	**P127**	**P16**	**P41**	**P17**	**P20**
1b34	13	17	3	12	16	13	11	15	7	16	3	15
1a53	16	13	14	15	9	2	10	11	16	9	16	17
1a31	9.5	4.5	4	10.5	1	9	12	11.5	2	2.5	1	11.5
1b38	12	12	5	2	8	7	1	14	13	8	4	7
1a154	13.5	9.5	10.5	9	11.5	8	13	10.5	6	10	9.5	11.5
1b09	7.5	12.5	8.5	4.5	13	9	11	13.5	9	13.5	7	9.5
1a123	14	6	4	7	2	3	12	2	1	2	2	9
1a80	6	1	2	14	15	12	7	6	12	15	13	11
1a157	7	8	10.5	7.5	10.5	11.5	9.5	9	6.5	8.5	7.5	8
1b21	11	11	8	11	10	10	9	11	11	11	11	11
1a09	4	5	7	8.5	6.5	5.5	2.5	5	8.5	5.5	6.5	3
1b58	4	14	6	10	5	8	5	4	15	5	14	12
1a72	11	5	11.5	4.5	3.5	4.5	7	6	7	5	6	3
1a38	2.5	6	6	4	4	3.5	7.5	4	8	5.5	9	3.5
1a116	9	10	10	10	8	7	11	9	6	9	7	6
1a142	8	3	11	11	11	6	6	1	4	11	10	14
1b52	3	9	3.5	3.5	4.5	9	2.5	6	6.5	5	8.5	3
1b14	2	10	13	5	7	15	3	3	8	7	8	4
1a129	4	1.5	10	9	9.5	8	7	6	9.5	7.5	10.5	3.5
strain	**P21**	**P22**	**P65**	**P28**	**P29**	**P30**	**C143**	**C47**	**C48**	**C110**	**C55**	**C57**
1b34	5	11	12	16	16	17	16	4	12	14	17	15
1a53	4	6	11	17	9	11	14	16	16	13	14	6
1a31	7.5	2	12	10	4	9	17	6	12	7.5	11.5	4.5
1b38	3	7	10	13	14	14	10	10	13	12	15	13
1a154	6	11.5	12	7	7.5	7	13	7.5	11.5	11.5	9	11
1b09	11	5	11.5	7	10.5	6	15	8	12	13.5	10.5	12.5
1a123	1	1	15	2	2	9	12	8	10	10	7	9
1a80	12	14	4	9	17	15	7	15	8	17	10	16
1a157	9.5	8	6	6	6	4.5	11	10.5	8.5	6	5	7
1b21	9	11	10	11	8	8		11	11	9	11	11
1a09	10.5	7	4.5	6	2.5	3	1	3.5	3.5	7	8.5	4.5
1b58	15	9	3	4	7	2	8	17	6	4	8	4
1a72	3.5	5.5	3.5	7.5	8.5	10.5	9	9	5.5	2	3	2
1a38	6.5	4	3.5	5	3.5	4.5	3	2	1.5	4.5	2.5	7.5
1a116	5	10	11	8	11	11		6	9	10	10	9

1a142	10	3	9	14	13	10	6	12	1	2	11	14
1b52	10	12.5	9.5	3.5	4.5	3	4	3	4.5	4.5	4	4.5
1b14	13	17	1	3	11	7	5	6	7	11	6	11
1a129	6.5	9.5	4	9	8.5	10	2	7.5	4	2	1	2
strain	**C117**	**C172**	**C112**	**C176**	**C116**	**C180**	**C181**	**C403**	**C430**	**C18**	**C19**	**C133**
1b34	17	16	2	17	17	4	3	1	13	1	5	14
1a53	16	12	1	8	13	1	14	4	10	15	16	16
1a31	6	9	9	3	5	1.5	2.5	4	12	11	9.5	10.5
1b38	13	15	16	14	15	16	12	17	12	17	13	11
1a154	12	10.5	12.5	9.5	11.5	11	8	12	12	11	14	8.5
1b09	12	13	10.5	11.5	7	10	9	11.5	12	10	8.5	7
1a123	8	8	4	5	8	5	1	12	3	8	12	12
1a80	11	6	5	16	16	17	17	9	5	3	6	1
1a157	9	4	11	4.5	5.5	6.5	8	5	9	8.5	11	9
1b21	11	11	11	11	11	11	10	11	11	10	10	10
1a09	7	4.5	5.5	6	4.5	6	6.5	8.5	4	3.5	6.5	5.5
1b58	1	7	6	12	12	14	10	5	8	5	1	5
1a72	4.5	5.5	6	3	6.5	6	3	6.5	3.5	9.5	5.5	9.5
1a38	3.5	2.5	7	5	5	6	5	6.5	6	5.5	4	2.5
1a116	7	10	7	10	10	8	9	9	10	11	4	11
1a142	12	4	10	11	11	15	15	16	11	11	8	2
1b52	2	8.5	7	6	2	4.5	5.5	8.5	6	3.5	6	7
1b14	7	9	13	13	7	13	13	6	2	2	4	9
1a129	2	3	3.5	2.5	2.5	6	10	2	2.5	5.5	5	4.5
strain	**C24**	**C26**	**C27**									
1b34	16	17	17									
1a53	7	13	1									
1a31	11.5	10	6									
1b38	9	16	16									
1a154	13	5.5	11.5									
1b09	13.5	10	3.5									
1a123	8	10	7									
1a80	10	7	6									
1a157	7	3	3.5									
1b21	1	10	9									
1a09	8.5	6	3									
1b58	3	1	14									
1a72	4.5	6.5	8									
1a38	3.5	6	8.5									
1a116	3	11	10									
1a142	6	15	13									

1b52	9	7	9									
1b14	5	5	15									
1a129	5	3	2.5									