**Supplementary Table S3.** Binding affinities and molecular interactions of dopamine and inhibitors with CsDAT and hDAT

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Ligand | CsDAT | | hDAT | | |
| Affinity  (kcal/mol) | Residue  (Å) | Affinity  (kcal/mol) | Residue  (Å) |
| Dopamine | -5.5 | Hydrophobic interactions  Y463 (3.62, 3.87), D572 (3.89)  Hydrogen bonds  R462 (2.68), G466 (3.43), A467 (2.35), D527 (3.26, 2.50, 2.53), T529 (3.00), T575 (3.61) | -5.3 | Hydrophobic interactions  W84 (3.78, 3.49), R85 (3.52, 3.59)  Hydrogen bonds  D385 (3.48), G386 (2.29) |
| Amfonelic acid | -7.8 | Hydrophobic interactions  I65 (3.72), I297 (3.68), Y463 (3.59), A467 (3.85)  Hydrogen bonds  Y463 (3.15), D527 (2.90) | -7.5 | Hydrophobic interactions  W84 (3.62), F472 (3.35), T473 (3.66), R476 (3.87)  Salt bridges  H477 (4.46), H547 (5.15) |
| Benztropine | -7.6 | Hydrophobic interactions  D527 (3.90), L531 (3.76), V568 (3.95), W572 (3.80)  Pi-stacking  W572 (3.85)  Salt bridges  D527 (4.50) | -7.2 | Hydrophobic interactions  R85 (3.56), L89 (3.65), T473 (3.65), H477 (3.52), P546 (3.89)  Pi-stacking  H477 (4.55)  Pi-cation interactions  R85 (3.98) |
| Bupropion | -6.0 | Hydrophobic interactions  I297 (3.57), Y463 (3.55), L531 (3.95), W572 (3.85) | -6.0 | Hydrophobic interactions  Y151 (3.80), F154 (3.51, 3.65), I230 (3.77), F462 (3.69), L474 (3.60), L475 (3.62, 3.77), L560 (3.65), I564 (3.68) |
| Vanoxerine | -8.6 | Hydrophobic interactions  W60 (3.55), R61 (3.68), I65 (3.77), V135 (3.77), P368 (3.79), V371 (3.59), F457 (3.57)  Halogen bonds  Q298 (3.16)  Salt bridges  D461 (5.29) | -8.2 | Hydrophobic interactions  R85 (3.92), T316 (3.70), D385 (3.57), T473 (3.42), F543 (3.80), Y548 (3.49)  Hydrogen bonds  R85 (2.99), H477 (2.23) |