

A

	H3-Brisbane 2007	H3-California 2004	H3-Moscow 1999	H3-Perth 2009	H3-Sydney 1997
56.a.09	2966000	3037000	2886000	2975000	3010000
M98A	3068000	3088000	2786000	3041000	3042000
F100A	55806	3907	1102	5379	9559
M98A-F100A	14033	12423	11793	14405	13726

	H1-California 2009	H3-Hong Kong 1968		H1-California 2009	H3-Hong Kong 1968
56.a.09	3033000	2987000	54.f.01	3138000	3097000
R52bA	3159000	3165000	R52bA	3196000	3164000
W55A	3235000	3203000	W55A	3175000	3133000
R52bA-W55A	3134000	3157000	R52bA-W55A	3167000	3140000

	H1-California 2009	H3-Hong Kong 1968		H1-California 2009	H3-Hong Kong 1968
56.a.09	3033000	2987000	54.f.01	3138000	3097000
g6-1CDRH2	3125000	3060000	g6-1CDRH2	3237000	3187000
4-39CDRH2	322916	4087	4-59*05CDRH2	3151000	3081000
4-61CDRH2	731879	11364	4-61CDRH2	3191000	1932000
4-30-2*05CDRH2	401561	90010	4-30-2*05CDRH2	2691000	5532
4-30-4CDRH2	128359	11716	4-31-CDRH2	3139000	654981

	H1-California 2009	H3-Hong Kong 1968		H1-California 2009	H3-Hong Kong 1968
56.a.09 gVDJ	3152000	3106000	54.f.01 gVDJ	1926000	6992
R52bA	2785000	237750	R52bA	6734	7433
W55A	3187000	3143000	W55A	540219	3194
R52bA-W55A	1748000	7493	R52bA-W55A	630.9	2176

	H1-California 2009	H3-Hong Kong 1968		H1-California 2009	H3-Hong Kong 1968
4-30-4CDRH2	1559	574.2	4-30-2CDRH2	5477	3788
4-30-2*05CDRH2	3432	2693	4-31CDRH2	5529	1687
4-39CDRH2	403.4	3063	4-59*05CDRH2	6326	4822
4-61CDRH2	3614	1127	4-61CDRH2	1966	3863

	H1-California 2009	H3-Hong Kong 1968		H1-California 2009	H3-Hong Kong 1968
gD3-3*01CDRH3	3158000	3088000	gD3-3*01CDRH3	2794000	3078000
D3-9fr1CDRH3	7926	20333			
D3-10fr3CDRH3	950	2105			
D3-10CDRH3-A	9591	2612000			
D6-13invfr2CDRH3	496.2	2938000			

B

	H3-Brisbane 2007	H3-California 2004	H3-Moscow 1999	H3-Perth 2009	H3-Sydney 1997
16.a.26	2911000	2887000	2808000	2865000	2797000
Q98A	3305000	3273000	3217000	3304000	3196000
V100aA	3458000	3389000	3354000	3439000	3330000
Q98A-V100aA	3180000	2345000	2512000	3069000	2623000

	H1-California 2009	H3-Hong Kong 1968		H1-California 2009	H3-Hong Kong 1968
16.g.07	2965000	3100000	16.a.26	3027000	3092000
16.g.07-S52N	23182	3082000	16.a.26-S52N	2979000	3105000
16.g.07-S52I	8512	3116000	16.a.26-S52I	2773000	3010000
16.g.07-G33Y	6355	37197	16.a.26-G33Y	3171000	3165000
16.g.07-G33S	2707000	1819000	16.a.26-G33S	3182000	3147000
16.g.07-HV1-45	5094	5907	16.a.26-HV1-45	no expression	no expression
16.g.07-HV1-68	no expression	no expression	16.a.26-HV1-68	no expression	no expression

	H3-Brisbane 2007	H3-California 2004	H3-Moscow 1999	H3-Perth 2009	H3-Sydney 1997
H-mature/L-UCA	3033000	2702000	2408000	2938000	2584000
H-UCA/L-mature	12395	13231	10772	15573	2128000
H-UCA/L-UCA	1016000	11991	10049	728902	12702

	H1-California 2009	H3-Hong Kong 1968		H1-California 2009	H3-Hong Kong 1968
16.g.07-gVDJ	5450	133960	16.a.26-gVDJ	6532	3104000

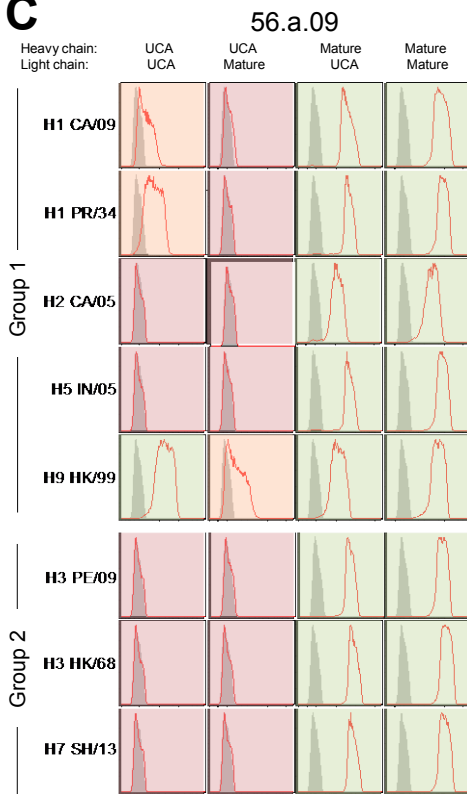
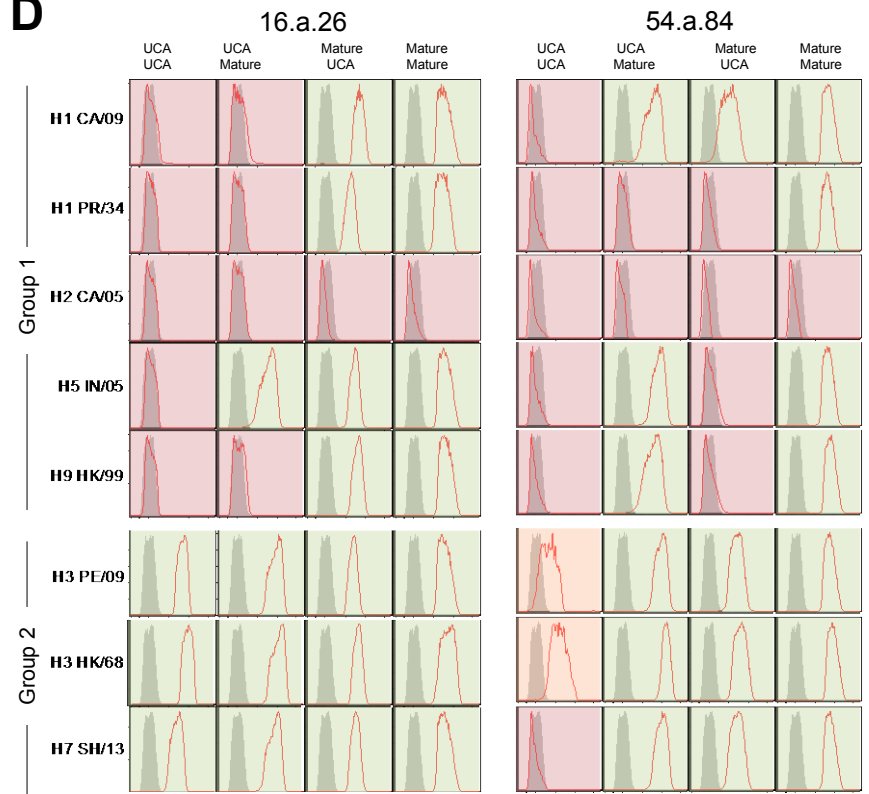
C**D**

Figure S7. Multidonor class recognition: binding of germline and contact residue variants, related to Figures 2-7. (A) HV6-1+HD3-3 antibody HA binding. (Top panel) critical contact residues from CDR H3 were mutated and assessed for binding to five H3 HA molecules by MSD-ECLIA with area under the curve indicated and colored from red (high binding) to blue (low binding). (Middle panel) CDR H2 residues were varied by mutation of individual residues or by replacement of entire CDR H2 region and assessed for binding to a H1 and H3 HA. (Lower panel) germline reverted versions and mutants were assessed for binding to a H1 and H3 HA. **(B)** HV1-18 (Q-x-x-V) antibody HA binding. (Top panel) critical contact residues from CDR H3 were mutated and assessed for binding to HA molecules. (Middle panel) HV1-18 framework residues G33 and S52, as well as HV gene replacement were assessed for their effect on HA binding. (Lower two panels) germline reverted antibodies were assessed for HA binding. **(C and D)** Cell surface expressed antibodies (mature and UCA combinations) were assessed for binding to group 1 and group 2 HA molecules by flow cytometry. Variant sequences are provided in Table S3.