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Fitness Epistasis and Constraints on Adaptation in a Human Immunodeficiency Virus Type 1 Protein Region

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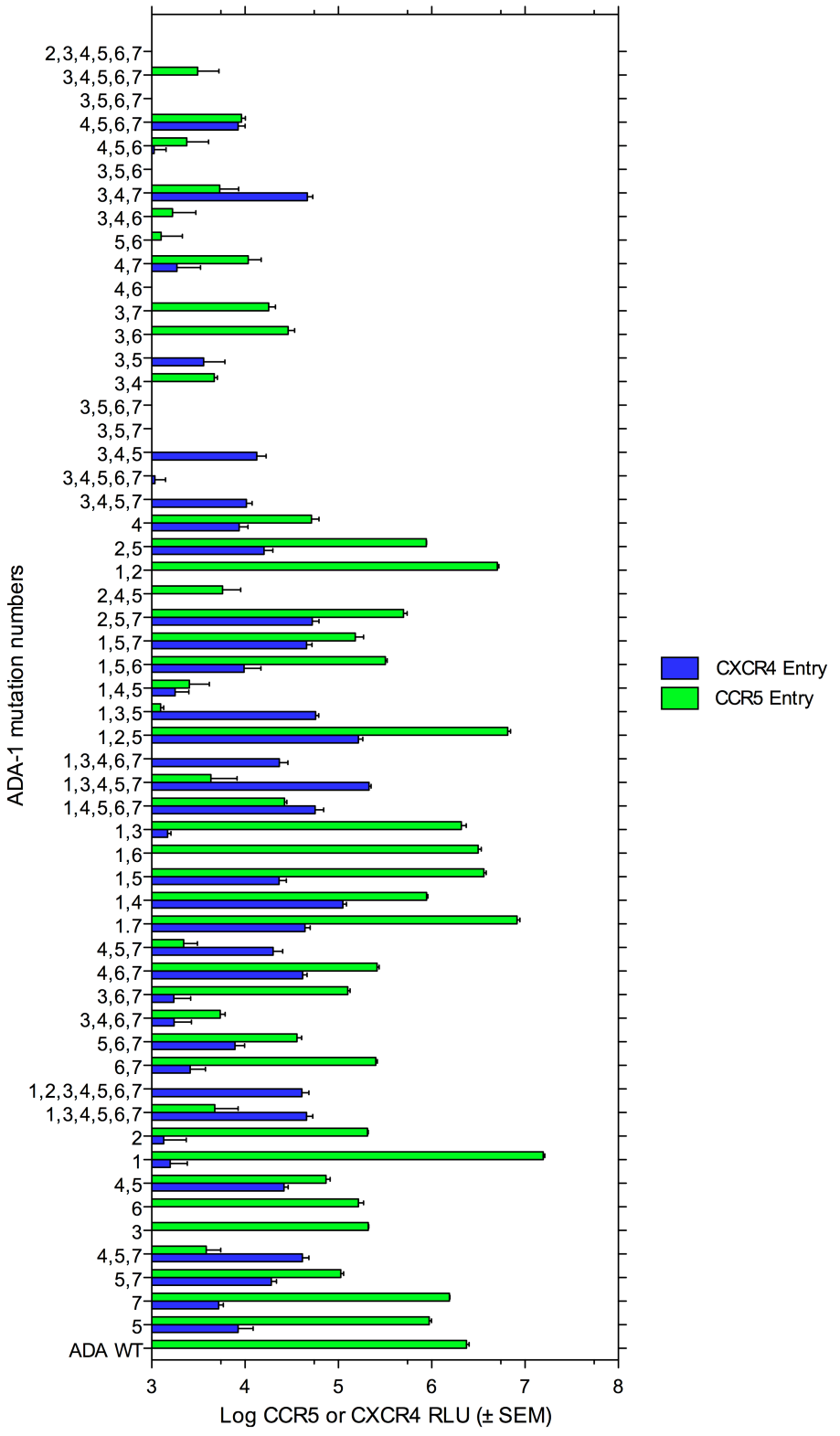

FIGURE S1.—The entry fitness of HIV-1 C2-V3 mutants on CCR5 and CXCR4 host cells in relative light units (RLU). Mutants were engineered with mutations observed for the ADA-1 CXCR4-adapted mutant on the ADA background. The method used to determine entry fitness is identical to that described in (PASTORE *et al.* 2006), with the exception that NP-2.CD4 target cells were used instead of U87.CD4 cells. Briefly, equivalent p24 levels of pseudotyped virus particles were added to each target cell line, and the luciferase activity of triplicate wells determined 48 hr. later. Experiments were repeated three times for all mutations that scored above background (~1000 RLU).

PASTORE, C., R. NEDELLEC, A. RAMOS, S. PONTOW, L. RATNER *et al.*, 2006 Human immunodeficiency virus type 1 coreceptor switching: V1/V2 gain-of-fitness mutations compensate for V3 loss-of-fitness mutations. Journal of Virology **80:** 750-758.

TABLE S1

Means and variances in fitness and epistatic deviation for assays on CCR5 and CXCR4 target cells

	CCR5										CXCR4									
Mutations	W	w	Var(w)	ε	Var(ε)	Sig.	E	ε'	Var(ε')	Sig.	W	w	Var(w)	ε	Var(ε)	Sig.	E	ε'	Var(ε')	Sig.
wt	2357403.7	1.0000	0.0147								441.1	0.0109	0.0000							
1	15717078.9	6.6671	0.1926								1584.3	0.0390	0.0012							
2	205870.3	0.0873	0.0000								1346.8	0.0331	0.0018							
3	209335.1	0.0888	0.0000								232.0	0.0057	0.0000							
4	51631.0	0.0219	0.0001								8656.0	0.2129	0.0082							
5	942373.0	0.3998	0.0015								8420.5	0.2071	0.0267							
6	163853.1	0.0695	0.0003								893.1	0.0220	0.0002							
7	1548272.5	0.6568	0.0002								5216.2	0.1283	0.0007							
12	5055976.9	2.1447	0.0202	1.5625	0.0219	*	0.5663				841.4	0.0207	0.0003	0.0194	0.0003		1.2050			
13	2078231.0	0.8816	0.0416	0.2895	0.0433		0.1729				1478.8	0.0364	0.0000	0.0362	0.0000	*	2.2137			
14	880760.1	0.3736	0.0005	0.2276	0.0032	*	0.4080				111577.6	2.7446	0.2023	2.7363	0.2024	*	2.5195			
15	3625942.7	1.5381	0.0258	-1.1271	0.1252	*	-0.2387				23136.3	0.5691	0.0398	0.5610	0.0399		1.8482			
16	3161239.0	1.3410	0.0301	0.8776	0.0436	*	0.4615				717.9	0.0177	0.0001	0.0168	0.0001		1.3144			
17	8238111.1	3.4946	0.1935	-0.8842	0.2846		-0.0980				44040.8	1.0833	0.0625	1.0783	0.0625	*	2.3358			
25	879624.7	0.3731	0.0000	0.3382	0.0000	*	1.0289				15978.0	0.3930	0.0279	0.3862	0.0280		1.7580			
34	4677.9	0.0020	0.0000	0.0000	0.0000		0.0087				356.4	0.0088	0.0000	0.0076	0.0000	*	0.8582			
35	480.4	0.0002	0.0000	-0.0353	0.0000	*	-2.2410				3612.0	0.0888	0.0112	0.0877	0.0112		1.8760			
36	28996.4	0.0123	0.0000	0.0061	0.0000		0.2995				646.2	0.0159	0.0000	0.0158	0.0000	*	2.1031			
37	17917.1	0.0076	0.0000	-0.0507	0.0000	*	-0.8850				329.9	0.0081	0.0000	0.0074	0.0000	*	1.0446			
45	73844.4	0.0313	0.0000	0.0226	0.0000	*	0.5536				26176.8	0.6439	0.0138	0.5998	0.0156	*	1.1644			
46	323.9	0.0001	0.0000	-0.0014	0.0000		-1.0445				351.2	0.0086	0.0000	0.0040	0.0000		0.2664			
47	10832.0	0.0046	0.0000	-0.0098	0.0000		-0.4956				1867.2	0.0459	0.0040	0.0186	0.0041		0.2256			
56	1265.5	0.0005	0.0000	-0.0272	0.0001	*	-1.7140				328.3	0.0081	0.0000	0.0035	0.0000		0.2491			
57	106531.5	0.0452	0.0000	-0.2174	0.0007	*	-0.7642				19148.7	0.4710	0.0117	0.4444	0.0122	*	1.2485			

67	252541.4	0.1071	0.0000	0.0615	0.0002	*	0.3705				2583.2	0.0635	0.0026	0.0607	0.0026		1.3530			
125	6550730.2	2.7788	0.1077	2.5460	0.1085	*	1.0770	1.7724	0.2556	*	164389.1	4.0436	0.5978	4.0434	0.5978	*	4.1796	3.0768	0.6661	*
135	1244.4	0.0005	0.0000	-0.2361	0.0008	*	-2.6516	0.6367	0.1693		57010.6	1.4023	0.0416	1.4023	0.0416	*	4.4835	0.7174	0.0927	
145	2542.6	0.0011	0.0000	-0.0573	0.0005		-1.7334	0.8196	0.1289		1781.2	0.0438	0.0010	0.0421	0.0010		1.4064	-3.8550	0.2588	*
156	320045.8	0.1358	0.0001	-0.0495	0.0026		-0.1350	0.2273	0.1715		9794.4	0.2409	0.0458	0.2407	0.0458		3.1331	-0.3406	0.0858	
157	152494.3	0.0647	0.0006	-1.6857	0.0448	*	-1.4323	0.5429	0.4553		45575.9	1.1211	0.0826	1.1200	0.0826	*	3.0344	-0.9638	0.1972	
245	5752.6	0.0024	0.0000	0.0017	0.0000		0.5040				883.5	0.0217	0.0004	0.0203	0.0004		1.1724			
257	499694.0	0.2120	0.0011	0.1890	0.0011	*	0.9659				52481.4	1.2909	0.1730	1.2901	0.1730	*	3.1662			
345	449.3	0.0002	0.0000	-0.0006	0.0000		-0.6106	0.0121	0.0001		13367.1	0.3288	0.0220	0.3286	0.0220		3.1161	-0.3665	0.0487	
346	1677.2	0.0007	0.0000	0.0006	0.0000		0.7212	-0.0042	0.0000		321.7	0.0079	0.0000	0.0079	0.0000	*	2.4719	-0.0194	0.0000	*
347	5376.8	0.0023	0.0000	0.0010	0.0000		0.2518	0.0615	0.0000	*	46615.1	1.1466	0.0777	1.1465	0.0777	*	3.8666	1.1129	0.0819	*
356	322.8	0.0001	0.0000	-0.0023	0.0000	*	-1.2557	0.0541	0.0001	*	310.8	0.0076	0.0000	0.0076	0.0000	*	2.4690	-0.0993	0.0112	
357	353.0	0.0001	0.0000	-0.0232	0.0000	*	-2.1923	0.2802	0.0008	*	366.5	0.0090	0.0000	0.0089	0.0000	*	1.7741	-0.5306	0.0234	*
367	126438.6	0.0536	0.0000	0.0496	0.0000	*	1.1216	0.0327	0.0002		1733.2	0.0426	0.0014	0.0426	0.0014		3.4233	-0.0413	0.0040	
456	2382.2	0.0010	0.0000	0.0004	0.0000		0.2203	0.0065	0.0001		1064.9	0.0262	0.0002	0.0252	0.0002		1.4320	-0.5821	0.0159	*
457	3851.5	0.0016	0.0000	-0.0041	0.0000		-0.5465	0.2005	0.0008	*	41248.0	1.0146	0.0895	1.0090	0.0896	*	2.2536	-0.0539	0.1215	
457	2198.6	0.0009	0.0000	-0.0048	0.0000		-0.7900	0.1998	0.0008	*	20073.9	0.4938	0.0494	0.4881	0.0495		1.9408	-0.5747	0.0814	
467	260575.8	0.1105	0.0001	0.1095	0.0001	*	2.0436	0.0592	0.0003	*	41540.0	1.0218	0.0407	1.0212	0.0407	*	3.2311	0.9379	0.0475	*
567	36089.6	0.0153	0.0000	-0.0029	0.0000		-0.0763	0.1802	0.0010	*	7841.0	0.1929	0.0077	0.1923	0.0077		2.5190	-0.3164	0.0225	
3456	3115.5	0.0013	0.0000	0.0013	0.0000		1.3884	-0.0320	0.0004		320.9	0.0079	0.0000	0.0079	0.0000	*	3.1546	0.3569	0.1027	
3457	466.8	0.0002	0.0000	-0.0003	0.0000		-0.4114	-0.2636	0.0025	*	10389.4	0.2556	0.0044	0.2555	0.0044	*	3.8984	-0.8115	0.3030	
3467	5438.3	0.0023	0.0000	0.0022	0.0000	*	1.4147	-0.1527	0.0008	*	1737.7	0.0427	0.0016	0.0427	0.0016		4.0962	-2.0614	0.1417	*
3567	436.1	0.0002	0.0000	-0.0014	0.0000	*	-0.9425	-0.2856	0.0030	*	359.3	0.0088	0.0000	0.0088	0.0000	*	3.4237	0.3770	0.0872	
3567	334.0	0.0001	0.0000	-0.0015	0.0000	*	-1.0583	-0.2856	0.0030	*	333.0	0.0082	0.0000	0.0082	0.0000	*	3.3907	0.3763	0.0872	
4567	9145.7	0.0039	0.0000	0.0035	0.0000	*	0.9871	-0.2711	0.0032	*	8461.9	0.2081	0.0046	0.2080	0.0046	*	3.2239	-0.6482	0.2265	
13457	4311.6	0.0018	0.0000	-0.0016	0.0000		-0.2698				213643.4	5.2552	0.2281	5.2552	0.2281	*	6.6208			
13467	559.1	0.0002	0.0000	-0.0004	0.0000		-0.3972				23371.1	0.5749	0.0547	0.5749	0.0547		6.6342			
14567	26450.9	0.0112	0.0000	0.0086	0.0000	*	0.6244				56417.9	1.3878	0.3193	1.3878	0.3193		5.4571			
34567	386.0	0.0002	0.0000	0.0001	0.0000	*	0.6640	0.3745	0.0143	*	1084.1	0.0267	0.0002	0.0267	0.0002		4.5751	1.7838	1.2635	

134567	4734.1	0.0020	0.0000	0.0018	0.0000		0.9288	45549.8	1.1204	0.1099	1.1204	0.1099	*	7.6078
234567	310.2	0.0001	0.0000	0.0001	0.0000	*	1.6279	340.4	0.0084	0.0000	0.0084	0.0000	*	5.5518
1234567	423.2	0.0002	0.0000	0.0002	0.0000	*	0.9389	40653.7	1.0000	0.1050	1.0000	0.1050	*	9.0382

W, absolute fitness; *w*, relative fitness; Var, variance; ε, overall epistatic deviation; ε', net epistatic deviation; E, epistasis magnitude; Sig., significant epistatic deviation at an experimentwise type-1 error rate of $\alpha' = 0.05$.