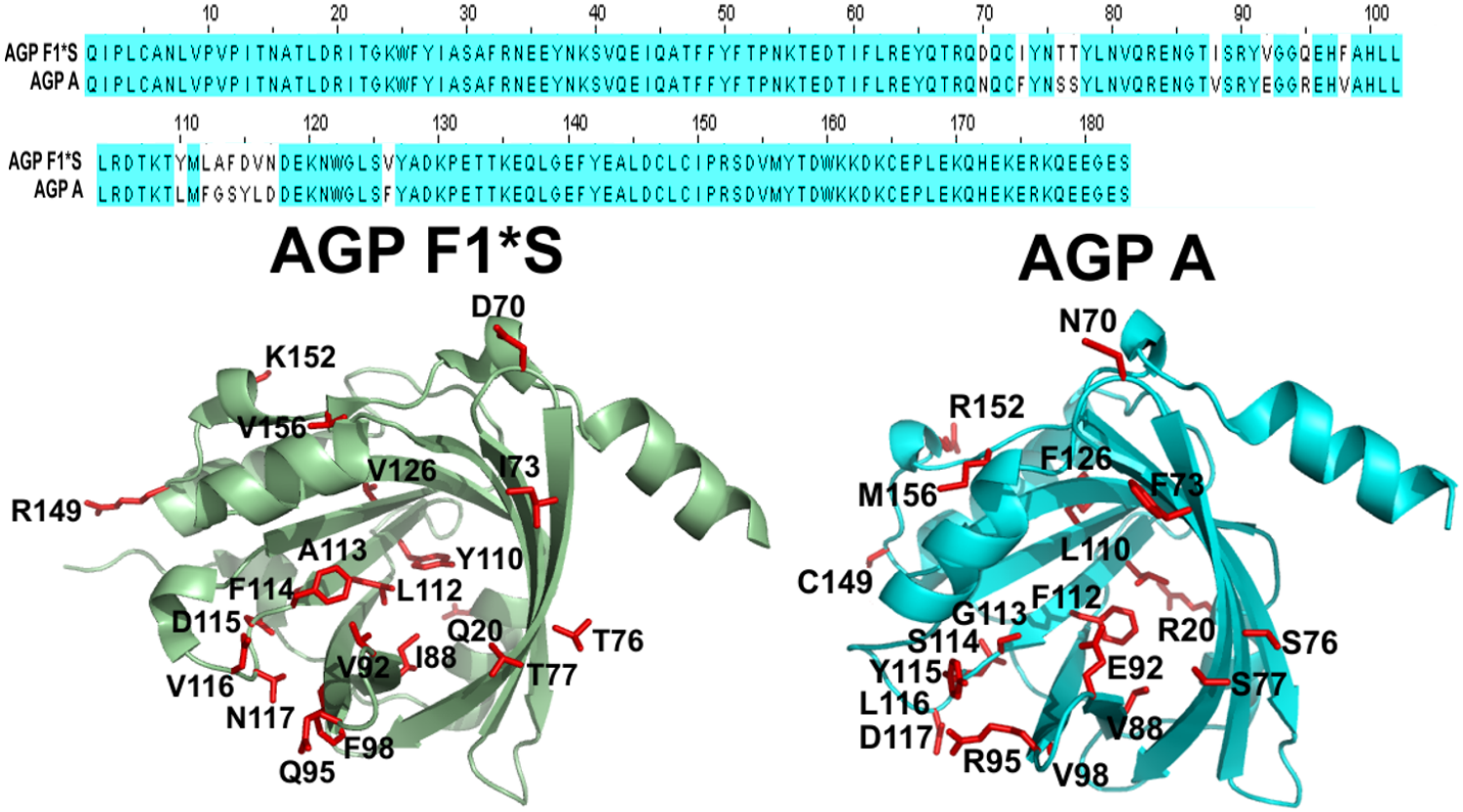
SUPPLEMENTARY INFORMATION

SI FIGURE CAPTIONS

SI Figure 1. Sequence differences in the crystallographic structures of the F1*S and A variants of human AGP. *Top panel.* The amino acid sequence alignment with conserved positions shaded. *Bottom panel.* The amino acid sequence differences mapped onto the crystallographic structure of each variant shown in ribbon representation with amino acid difference in stick representation and labeled in single letter code.

SI Figure 1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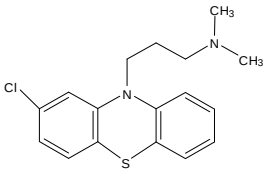
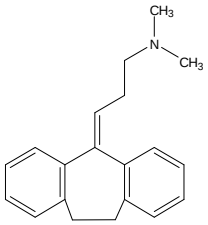
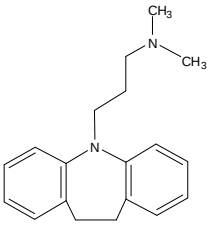
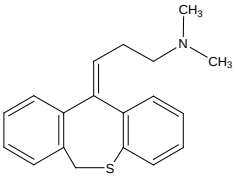
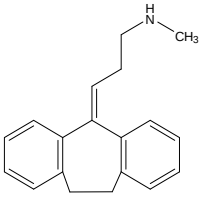
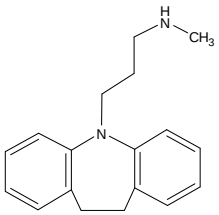
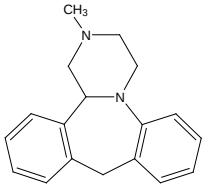
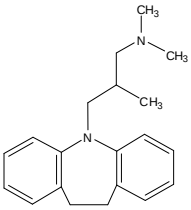
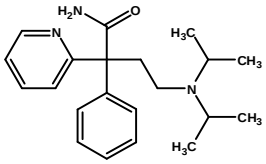
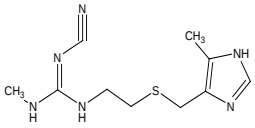
AGP F1*S QIPLCANLVPVPITNATLDRITGKWFYIASAFRNEEYNKSVQEIQATFFYFTPNKTEDTIFLREYQTRQDQCIYNTTYLNVQRENGTISRYVGGQEHFAHLL
AGP A QIPLCANLVPVPITNATLDRITGKWFYIASAFRNEEYNKSVQEIQATFFYFTPNKTEDTIFLREYQTRQNQCFYNSSYLNVQRENGTVSRYEGGREHVAHLL
110 120 130 140 150 160 170 180
AGP F1*S LRDTKTYMLAFDVNDEKNWGLSVYADKPETTKEQLGEFYEALDCLCIPRSDVMYTDWKKDKCEPLEKQHEKERKQEEGES
AGP A LRDTKTLMFGSYLDDEKNWGLSFYADKPETTKEQLGEFYEALDCLCIPRSDVMYTDWKKDKCEPLEKQHEKERKQEEGES
AGP F1*S
D70
K152
V156
V126
I73
R149
A113
Y110
F114
L112
D115
Q20
T76
V92
I88
T77
V116
N117
F98
Q95
AGP A
N70
R152
F126
F73
M156
L110
C149
F112
G113
R20
S76
S114
E92
Y115
S77
L116
V88
D117
R95
V98

SI Table 1. Isothermal titration calorimetric parameters for binding of basic drugs to AGP at 30ºC in 20 mM HEPES pH 7.4

Parameter	Chlorpromazine	Amitriptyline	Imipramine	Dothepin	Nortriptyline
					
[a]clogD pH 7.4	3.2	4.3	2.4	3.8	3.1
PSA	6.5	3.2	6.5	3.2	12
n	0.97	1.93	2.81	2.58	2.13
K_d (μM)	21.9	32.9	69.9	84.7	123
ΔH (kcal/mol)	-3.91	-1.40	-3.27	-4.10	-2.88
TΔS (kcal/mol)	2.50	4.85	2.48	1.55	2.54
ΔG_o (kcal/mol)	-6.41	-6.25	-5.75	-5.65	-5.42

Parameter	Desimipramine	Miaserine	Triimipramine	Disopyramide	Cimetidine
					
[a]clogD pH 7.4	1.2	2.8	2.9	0.31	0.2
PSA	15	6.5	6.5	59	85
n	1.88	2.55	2.80	1.50	2.36
K_d (μM)	149	219	404	29.6	38.9
ΔH (kcal/mol)	-2.52	-2.94	-13.8	-2.37	-3.69
TΔS (kcal/mol)	2.78	2.14	-9.16	4.03	2.42
ΔG_o (kcal/mol)	-5.30	-5.08	-4.64	-6.40	-6.11

[a]Calculated logD pH 7.4