

Supporting Information

Structures of Ebolavirus Glycoprotein Complexes with Tricyclic Antidepressant and Antipsychotic Drugs

Yuguang Zhao, Jingshan Ren, Elizabeth E. Fry, Julia Xiao, Alain R. Townsend, and David I. Stuart

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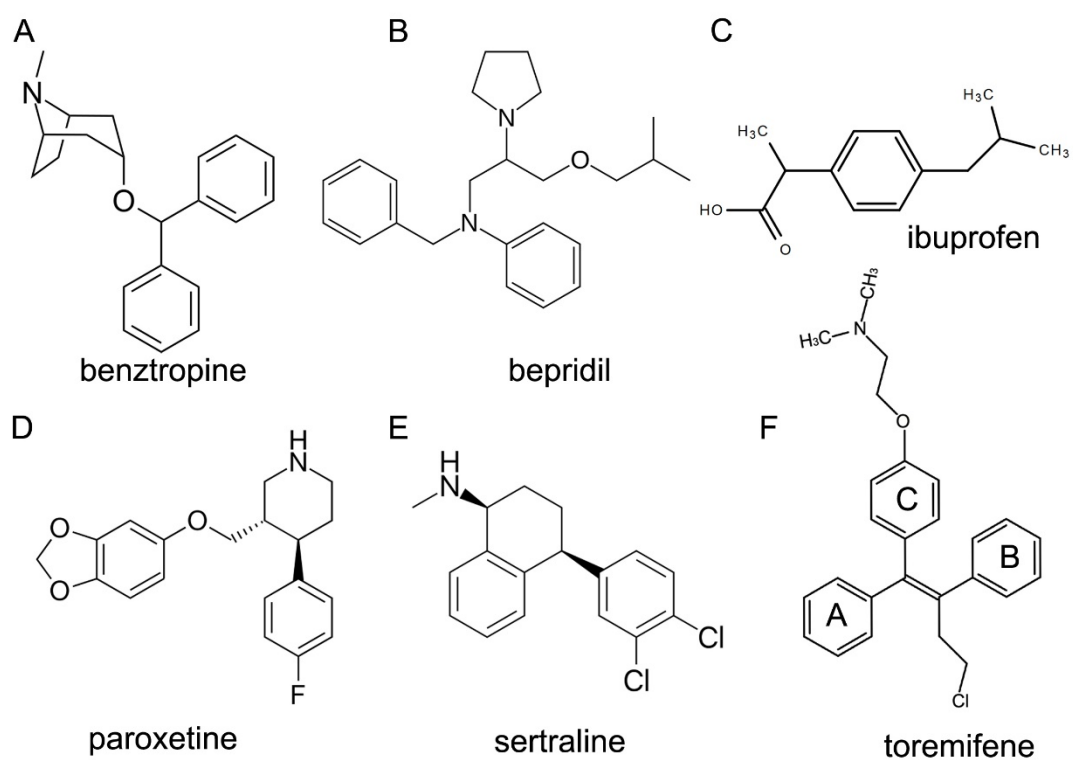


Figure S1. Chemical structures of drugs whose complex structures with EBOV GP have been reported previously.

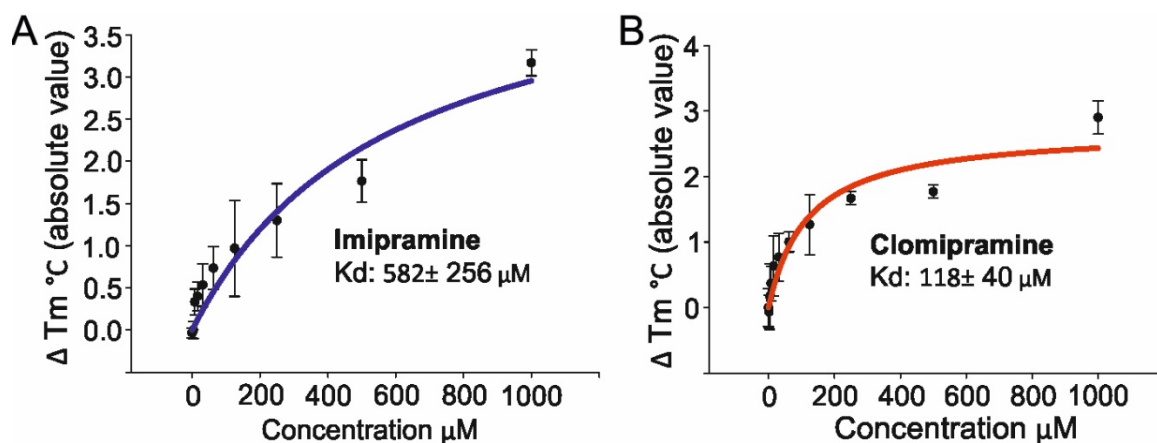


Figure S2. Summary of thermal shift assay results. Shifts in melting temperature (ΔT_m °C in absolute value) are plotted against concentrations of imipramine (A) and clomipramine (B) at pH 5.2. Data are mean \pm s.d. ($n = 3$). The affinity constant K_d is calculated by a ligand binding 1:1 saturation fitting with the SigmaPlot version 13 (Systat Software Inc.).

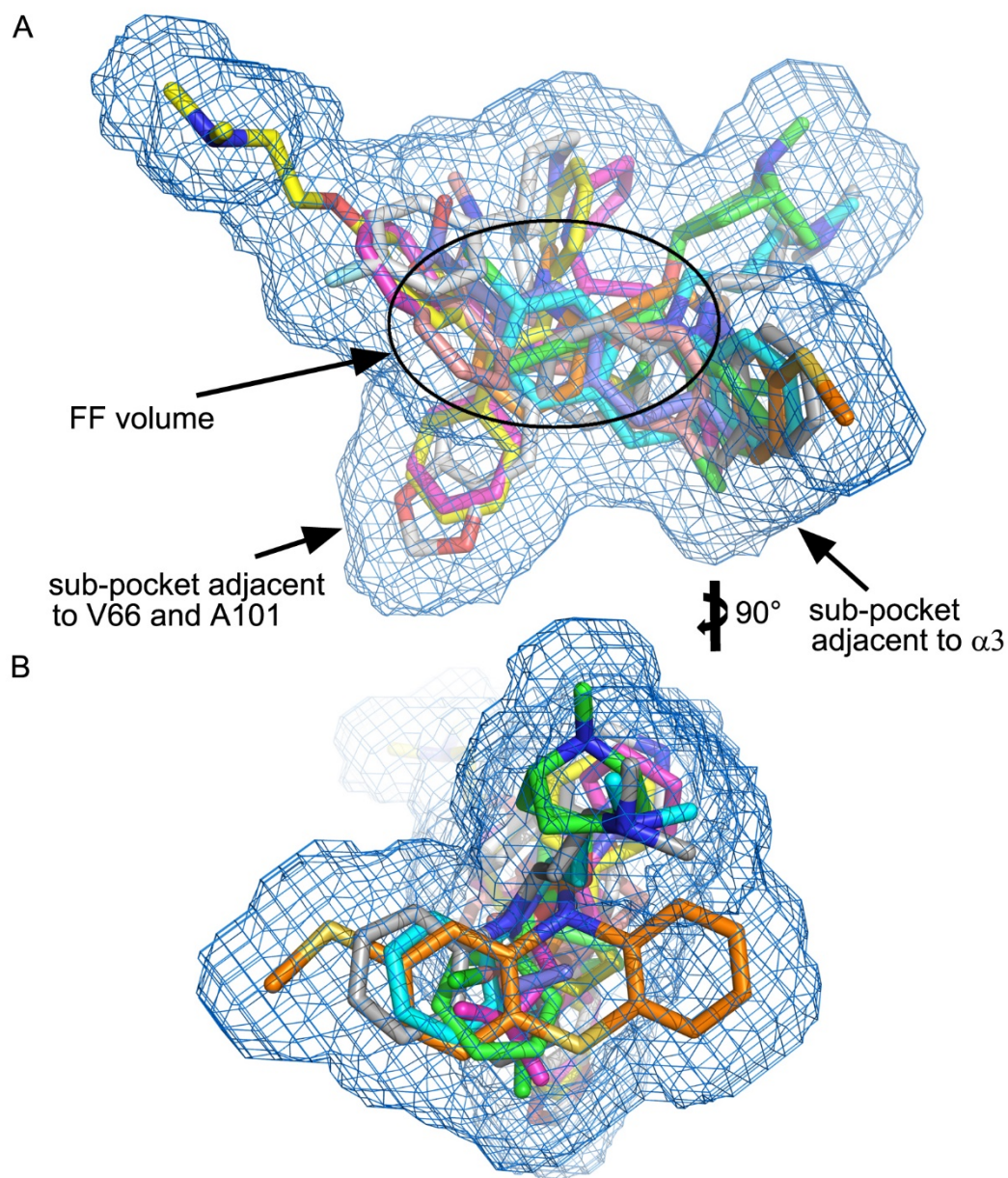


Figure S3. Molecular volumes. (A) Overall volume of EBOV GP drug-binding cavity exploited by the nine FDA approved drugs, imipramine (grey), clomipramine (cyan), thioridazine (orange), toremifene (yellow), bepridil (magenta), paroxetine (light grey), sertraline (pink), ibuprofen (blue) and benztropine (green). (B) 90° rotation of A to show the unique volume exploited by thioridazine (lower right portion of the volume).

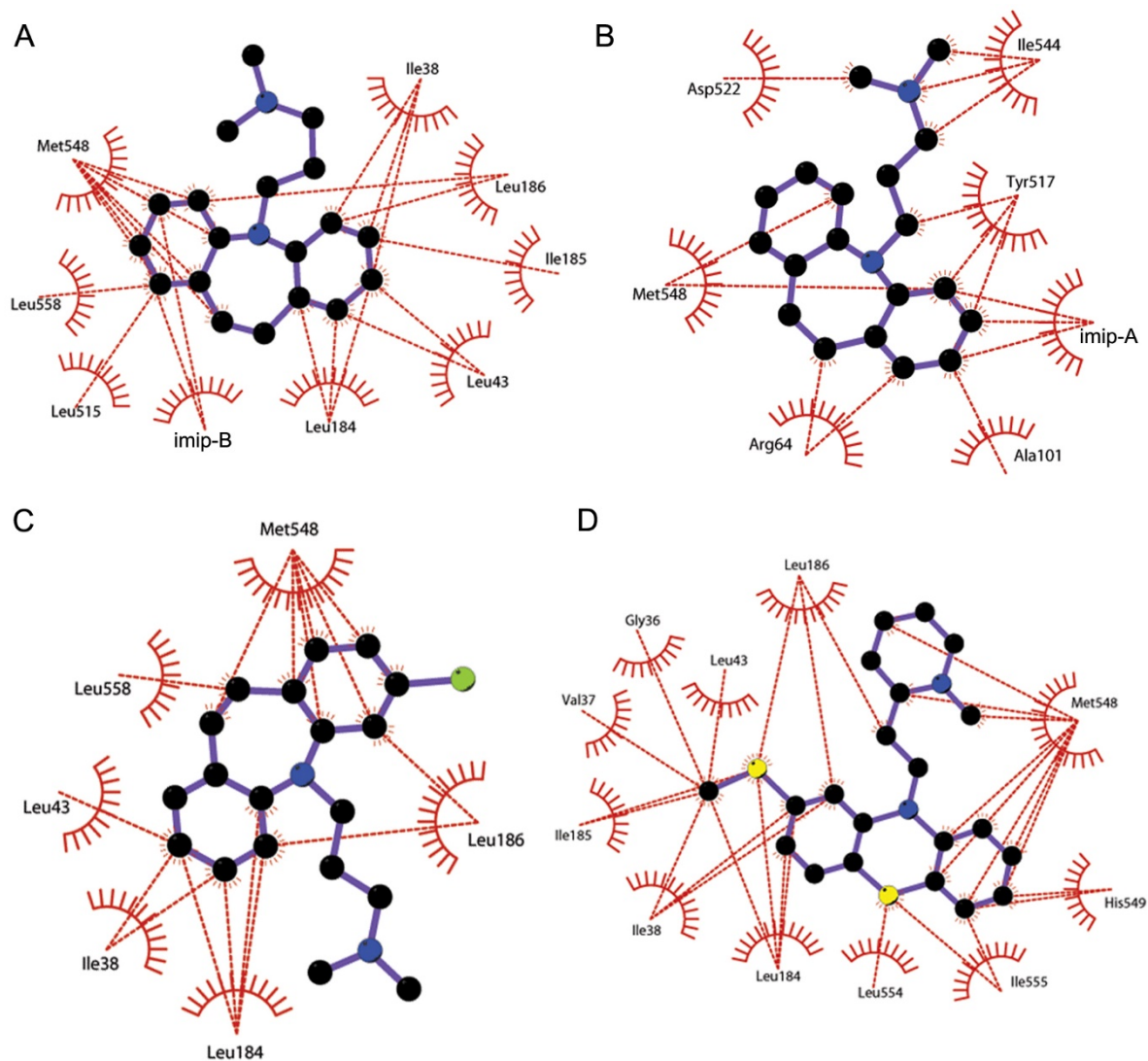


Figure S4. Ligplot figures of protein inhibitor interactions. (A) Imipramine-A, (B) imipramine-B, (C) clomipramine and (D) thioridazine. Interactions are shown where distances between protein and inhibitor are less than 3.9 Å.

Table S1. Data collection and refinement statistics

Data collection			
Data set	GP-imipramine	GP-clomipramine	GP-thioridazine
Space group	<i>R</i> 32		
Cell dimensions (Å)	<i>a</i> =114.2, <i>b</i> =114.2, <i>c</i> =305.6	<i>a</i> =114.2, <i>b</i> =114.2, <i>c</i> =306.4	<i>a</i> =114.0, <i>b</i> =114.0, <i>c</i> =305.7
Resolution (Å)	83.0–2.26 (2.30–2.26)*	60.6–2.19 (2.23–2.19)	82.9–2.31 (2.35–2.31)
Unique reflections	36357 (1787)	40019 (1962)	33894 (1662)
<i>R</i> _{merge}	0.083(---)	0.080 (---)	0.083 (---)
CC ₅₀	1.000 (0.71)	1.000 (0.94)	1.000(0.67)
<i><I> / <σI></i>	18.5(1.2)	26.9 (2.6)	30.8(1.6)
Completeness (%)	99.9(98.3)	100 (100)	99.8(99.6)
Redundancy	18.5(11.4)	38.9 (33.4)	35.6(10.5)
Refinement			
Resolution (Å)	83.0–2.26	60.6–2.19	52.0–2.31
No. reflections	34223/1894	37751/2036	32231/1652
<i>R</i> _{work} / <i>R</i> _{free}	0.208/0.227	0.201/0.216	0.187/0.212
No. atoms	3246	3316	3328
Average <i>B</i> -factors (Å ²)	76	52	59
r.m.s. deviations			
Bond lengths (Å)	0.007	0.008	0.007
Bond angles (°)	1.3	1.3	1.1

*, Numbers in brackets refer to the highest resolution shell of data