

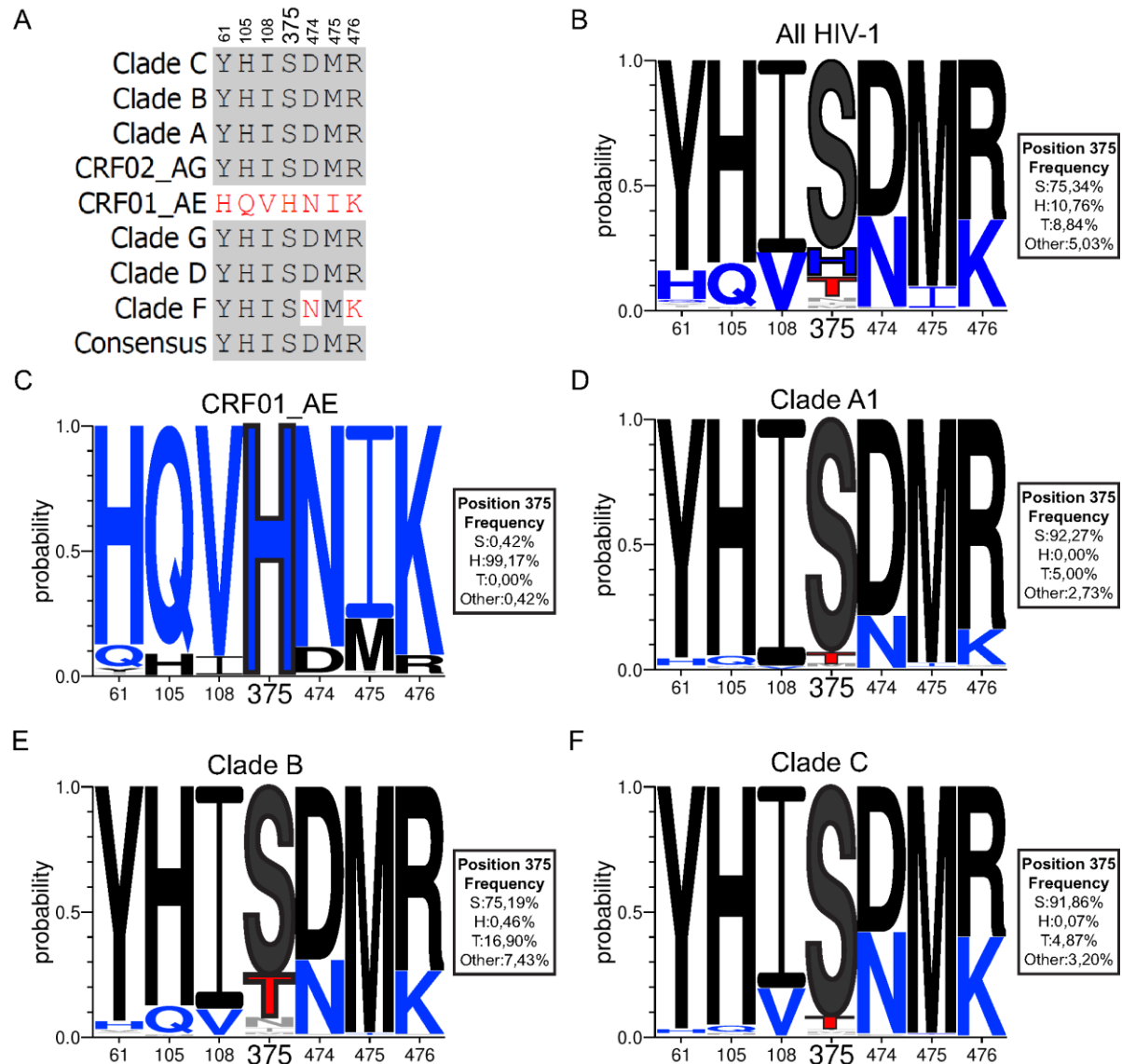


A complex interplay between the HIV-1 Env gp120 inner domain and the Phe43 cavity shapes the CD4-binding site

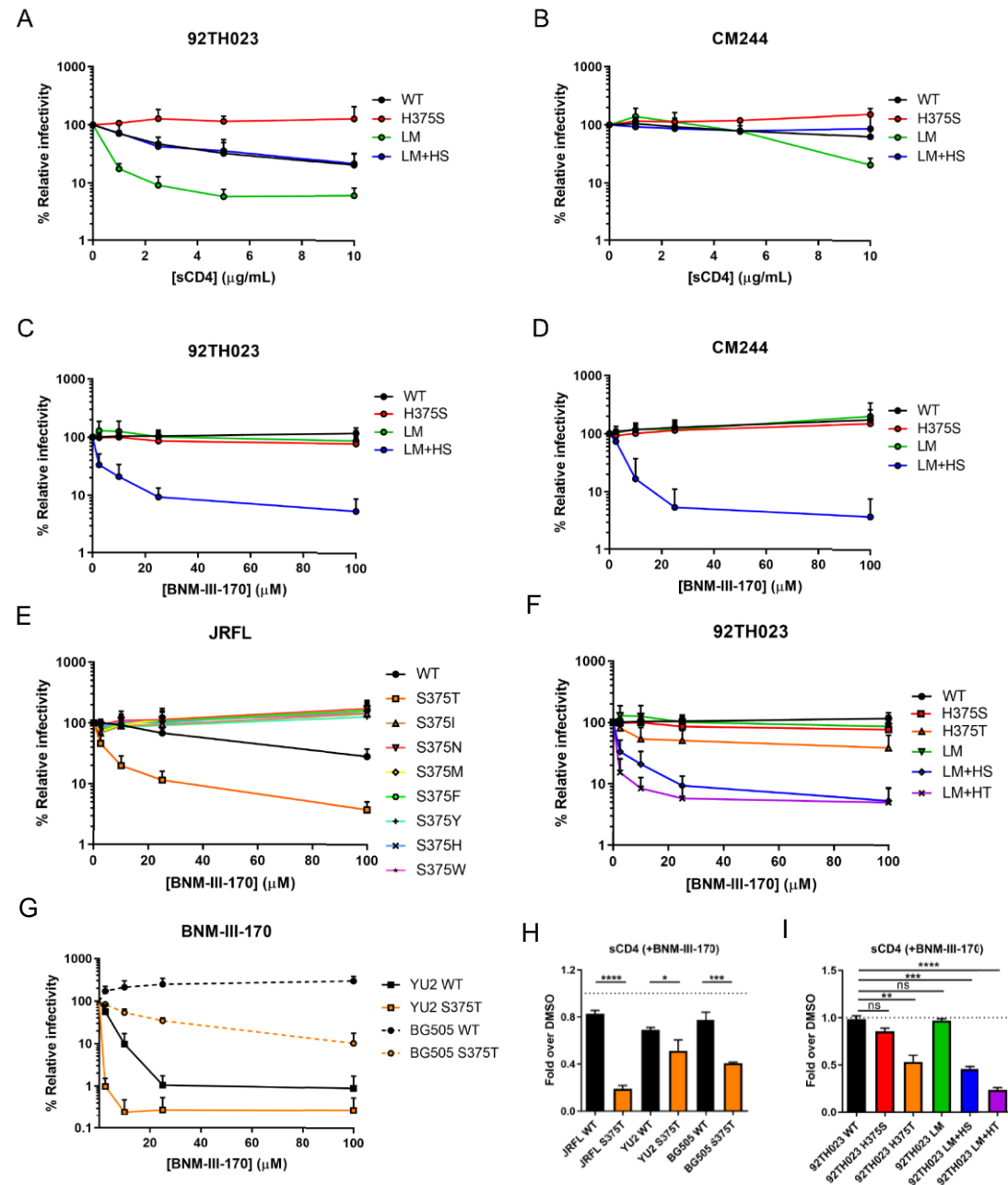
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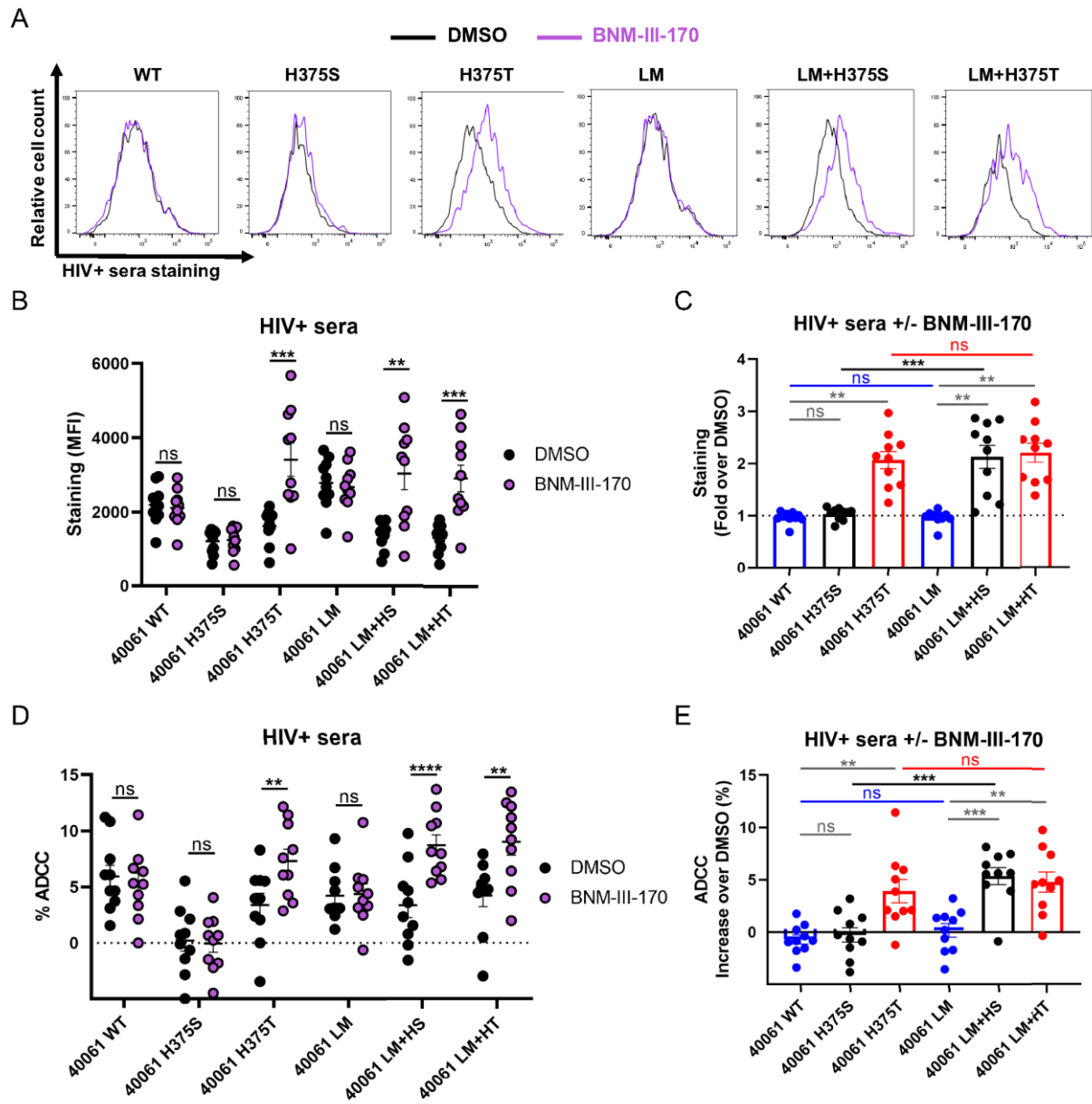
Sequence alignment of gp120 Phe43 cavity and inner domain layers residues of different HIV-1 isolates



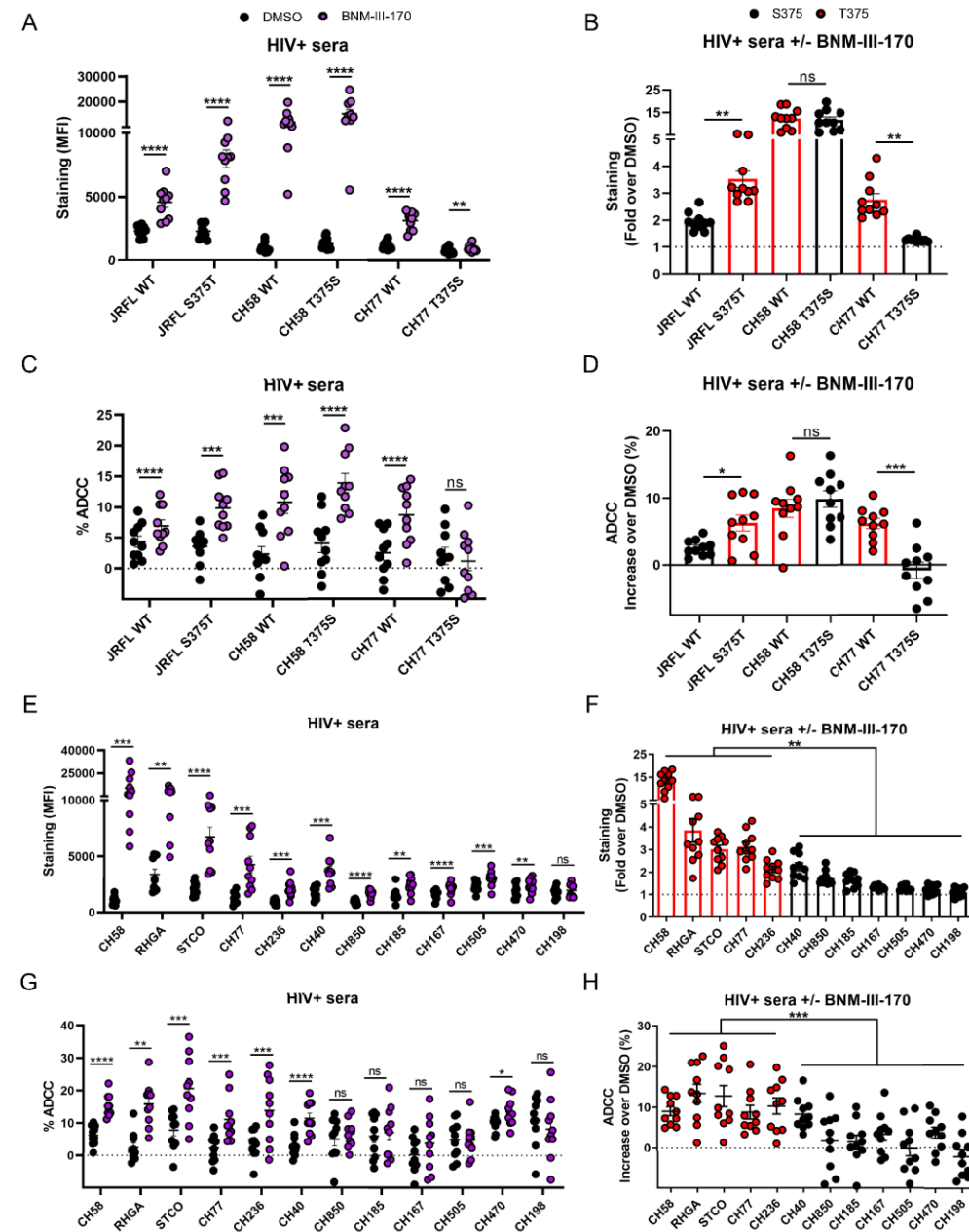
Effect of gp120 layer mutations and Phe43 cavity changes on neutralization by CD4mc



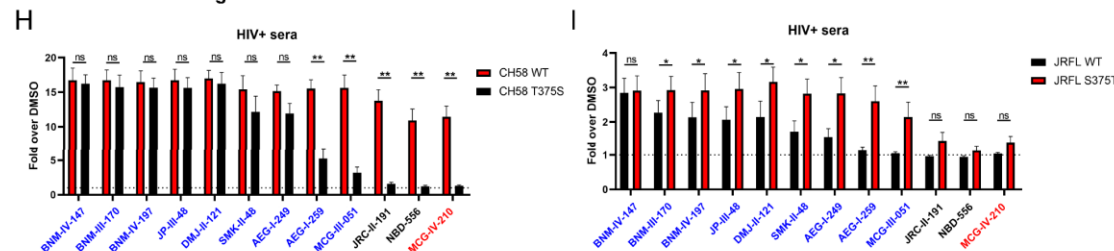
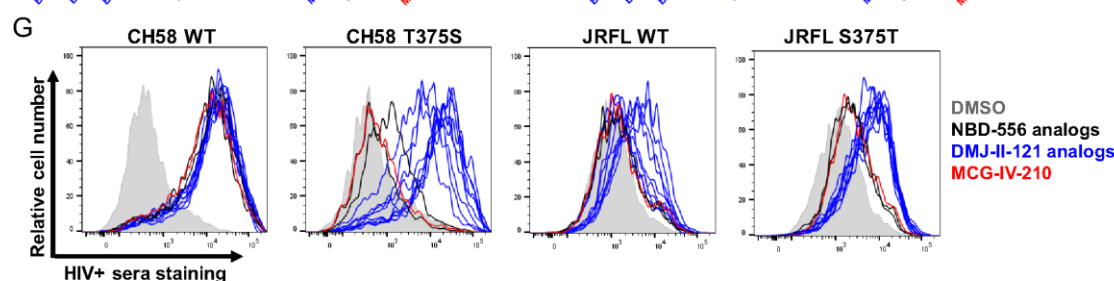
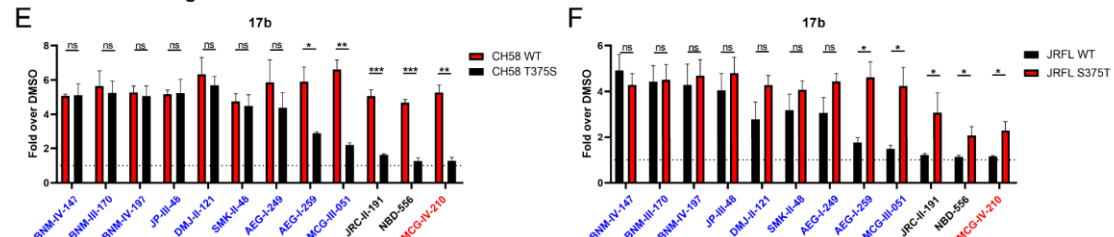
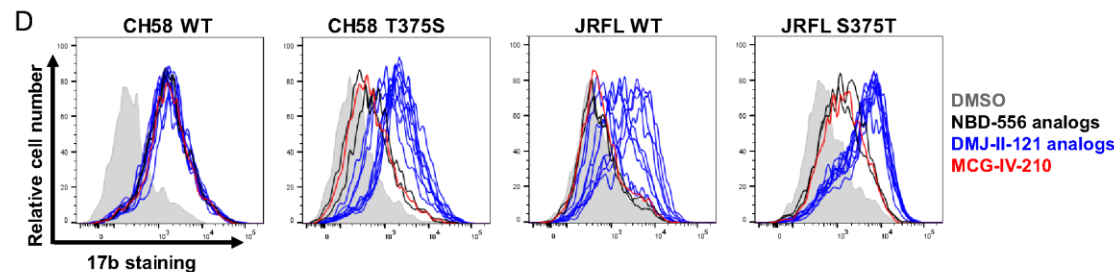
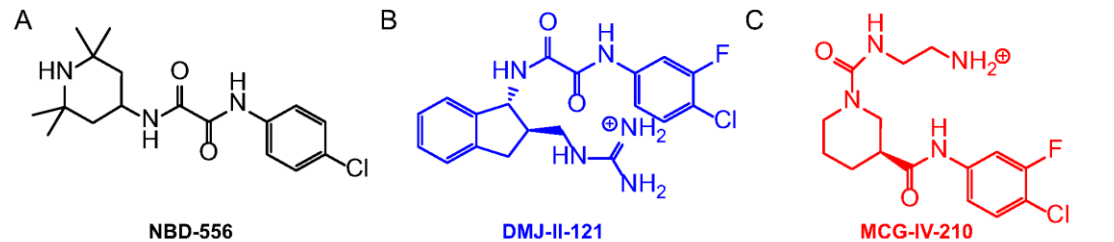
CRCHUM Phe43 cavity and inner domain changes enhance susceptibility of the CRF01_AE strain to ADCC responses mediated by HIV+ sera in the presence of CD4mc



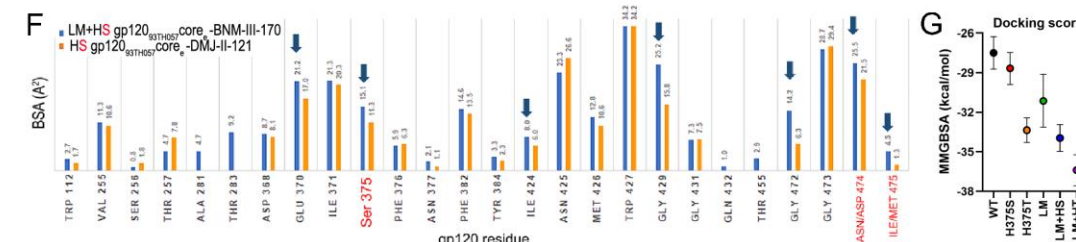
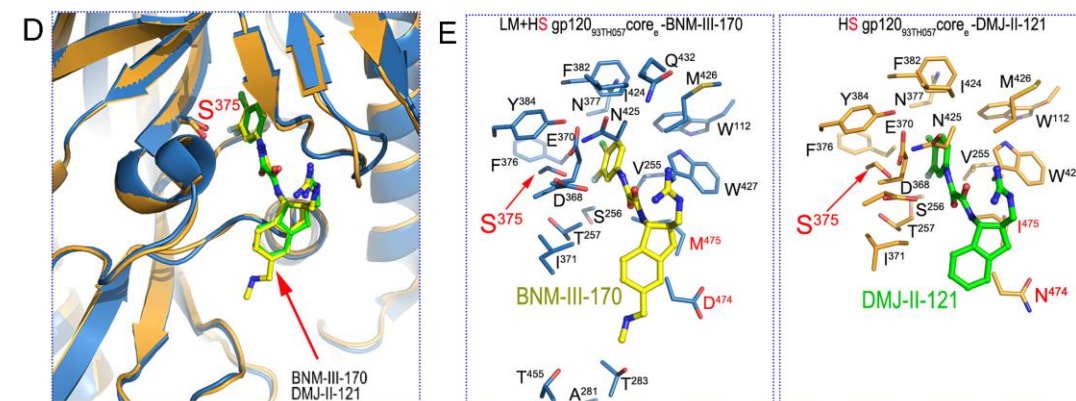
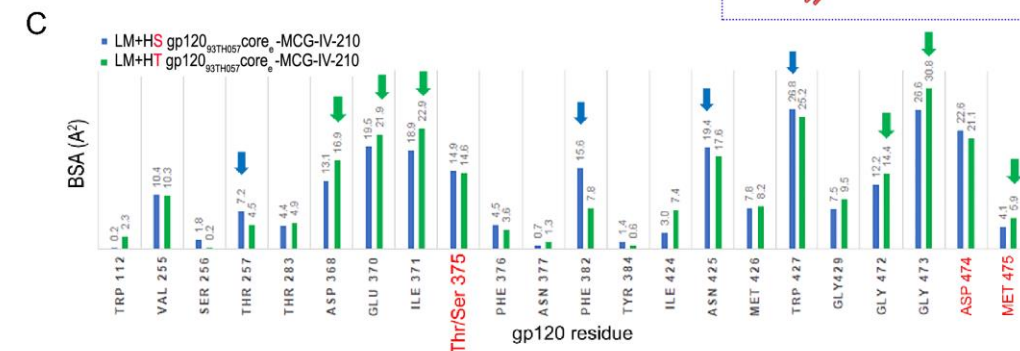
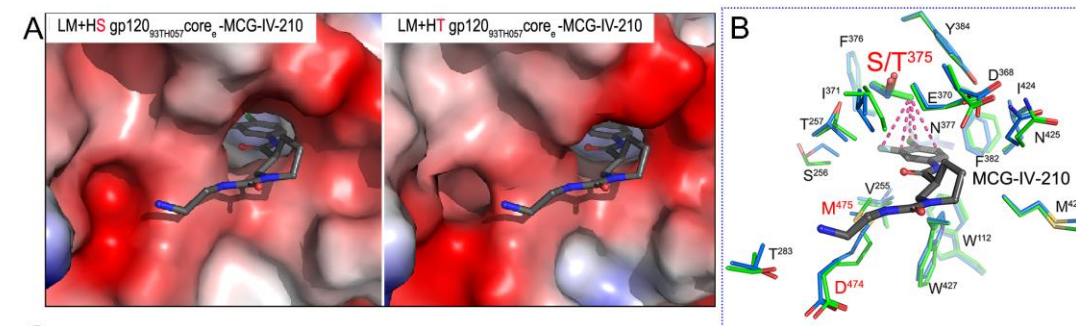
Primary viruses harboring a T375 residue are highly susceptible to ADCC responses mediated by HIV+ sera in the presence of CD4mc

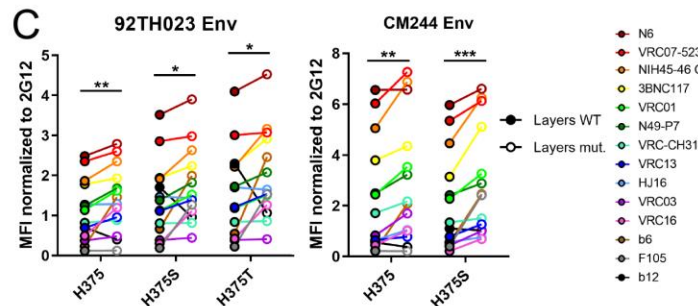
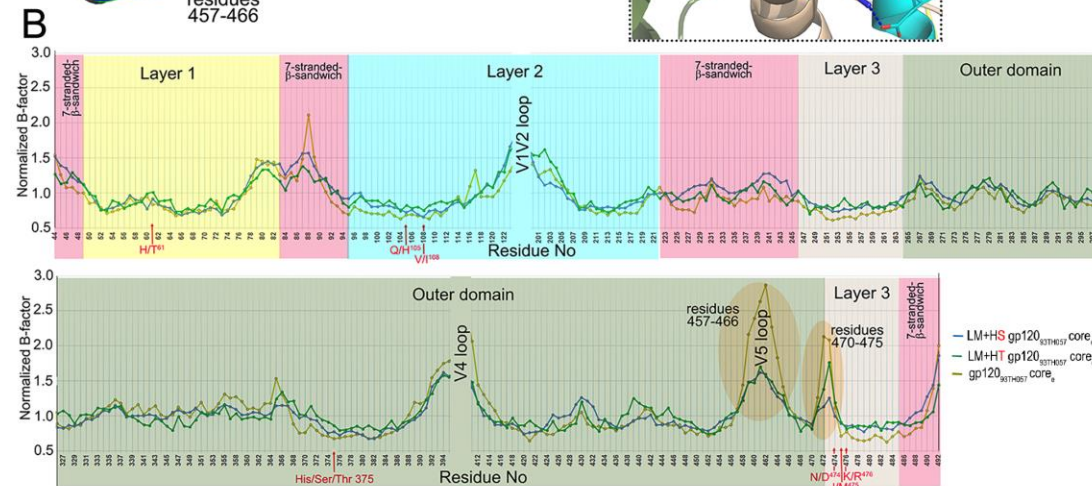
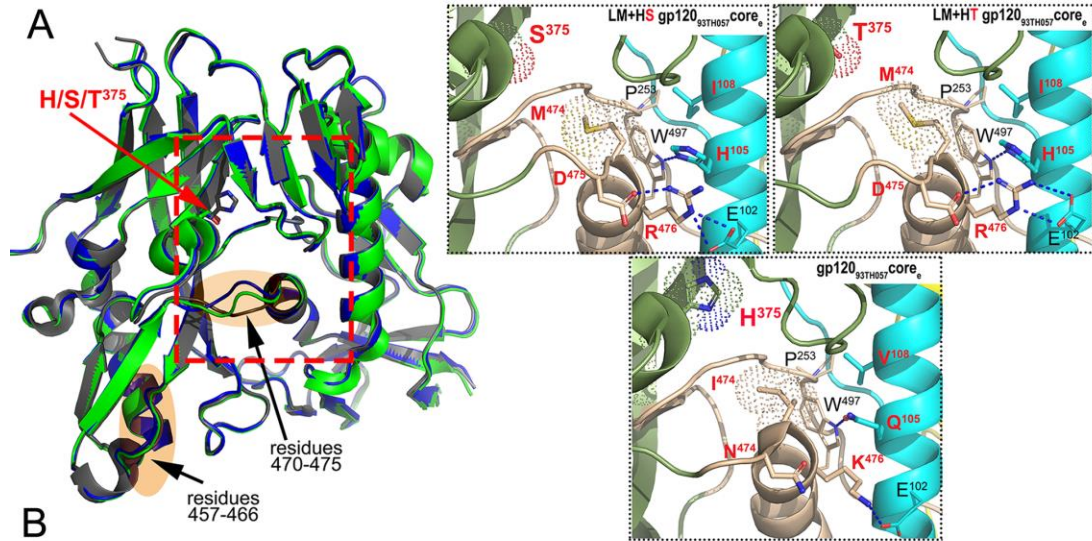


Residue 375 modulates Env sensitivity to different families of CD4mc



Structural effects of Phe43 cavity and inner domain changes on CD4mc docking into the Phe43 cavity





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Neutralization IC₅₀ (μg/mL)

	92TH023	VRC01	VRC13	VRC16	b12
WT		4.08	3.83	>10	>10
LM		2.10	3.60	3.44	>10
H375S		>10	3.59	>10	3.74
LM+HS		3.55	3.44	9.97	9.98

Legend

Legend	IC ₅₀ < 5	5 < IC ₅₀ < 10	IC ₅₀ > 10
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- Phe43 cavity and gp120 inner domain layer mutations render CRF01_AE strains susceptible to CD4mc antiviral activities.
- Phe43 cavity and inner domain changes modulate the sensitivity of HIV-1 from major clades to CD4mc antiviral activities.
- Phe43 cavity and gp120 inner domain substitutions affect the sensitivity to a broad range of CD4 binding site probes.
- Structural analysis reveals how the Phe43 cavity and inner domain residues shape the CD4 binding site.

Acknowledgements

Canada Research
ChairsChaires de recherche
du Canada**Fonds de recherche
Santé**

Québec 



CIHR IRSC

Canadian Institutes of Health Research Instituts de recherche en santé du Canada

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