

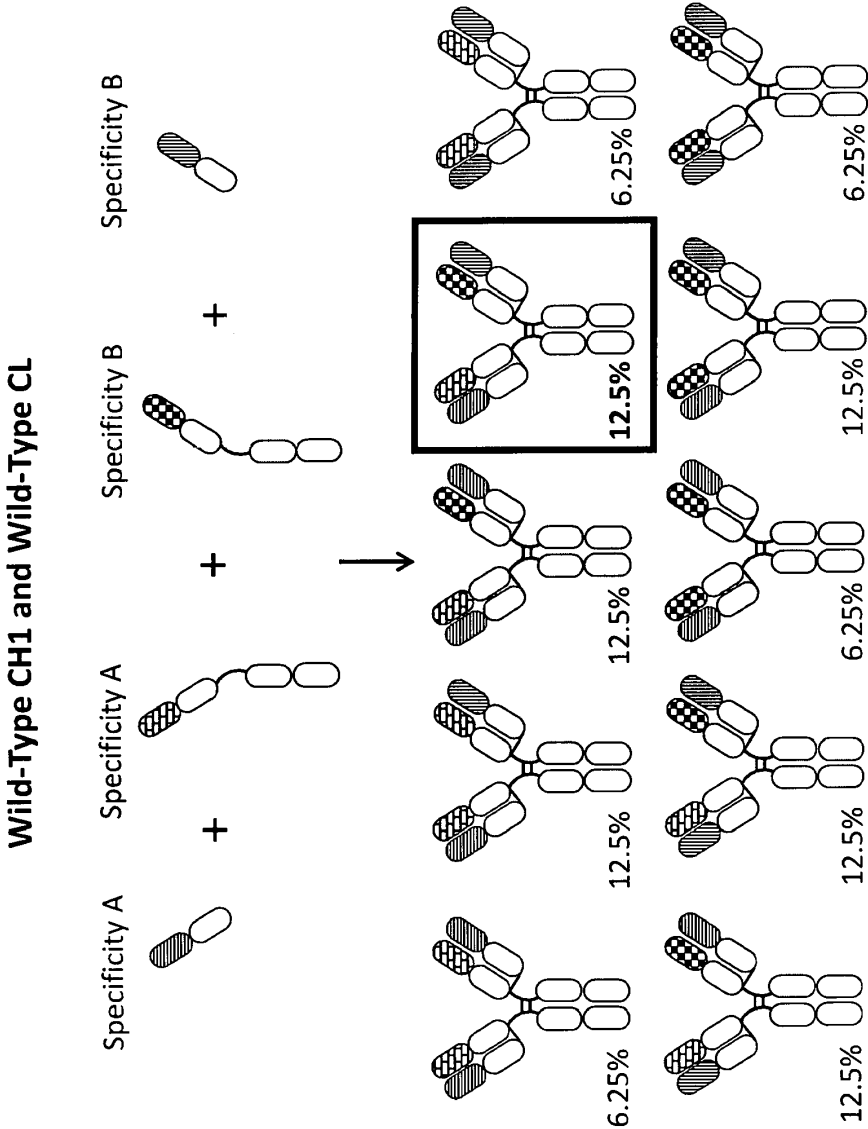


FIG. 1A

Wild-Type CH1 and Wild-Type CL (i.e., WT CH1-CL κ set or WT CH1-CL λ set)
combined with heavy chain heterodimerizing technology

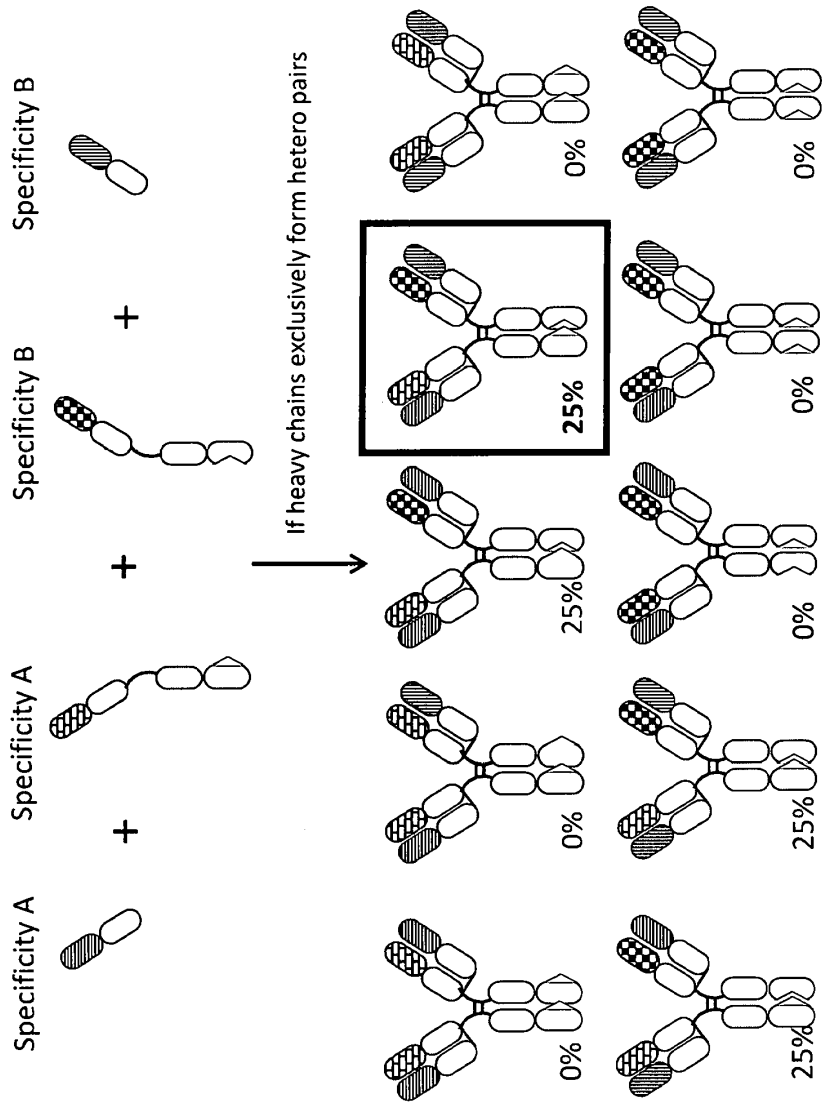


FIG. 1B

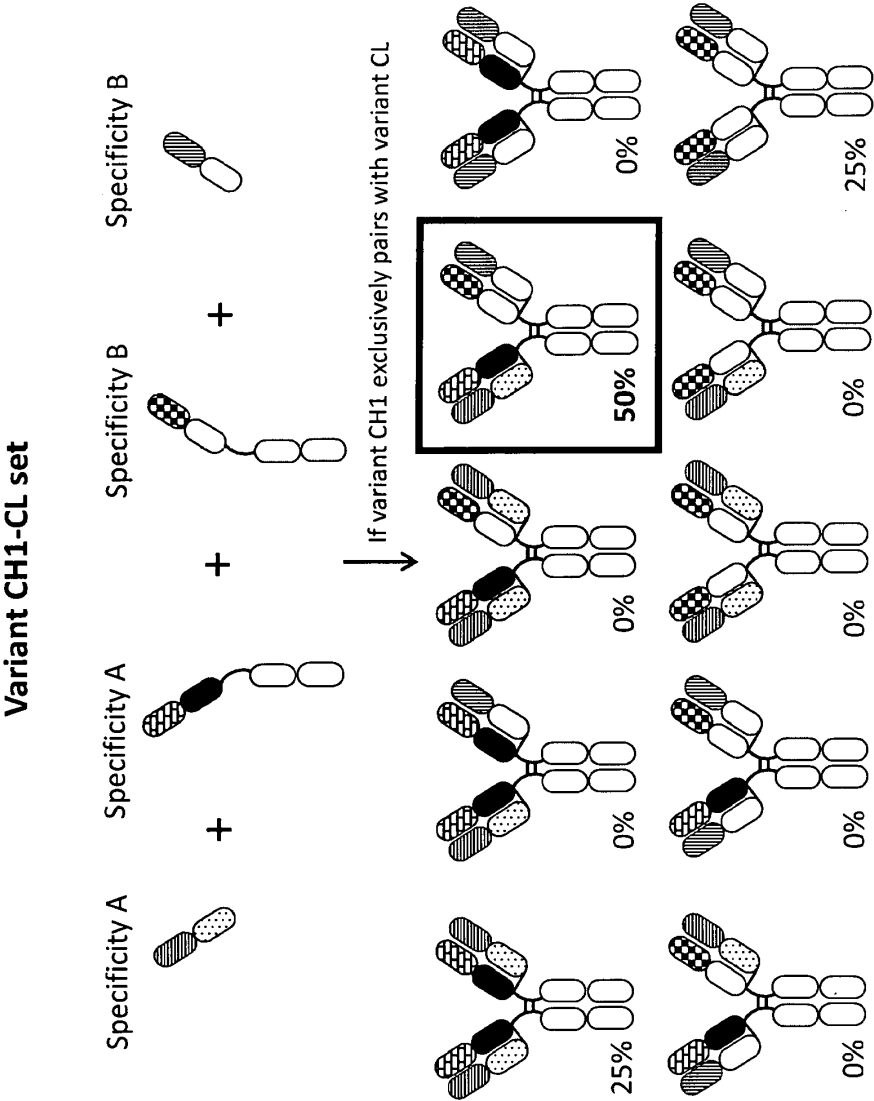


FIG. 1C

Variant CH1-CL set combined with heavy chain heterodimerizing technology

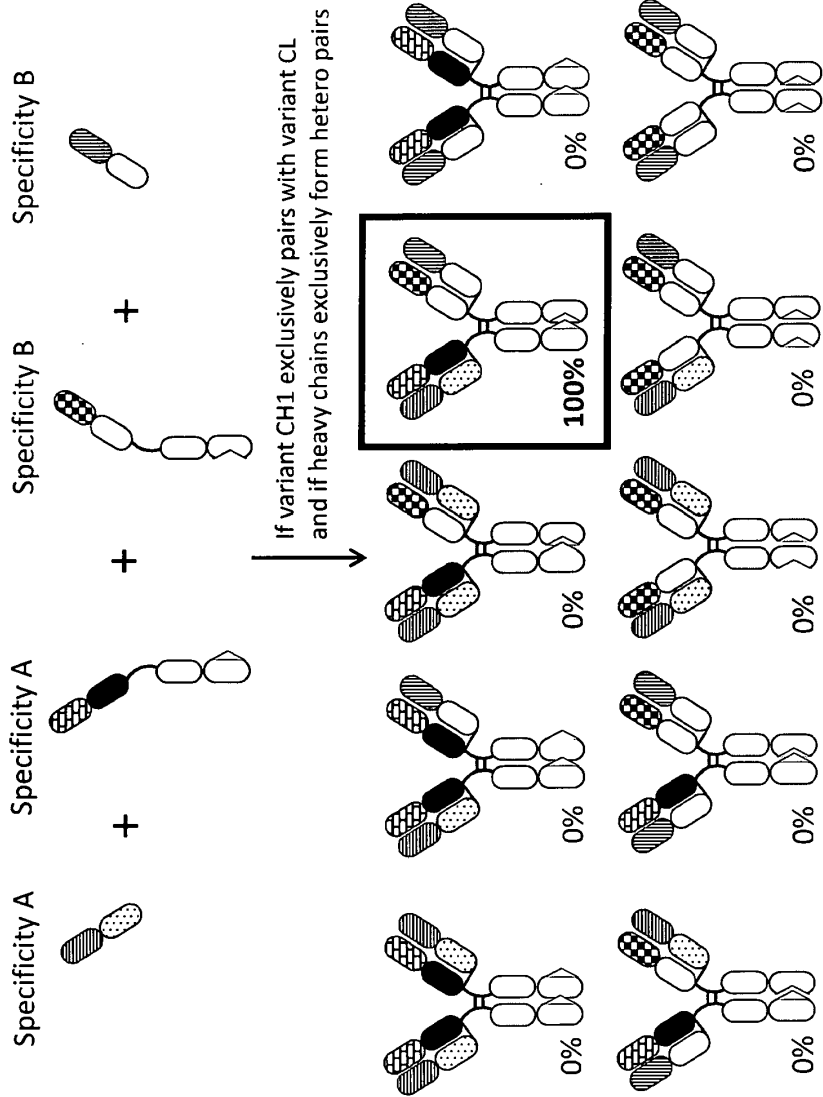


FIG. 1D

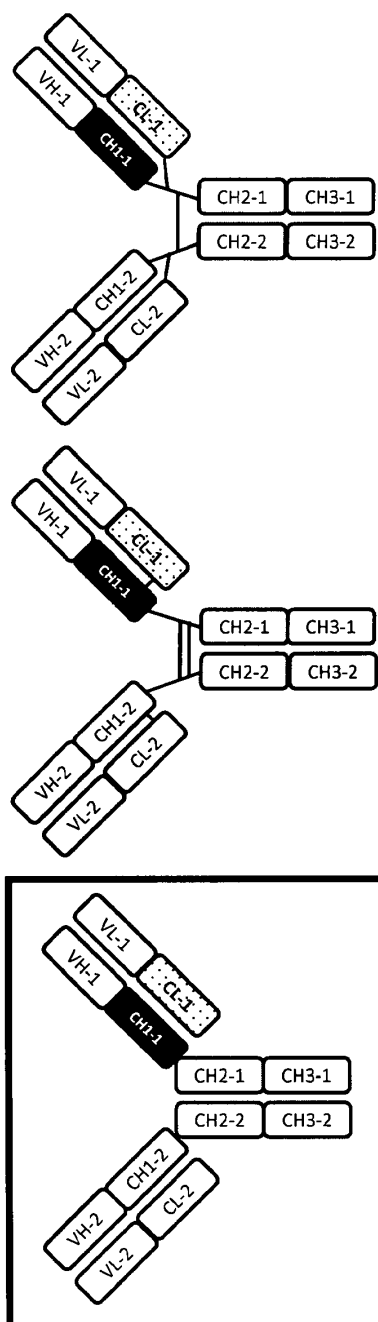
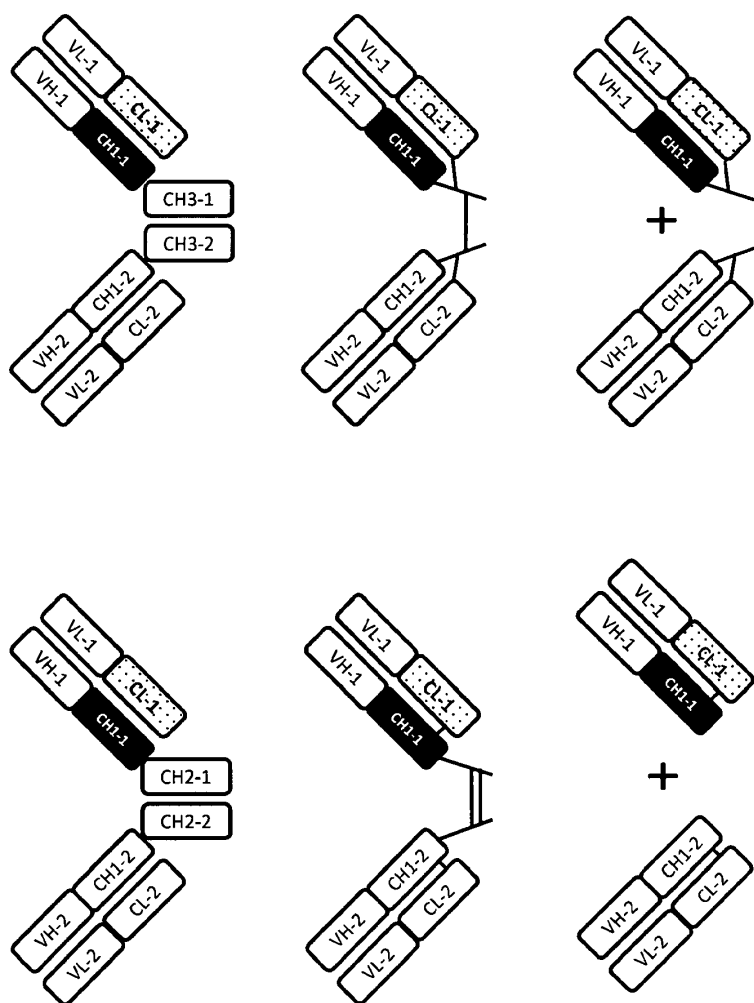


FIG. 2A

**FIG. 2B**

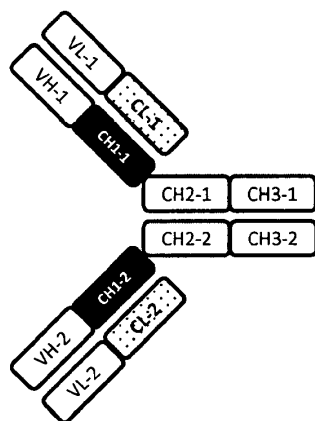


FIG. 2C

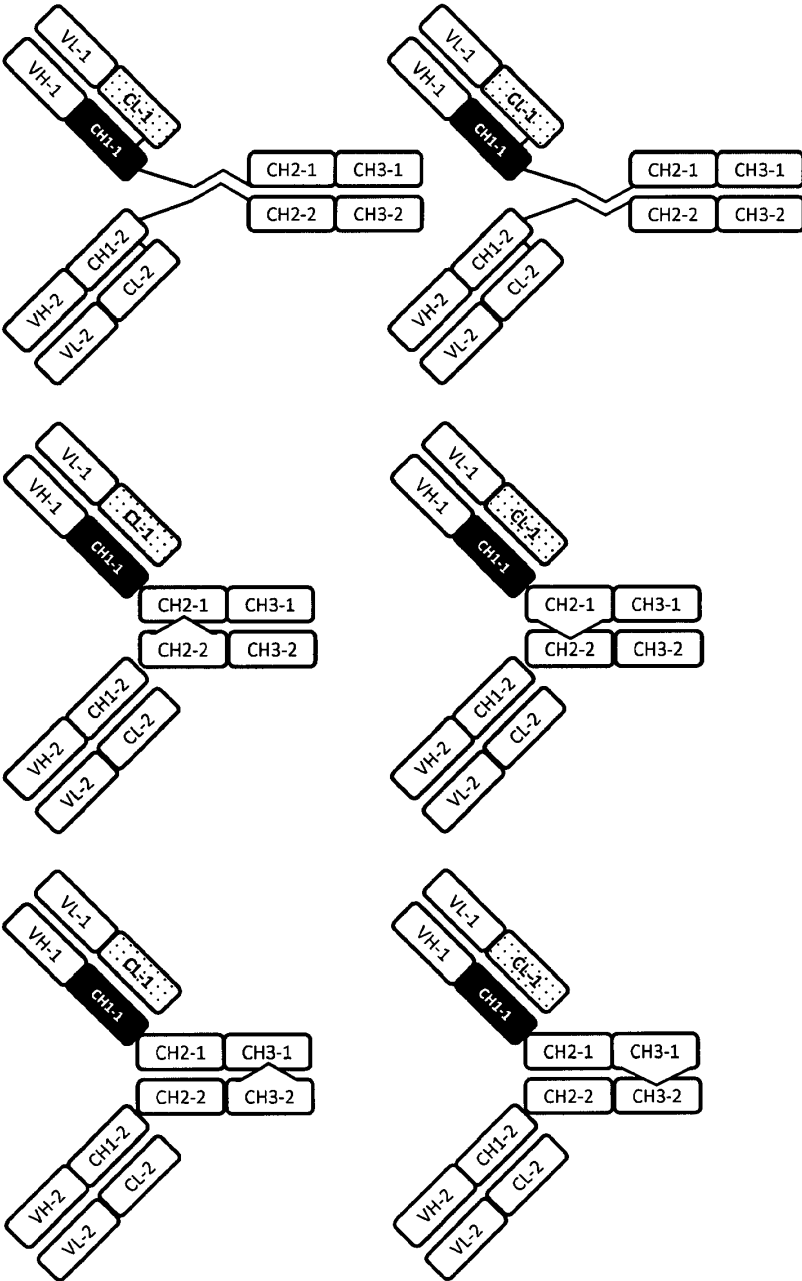


FIG. 2D

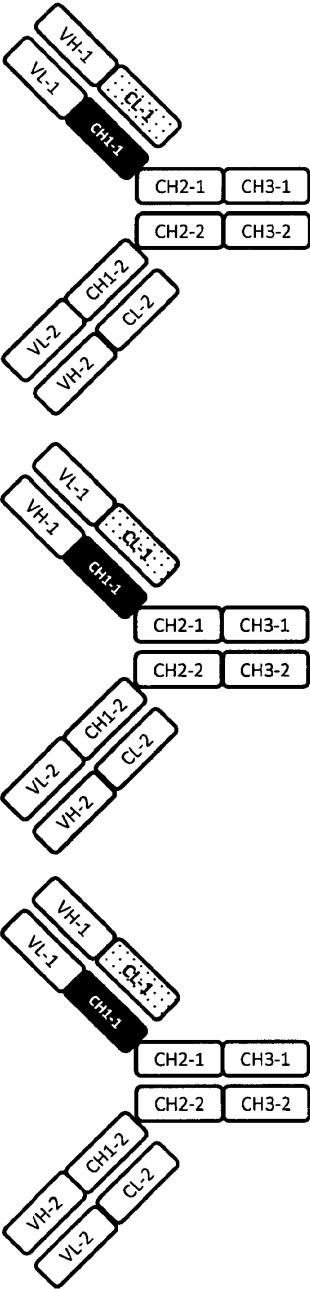


FIG. 3

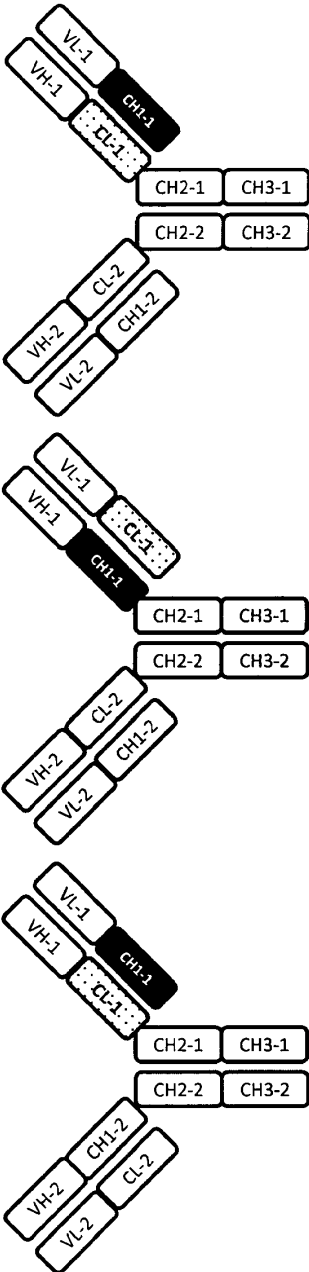


FIG. 4A

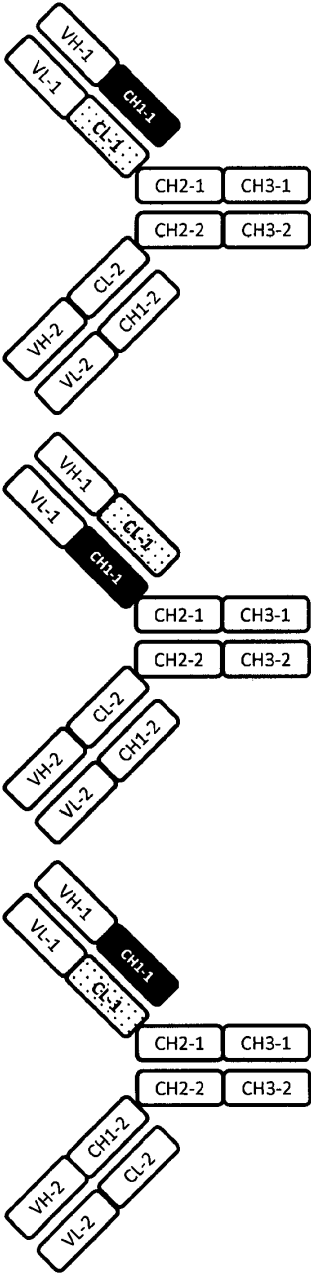


FIG. 4B

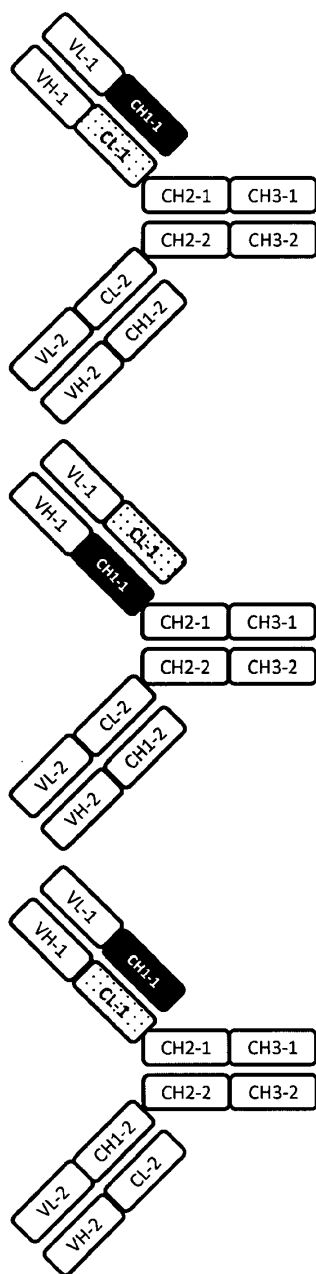


FIG. 4C

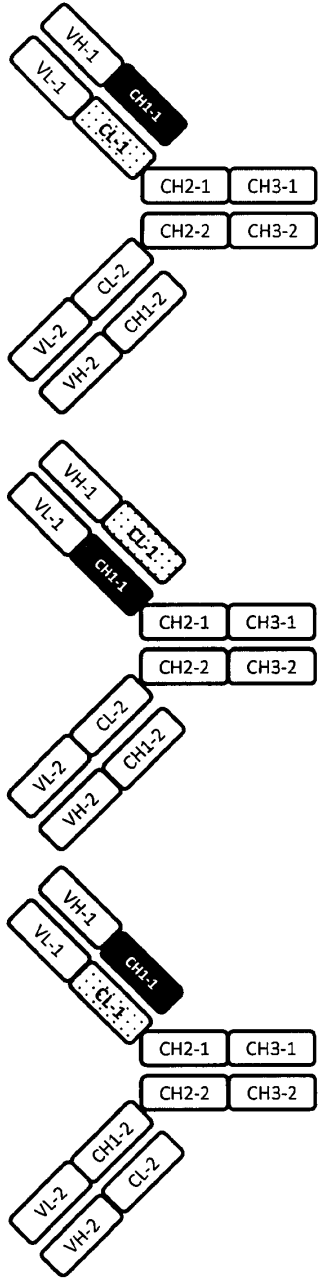
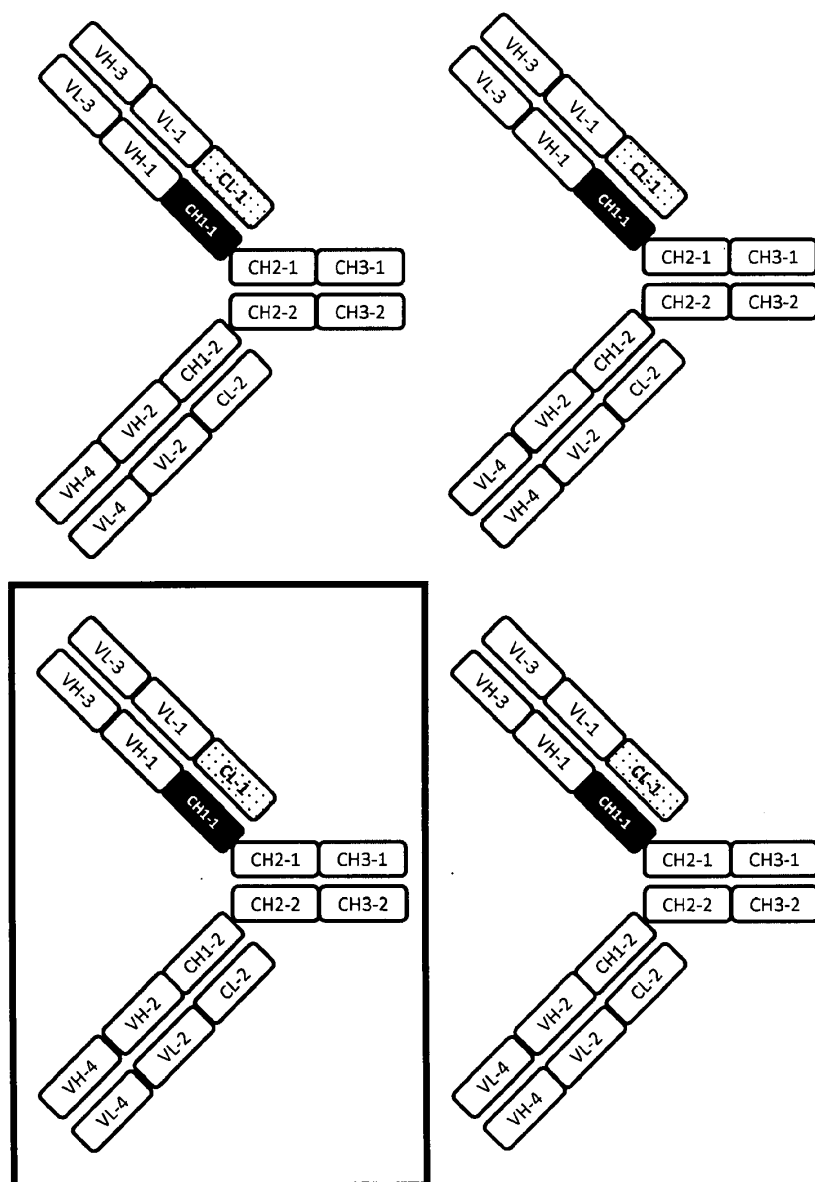


FIG. 4D

**FIG. 5A**

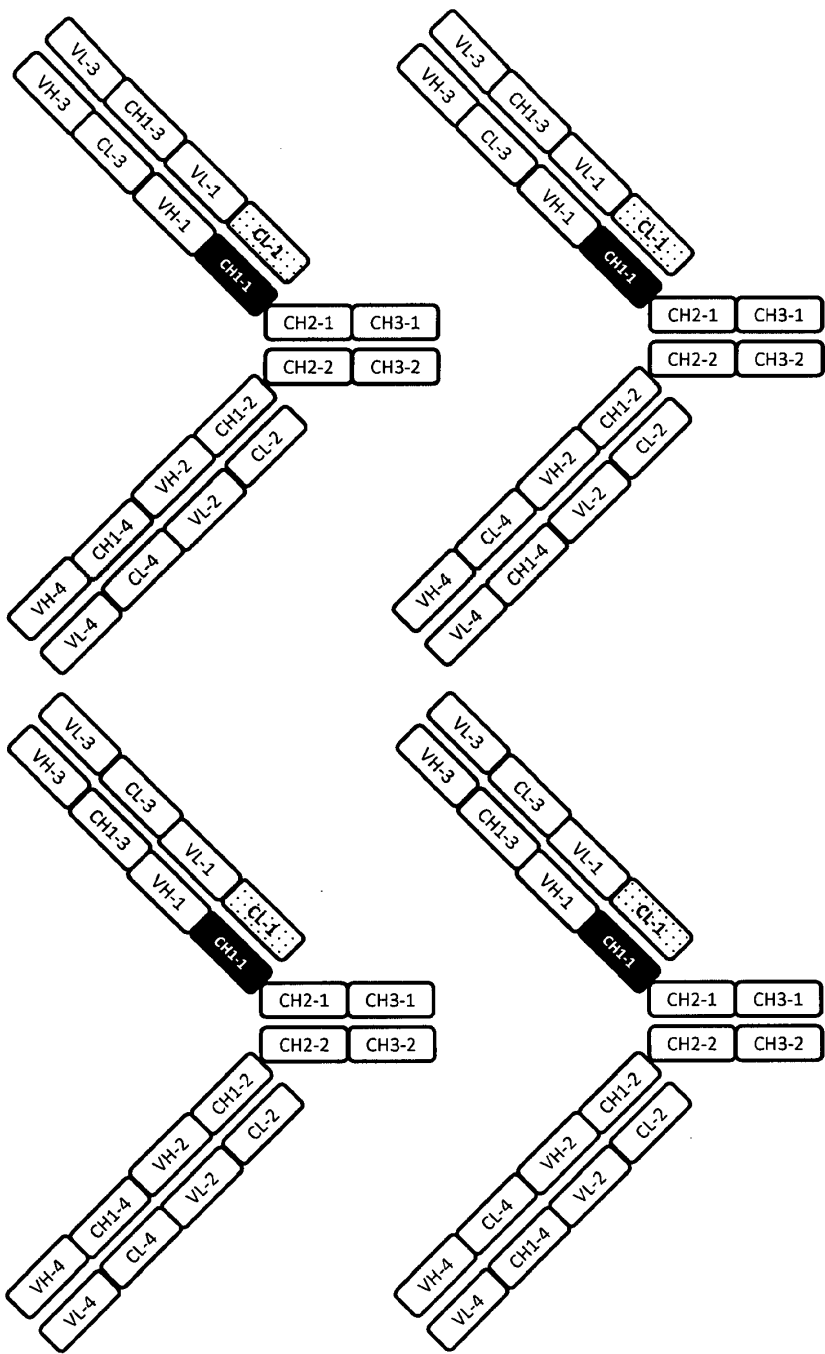


FIG. 5B

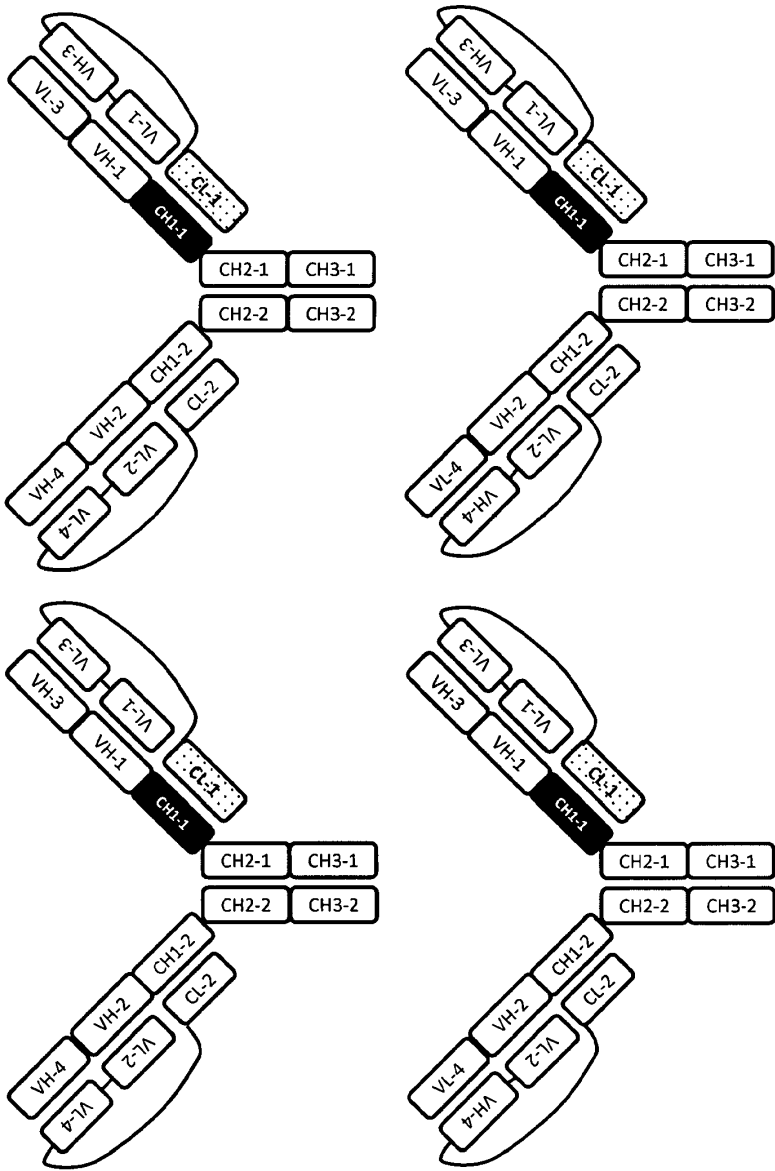


FIG. 5C

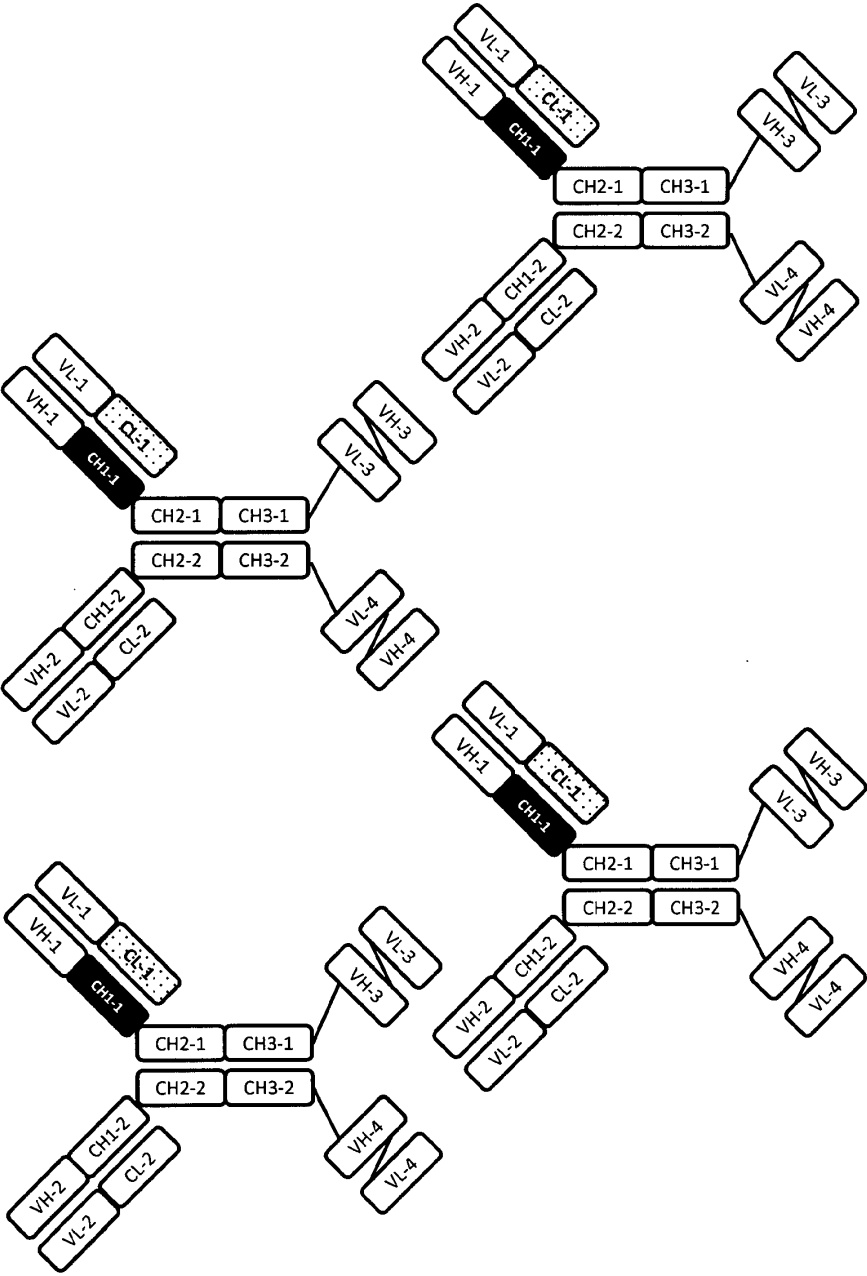


FIG. 6A

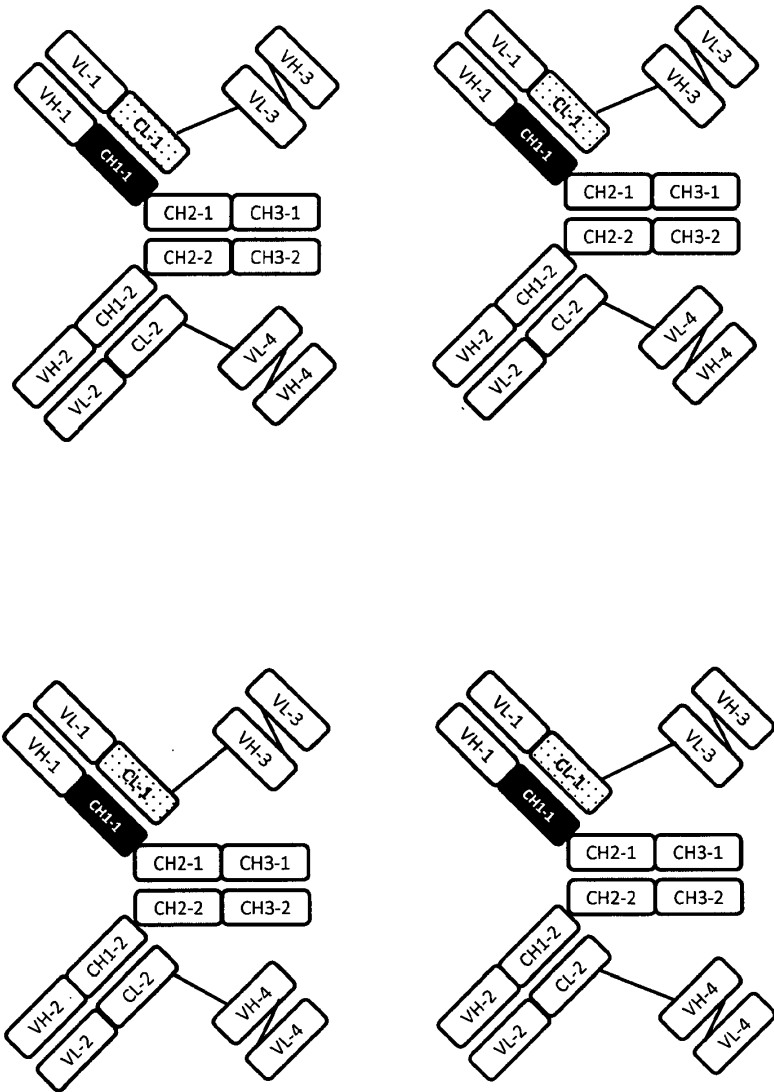


FIG. 6B

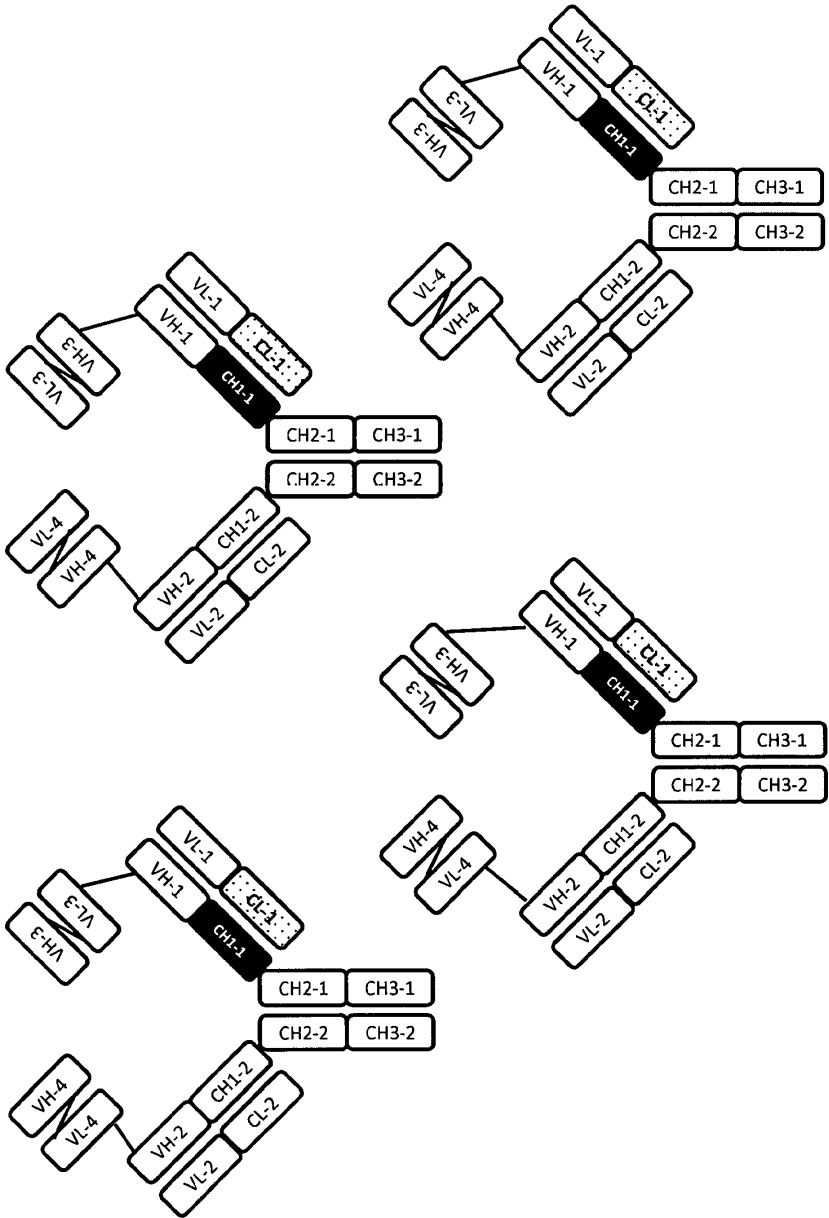


FIG. 6C

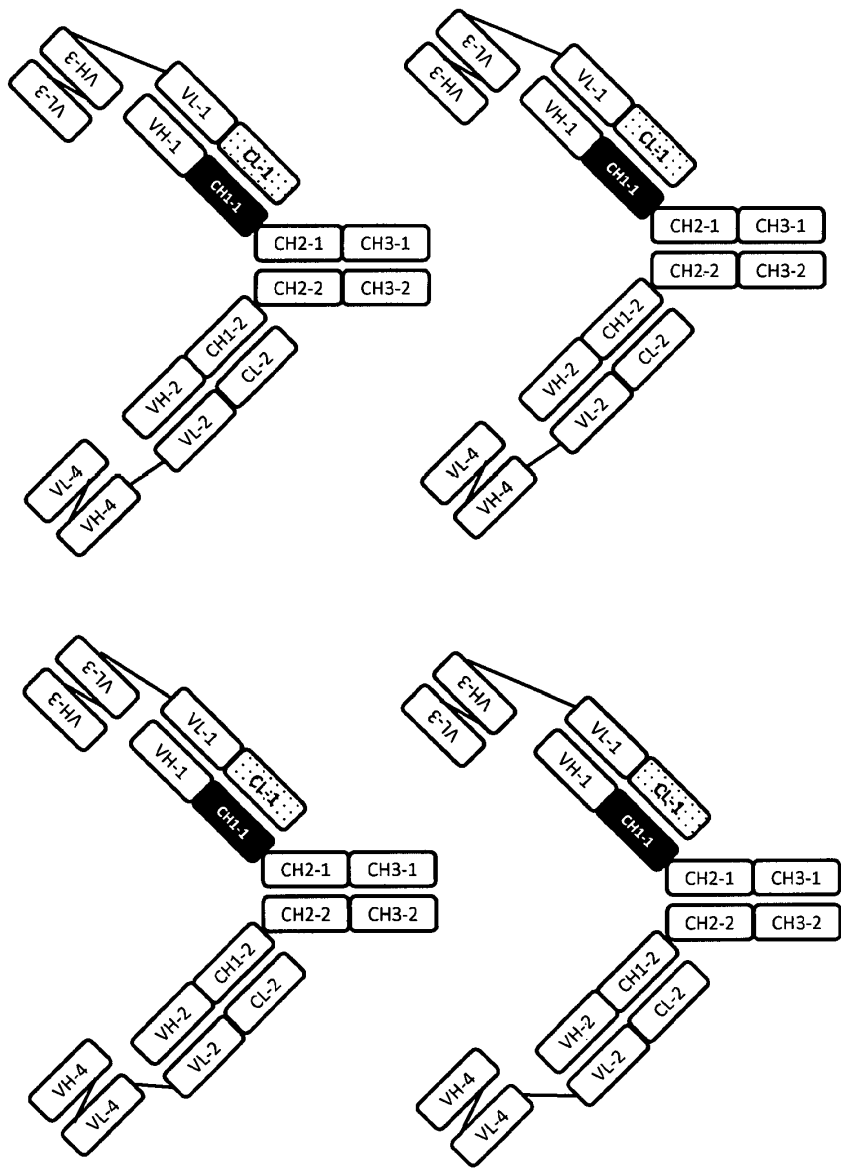


FIG. 6D

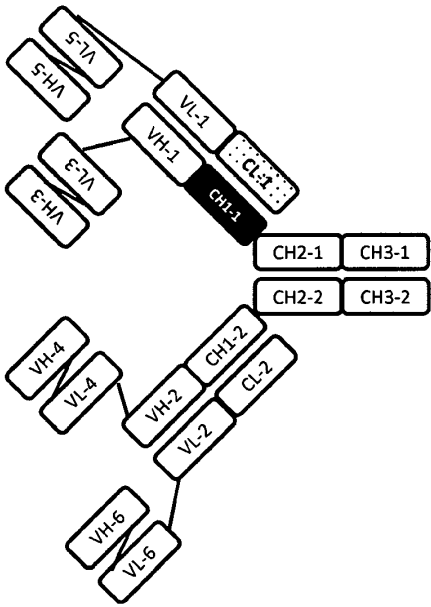
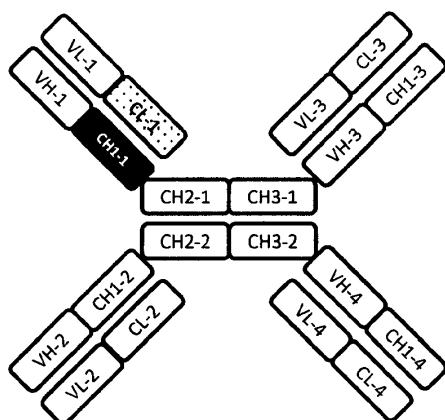


FIG. 6E

**FIG. 7A**

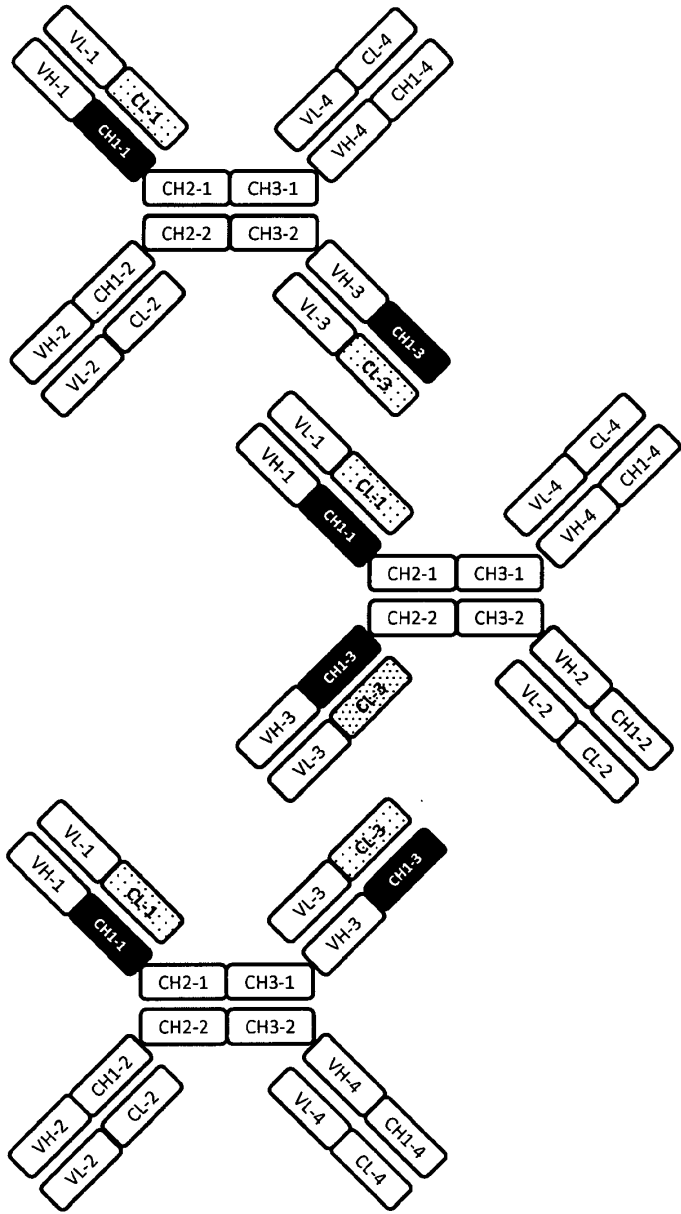


FIG. 7B

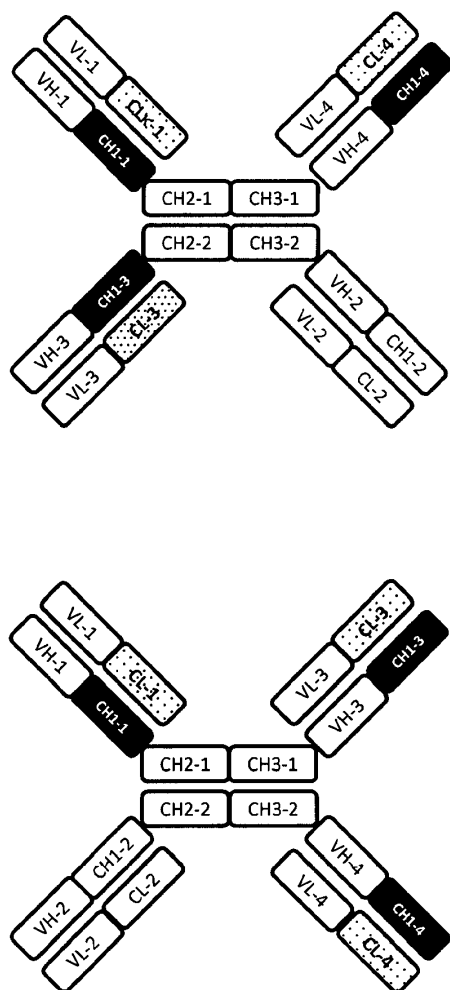
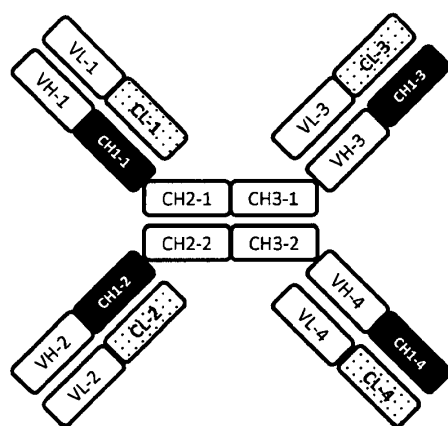


FIG. 7C

**FIG. 7D**

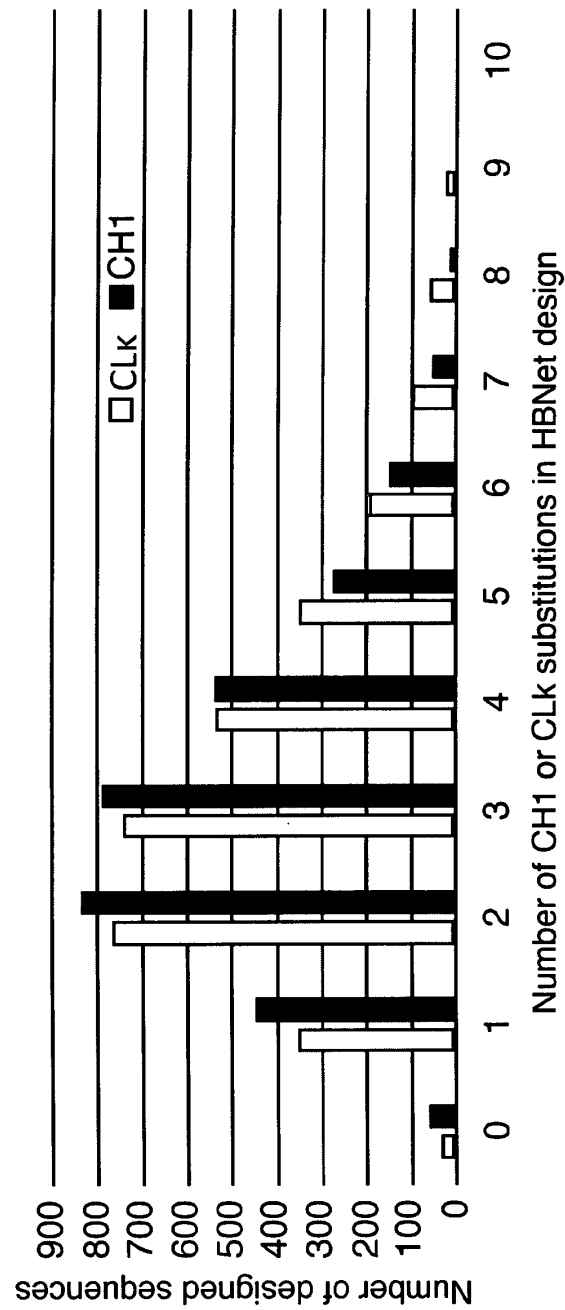


FIG. 8A

	0	1	2	3	4	5	6	7	8	9	10	Row-total
0	1	6	19	14	12	4	1	1	0	0	0	58
1	8	73	162	116	64	18	5	2	0	0	0	448
2	16	160	256	218	110	53	16	5	2	0	0	836
3	6	83	207	194	139	85	44	18	8	4	1	789
4	0	29	90	122	115	79	51	28	18	6	1	539
5	0	4	20	50	59	58	37	21	19	7	2	277
6	0	1	8	21	27	36	23	15	11	6	0	148
7	0	0	3	6	7	15	12	9	1	0	0	53
8	0	0	0	2	3	4	4	1	0	0	0	14
9	0	0	0	0	0	1	1	0	0	0	0	2
Column-total	31	356	765	743	536	353	194	100	59	23	4	

FIG. 8B

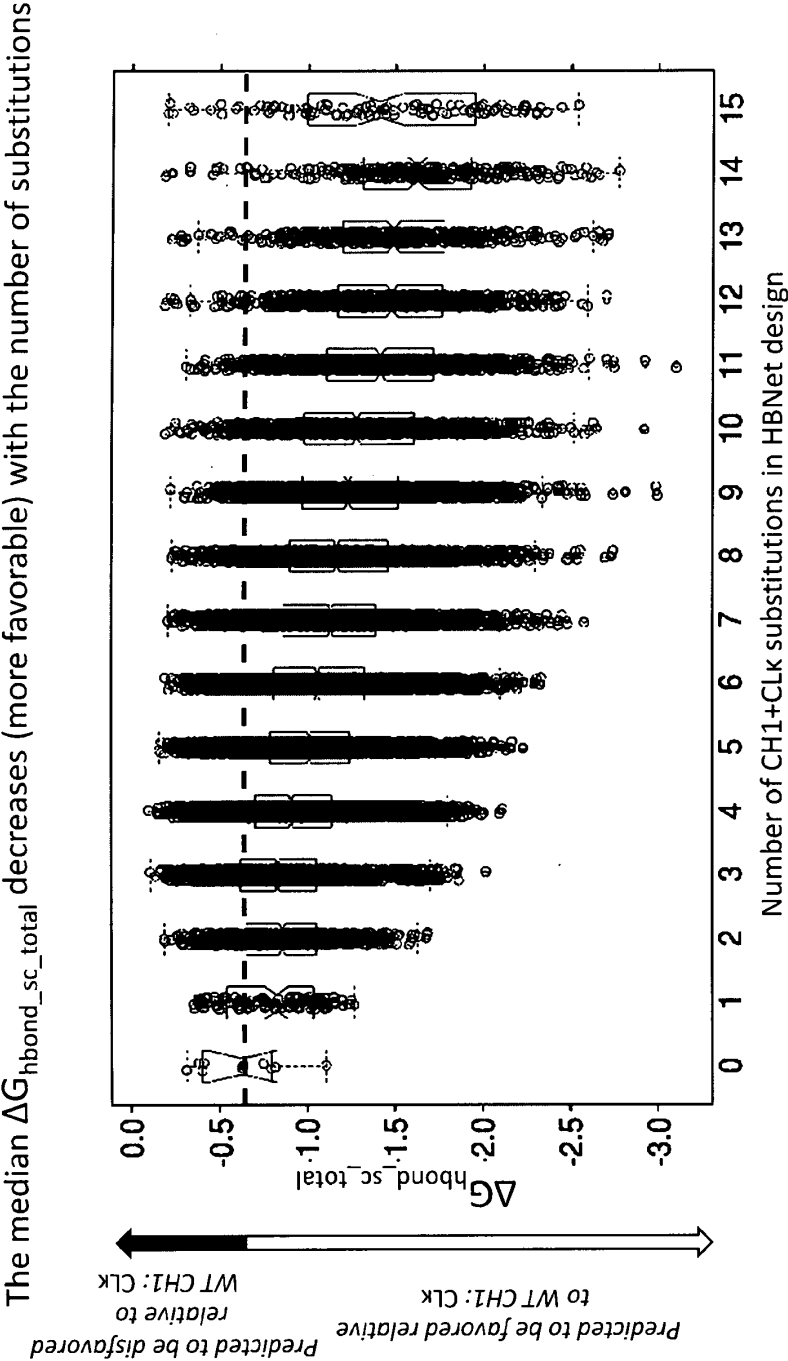


FIG. 8C

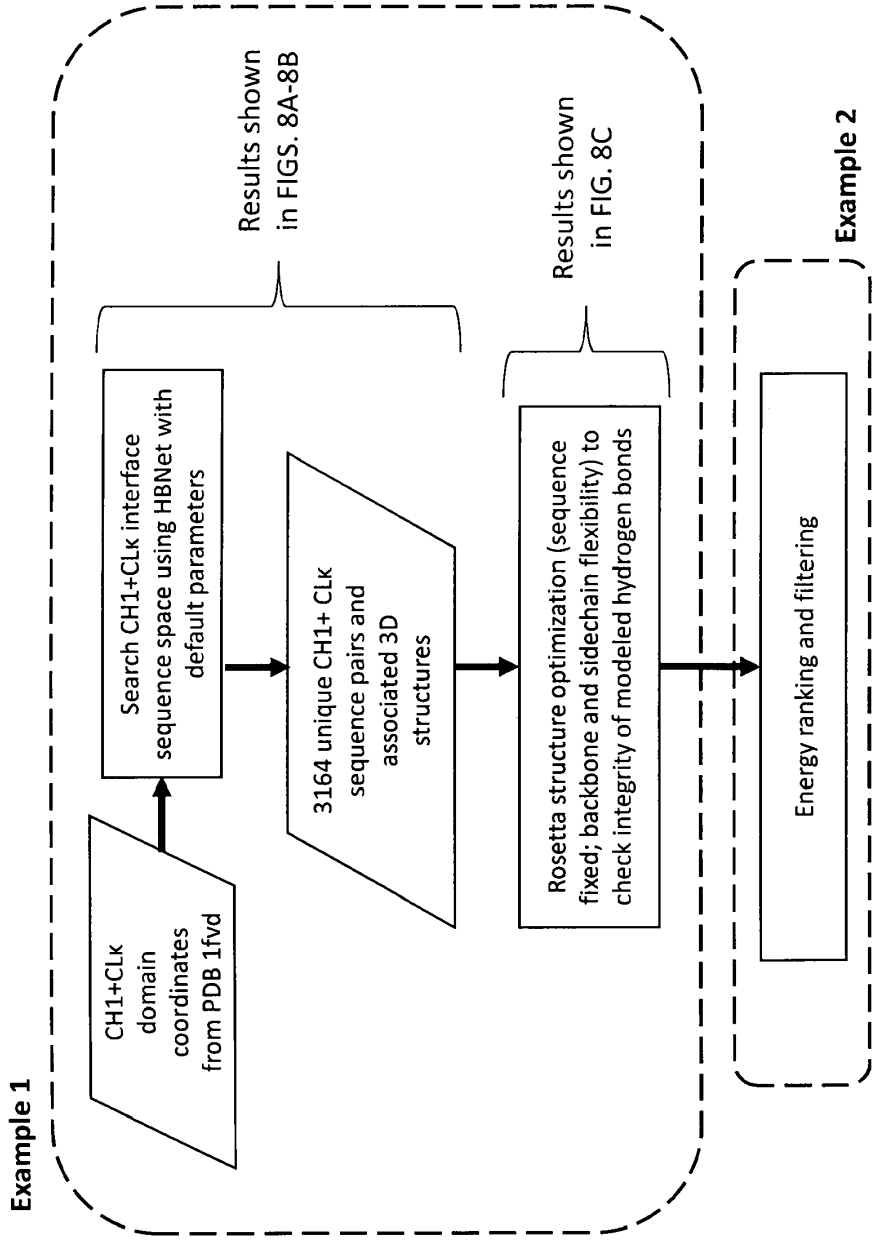


FIG. 8D

Final filtering produces a set of 20 design nominees for production

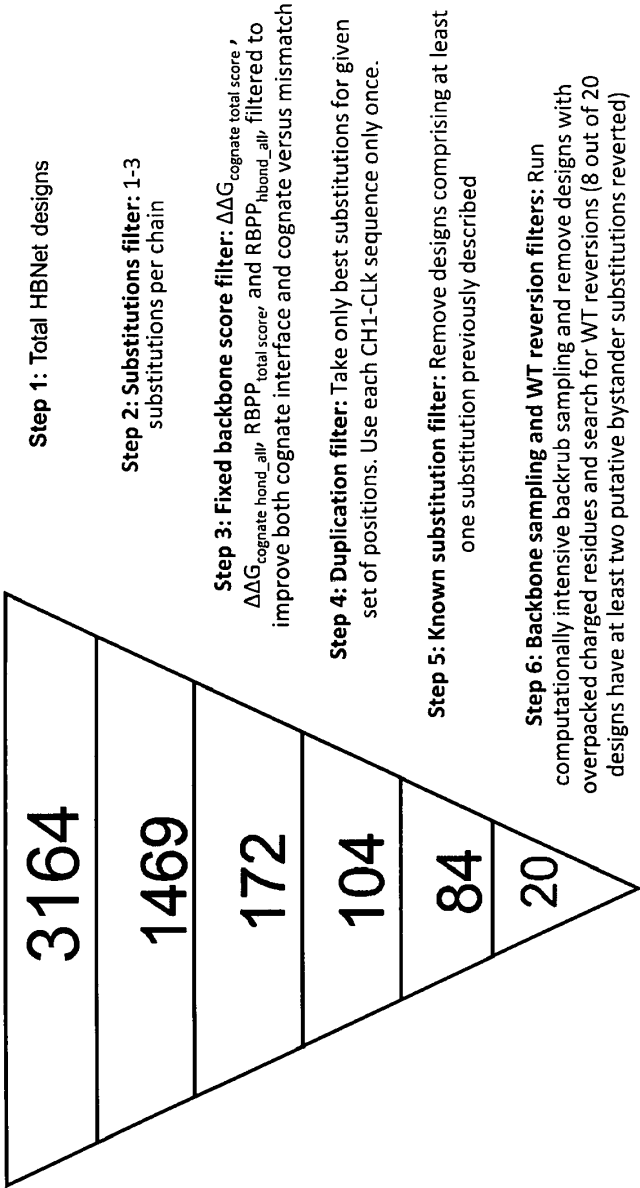


FIG. 9A

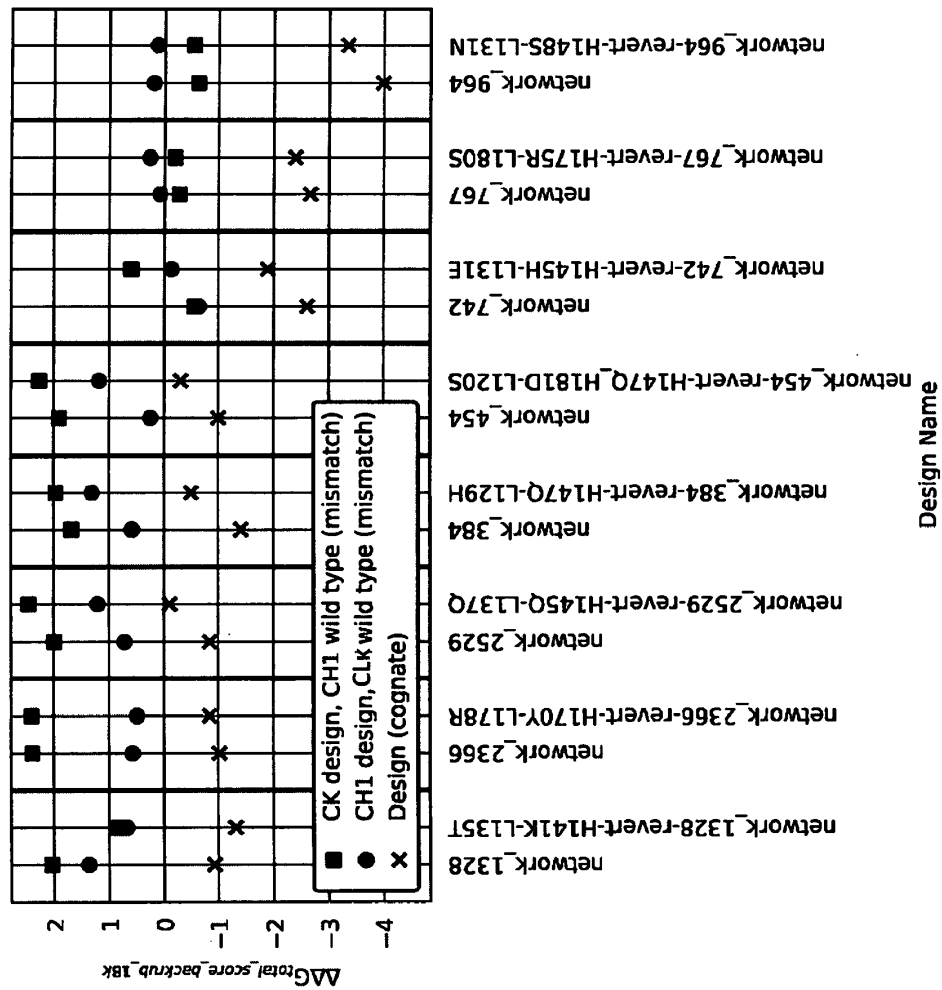


FIG. 9B

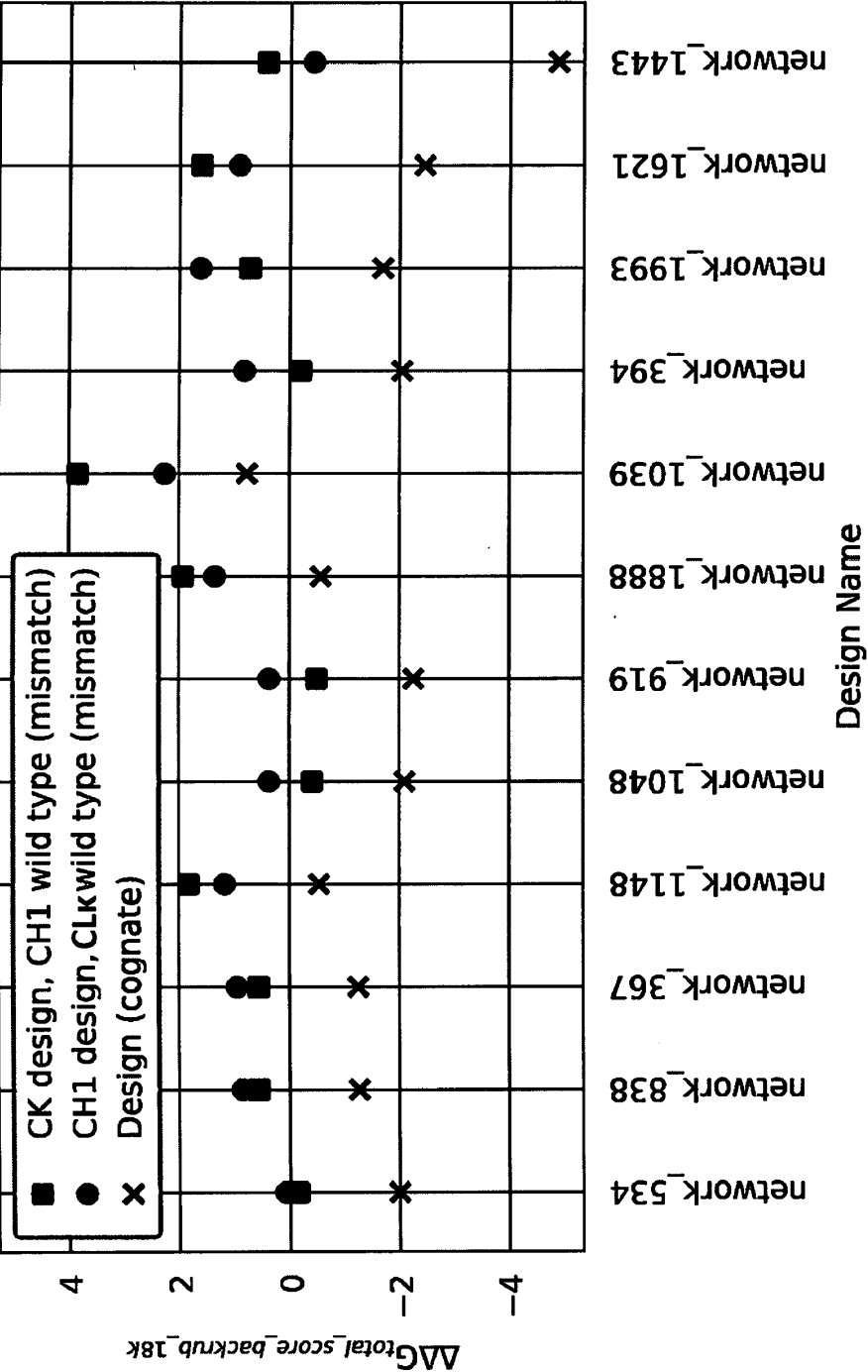
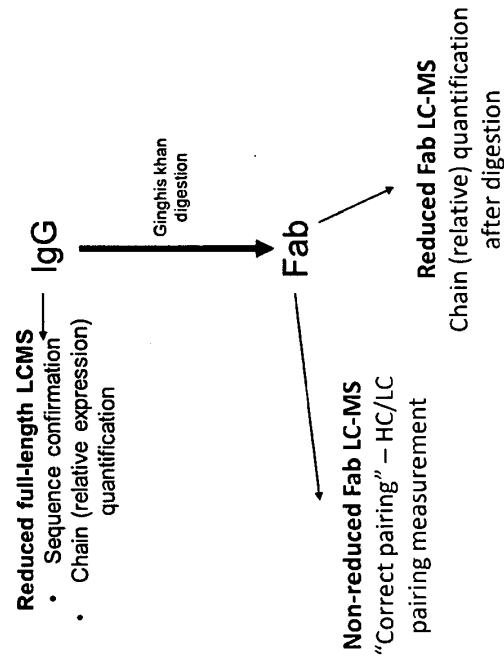


FIG. 9C

LC-MS workflow:



Example data:

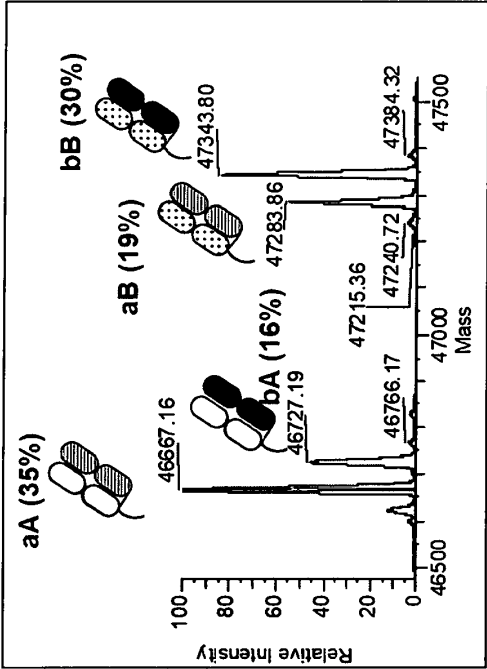


FIG. 10

	network_1443	network_1993	network_1328	network_367	network_1039	network_964	network_2366	network_767	network_1888	network_2529	network_742	network_384	network_454	network_1148	network_534
network_1443	-6.1	-4.2	-5.3	-4.1	-5.0	-4.0	-1.0	-3.8	-2.4	-0.9	-2.6	-3.7	-2.7	-2.0	
network_1993	-6.1	-3.2	-2.3	-2.9	-2.4	-3.1	-3.1	-2.9	-3.6	-2.8	-2.6	-1.7	-2.4	-2.3	
network_1328	-4.2	-3.2	-2.7	-3.6	-2.7	-3.1	-2.8	-2.3	-3.0	-2.5	-2.6	-2.7	-2.5	-2.2	
network_367	-5.3	-2.3	-2.7	-2.7	-0.8	-2.9	-3.9	-2.6	-4.0	-3.5	-2.2	-1.6	-2.1	-1.6	
network_1039	-4.1	-2.9	-3.6	-2.7	-2.5	-2.7	-2.7	-2.0	-2.8	-2.7	-2.5	-2.3	-2.4	-2.1	
network_964	-5.0	-2.4	-2.7	-0.8	-2.5	-2.6	-3.4	-2.2	-3.7	-2.7	-2.2	-1.5	-2.0	-1.6	
network_2366	-4.0	-3.1	-2.9	-2.7	-2.6	-2.5	-2.3	-1.0	-0.7	-2.3	-2.3	-2.3	-2.2	-2.2	
network_767	-1.0	-3.1	-2.8	-3.9	-2.7	-3.4	-2.5	-2.3	-1.6	-0.4	-2.1	-2.3	-2.0	-1.9	
network_1888	-3.8	-2.9	-2.3	-2.6	-2.0	-2.2	-1.0	-2.3	-1.0	-2.2	-2.3	-2.3	-2.3	-1.8	
network_2529	-2.4	-3.6	-3.0	-4.0	-2.8	-3.7	-0.7	-1.6	-1.0	-1.3	-1.9	-1.9	-1.7	-1.4	
network_742	-0.9	-2.8	-2.5	-3.5	-2.7	-2.7	-2.3	-0.4	-2.2	-1.3	-1.9	-2.0	-1.8	-1.2	
network_384	-2.6	-2.6	-2.2	-2.5	-2.2	-2.3	-2.1	-2.3	-1.9	-1.9	0.0	0.0	0.0	-0.4	
network_454	-3.7	-1.7	-2.7	-1.6	-2.3	-2.3	-2.3	-2.3	-1.9	-2.0	0.0	0.0	0.0	-0.4	
network_1148	-2.7	-2.4	-2.5	-2.1	-2.4	-2.0	-2.2	-2.3	-1.7	-1.8	0.0	0.0	0.0	-0.2	
network_534	-2.0	-2.3	-2.2	-1.6	-2.1	-1.6	-2.2	-1.9	-1.4	-1.2	-0.4	-0.4	-0.2	-0.2	

Left → right columns sorted by descending. mean column value
($RBPP_{\text{hbond+electrostatic backrun 18k score}}$)

FIG. 11

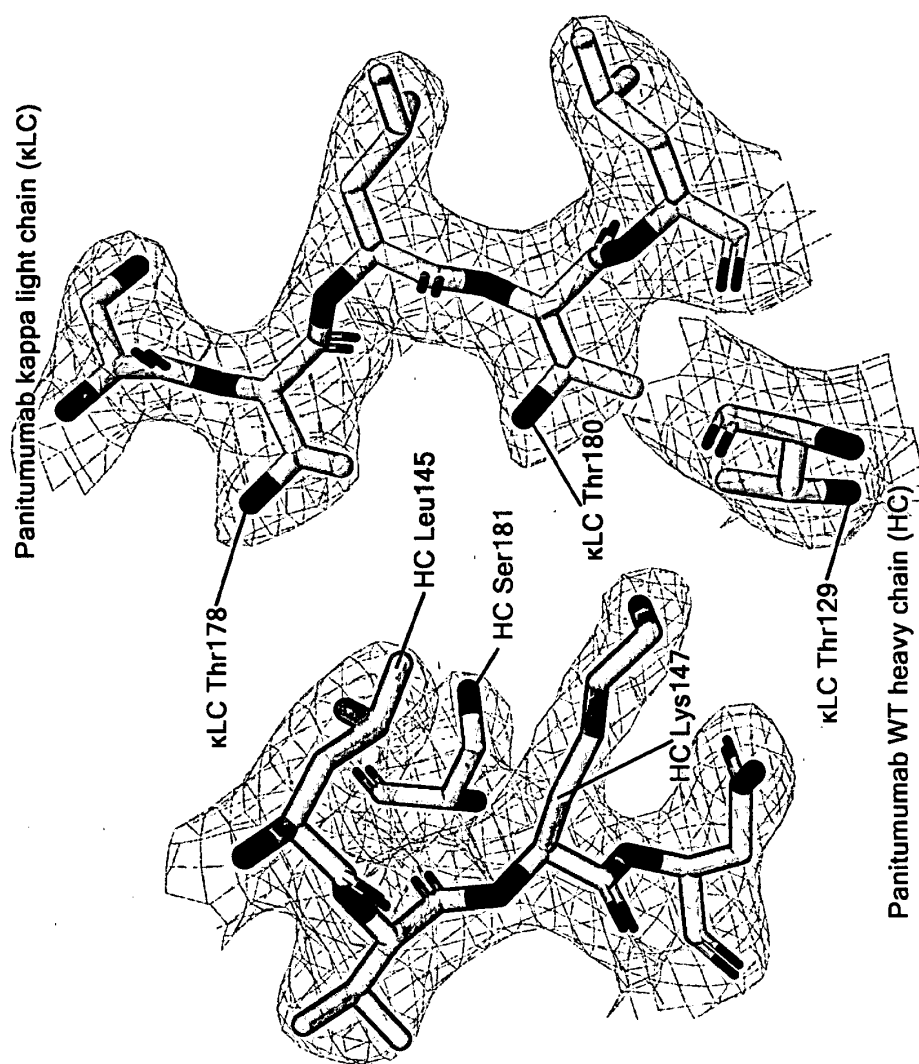


FIG. 12

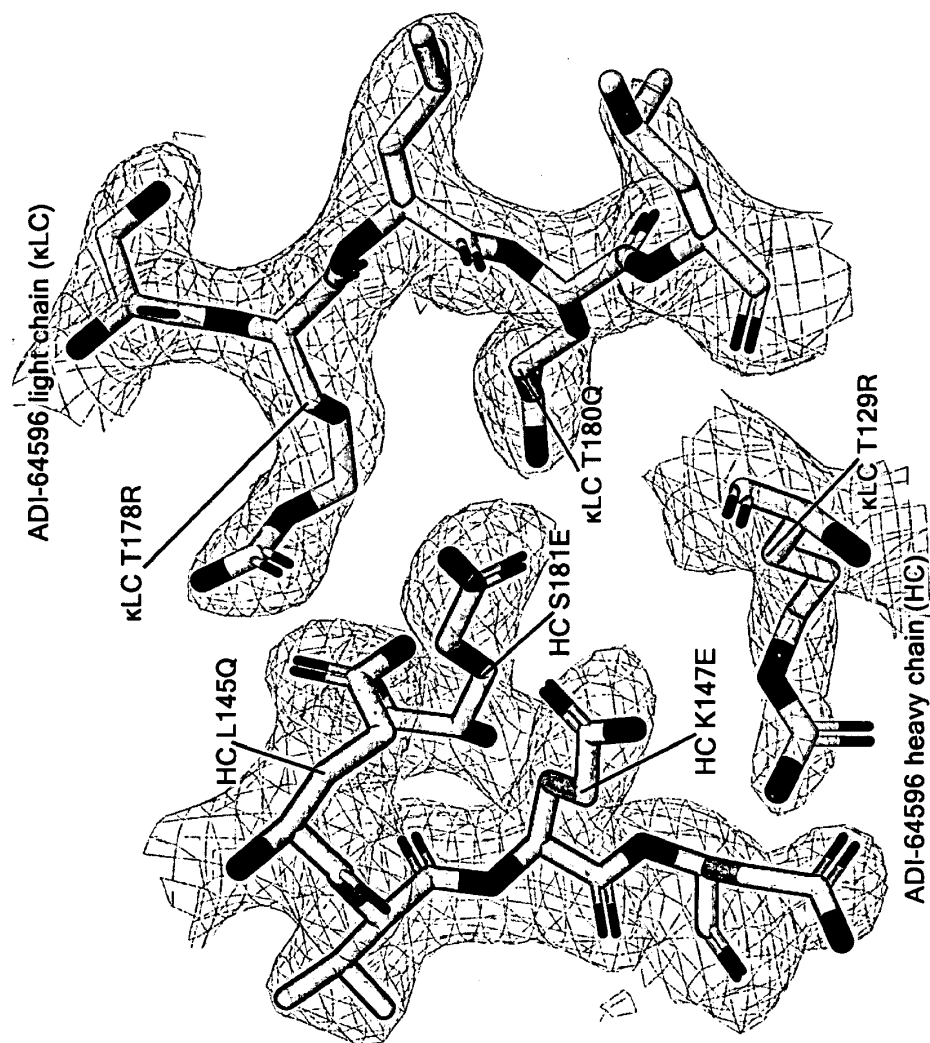


FIG. 13

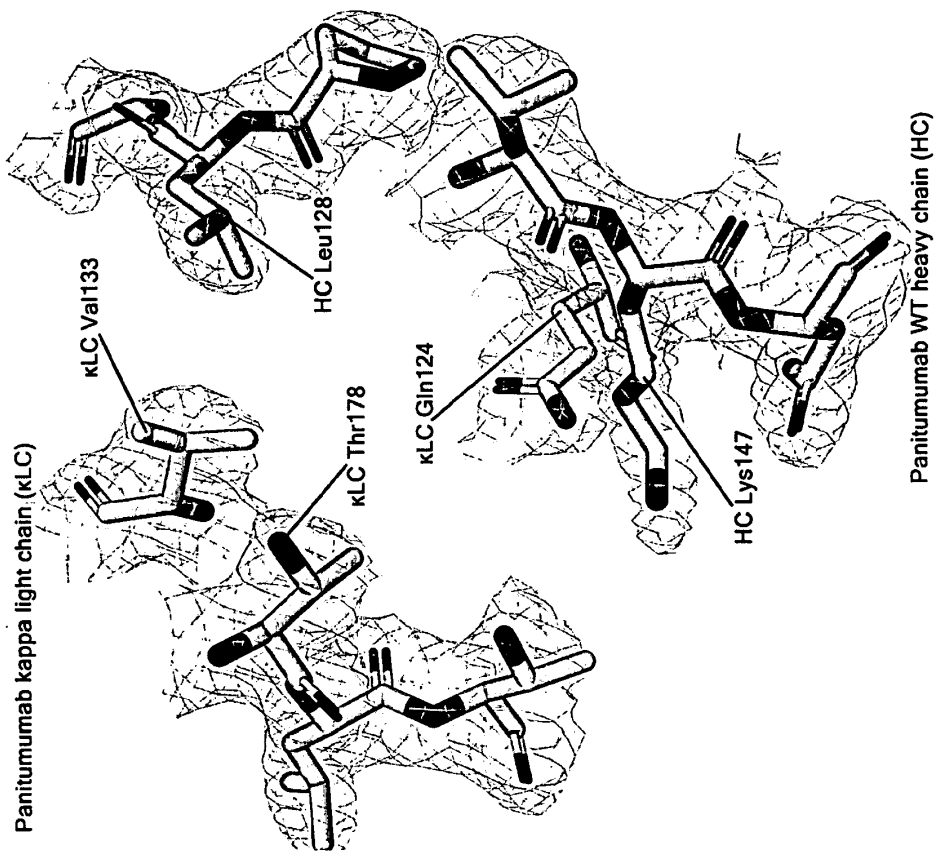


FIG. 14

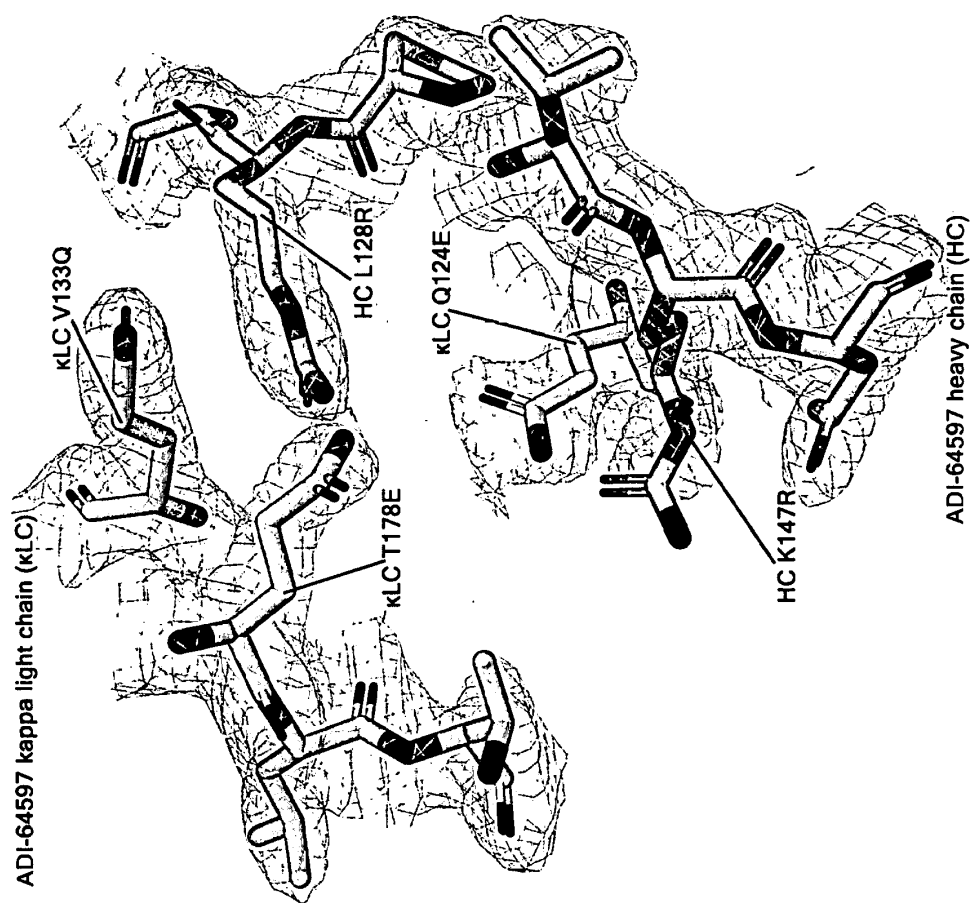


FIG. 15

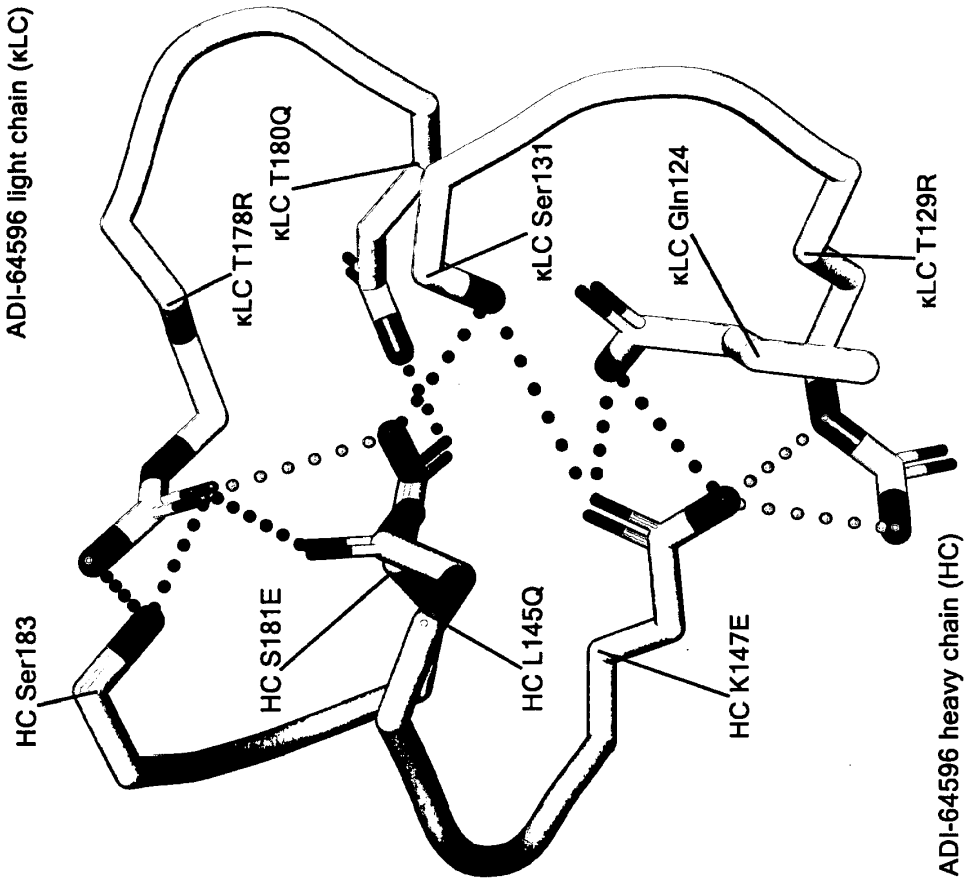


FIG. 16

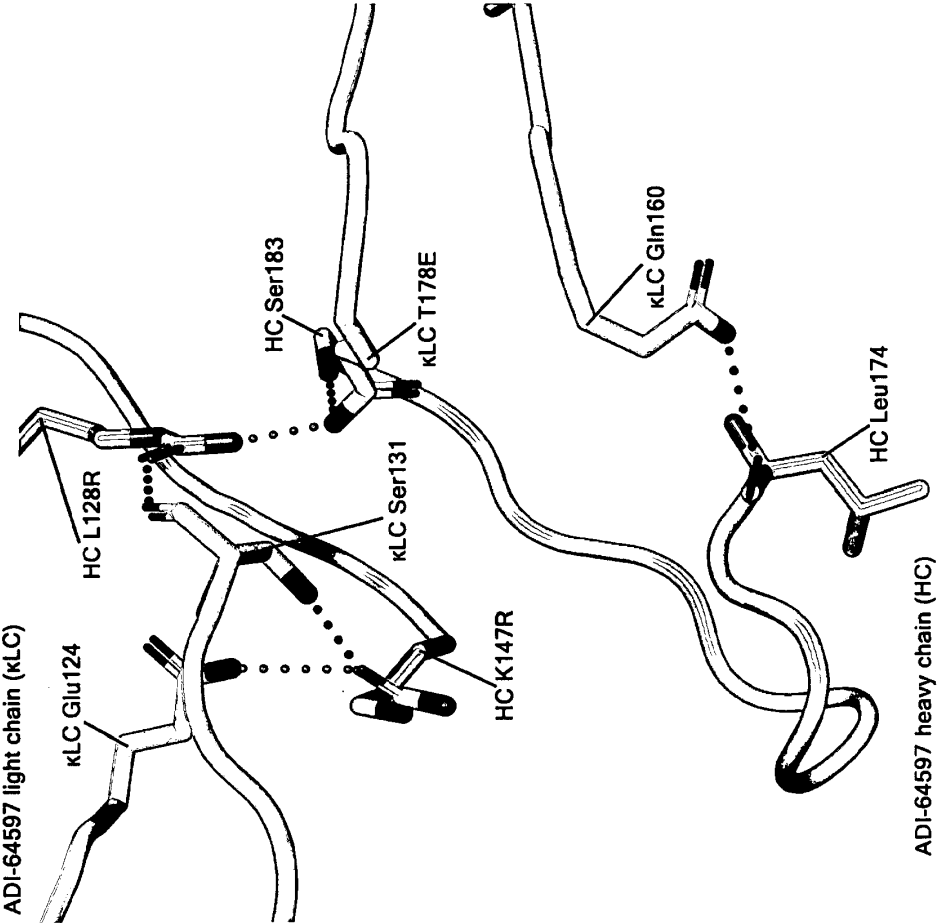


FIG. 17

ADI-64597 heavy chain (HC) and ADI-64596 light chain (κLC)

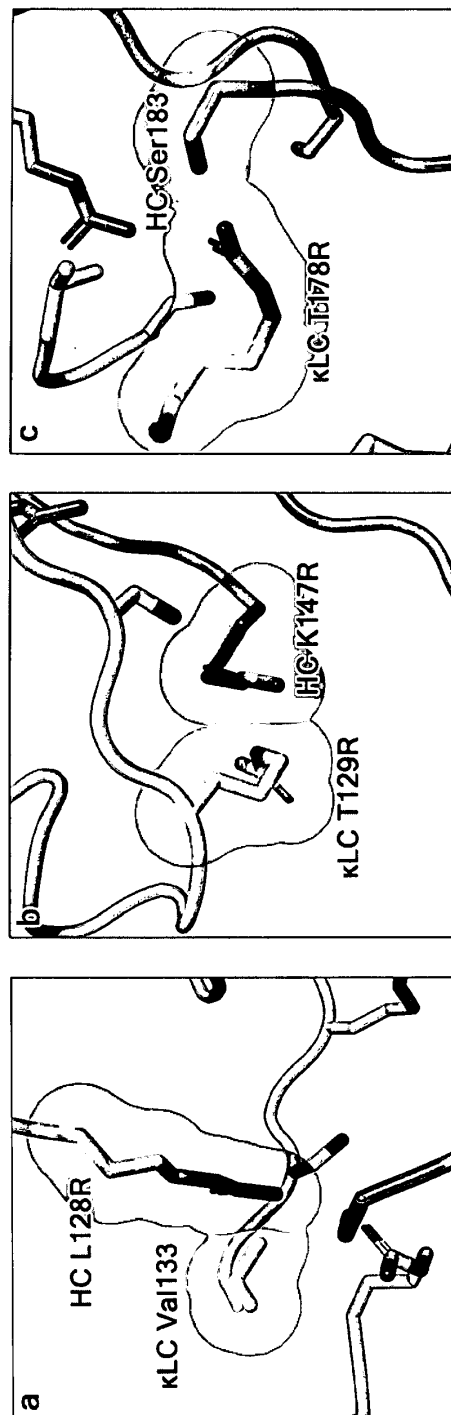


FIG. 18

Net work	367	964	1443	1621	2366	2529	1993	1888	534	394	742	1039	767	1048	384	454	1328	1148	838	919
367		-0.4	-4.0	-4.8	-2.9	-4.1	-3.0	-2.6	-1.0	-0.6	-3.0	-2.6	-3.1	-2.2	-2.5	-2.6	-2.3	-2.6	-2.3	-0.5
964	-0.4		-4.7	-4.1	-2.6	-3.7	-1.8	-2.0	-1.4	-0.6	-2.9	-2.1	-3.2	-1.9	-2.1	-2.2	-1.8	-2.2	-1.8	-1.3
1443	-4.0	-4.7		-0.6	-2.5	-1.4	-3.6	-2.4	-2.3	-2.7	-0.5	-2.3	-0.3	-1.0	-1.5	-1.7	-2.0	-1.7	-1.8	-1.8
1621	-4.8	-4.1	-0.6		-2.4	-1.3	-2.0	-2.1	-1.9	-2.8	-0.6	-2.0	-0.7	-2.2	-0.8	-1.1	-1.7	-0.9	-1.7	-1.8
2366	-2.9	-2.6	-2.5	-2.4		-0.2	-1.0	-1.2	-1.8	-1.2	-1.3	-0.8	-1.2	-1.3	-1.6	-1.5	-1.2	-1.6	-1.1	-1.2
2529	-4.1	-3.7	-1.4	-1.3	-0.2		-1.4	-1.2	-1.9	-2.1	-0.4	-1.1	-0.5	-1.1	-1.2	-1.3	-1.4	-1.3	-1.3	-1.4
1993	-3.0	-1.8	-3.6	-2.0	-1.0	-1.4		-1.0	-1.5	-1.9	-0.6	-0.6	-0.7	-1.7	-1.4	-0.3	-0.5	-0.3	-0.7	-0.9
1888	-2.6	-2.0	-2.4	-2.1	-1.2	-1.2	-1.0		-1.5	-0.8	-1.1	-0.4	-0.9	-0.9	-1.1	-1.2	-0.7	-1.1	-0.6	-0.7
534	-1.0	-1.4	-2.3	-1.9	-1.8	-1.9	-1.5	-1.5		-0.7	-1.5	-1.2	-1.9	-1.1	-0.9	-0.6	-1.2	-0.6	-0.9	0.3
394	-0.6	-0.6	-2.7	-2.8	-1.2	-2.1	-1.9	-0.8	-0.7		-1.8	-0.7	-1.9	-0.5	-0.6	-0.8	-0.6	-0.7	-0.7	0.1
742	-3.0	-2.9	-0.5	-0.6	-1.3	-0.4	-0.6	-1.1	-1.5	-1.8		-0.9	0.2	-1.1	-0.9	-1.2	-0.9	-1.1	-0.7	-1.3
1039	-2.6	-2.1	-2.3	-2.0	-0.8	-1.1	-0.6	-0.4	-1.2	-0.7	-0.9		-0.8	-0.5	-1.2	-0.9	-0.8	-1.0	-0.6	-0.5
767	-3.1	-3.2	-0.3	-0.7	-1.2	-0.5	-0.7	-0.9	-1.9	-1.9	0.2	-0.8		-0.8	-0.6	-0.8	-0.6	-0.7	-0.4	-1.2
1048	-2.2	-1.9	-1.0	-2.2	-1.3	-1.1	-1.7	-0.9	-1.1	-0.5	-1.1	-0.5	-0.8		-0.7	-0.9	-0.5	-0.9	-0.4	0.6
384	-2.5	-2.1	-1.5	-0.8	-1.6	-1.2	-1.4	-1.1	-0.9	-0.6	-0.9	-1.2	-0.6	-0.7		0.0	-0.8	0.0	-0.8	-0.3
454	-2.6	-2.2	-1.7	-1.1	-1.5	-1.3	-0.3	-1.2	-0.6	-0.8	-1.2	-0.9	-0.8	-0.9	0.0		-0.9	0.0	-0.8	-0.2
1328	-2.3	-1.8	-2.0	-1.7	-1.2	-1.4	-0.5	-0.7	-1.2	-0.6	-0.9	-0.8	-0.6	-0.5	-0.8	-0.9		-0.8	0.0	-0.3
1148	-2.6	-2.2	-1.7	-0.9	-1.6	-1.3	-0.3	-1.1	-0.6	-0.7	-1.1	-1.0	-0.7	-0.9	0.0	0.0	-0.8		-0.7	-0.3
838	-2.3	-1.8	-1.8	-1.7	-1.1	-1.3	-0.7	-0.6	-0.9	-0.7	-0.7	-0.6	-0.4	-0.4	-0.8	-0.8	0.0	-0.7		-0.5
919	-0.5	-1.3	-1.8	-1.8	-1.2	-1.4	-0.9	-0.7	0.3	0.1	-1.3	-0.5	-1.2	0.6	-0.3	-0.2	-0.3	-0.3	-0.5	

Left → right columns sorted by descending mean column value
($\text{RBPP}_{\text{hbond+electrostatic backrun 18k}}$ score)

FIG. 19