**Supporting Information**

# Interaction of the neutral amino acid transporter ASCT2 with basic amino acids

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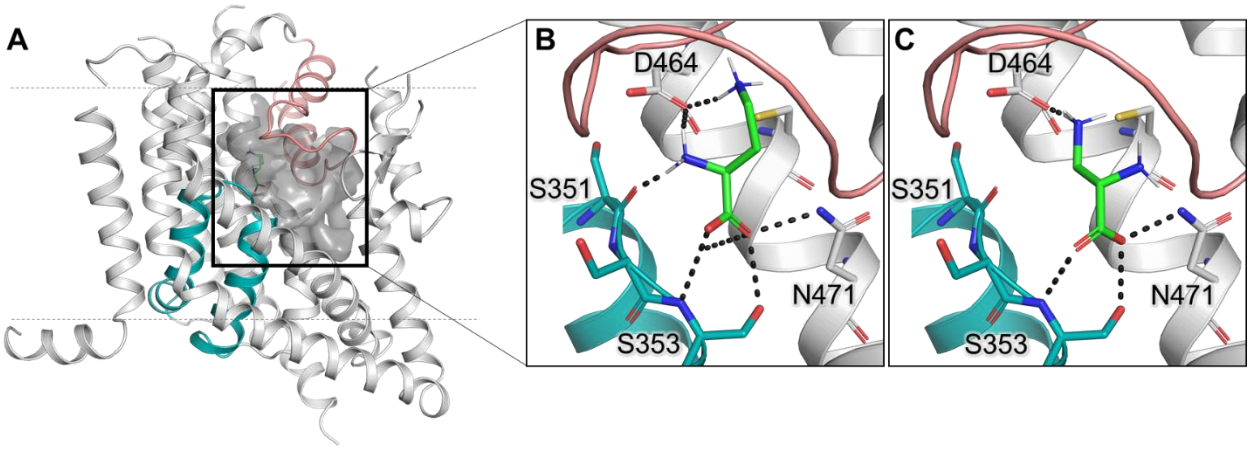
| ASCT2 outward-occluded | | |
|---|---|---|
| Rank | Ligand | Glide Score |
| 1 | L-DAP (positively charged) (Figure 1G) | -6.88 |
| 2 | L-DAB (Figure 1B) | -6.36 |
| 3 | L-DAP (negatively charged) (Figure 1D) | -6.26 |
| 4 | L-Asparagine | -6.24 |
| 5 | L-DAP (neutral beta) (Figure 1F) | -6.21 |
| 6 | L-DAP (neutral alpha) (Figure 1E) | -6.09 |
| 7 | L-Cysteine | -5.30 |
| 8 | L-Serine | -5.15 |
| 9 | L-Glutamine | -5.01 |
| 10 | L-Threonine | -4.85 |
| 11 | L-Alanine | -4.72 |
| 12 | L-Leucine | -4.66 |
| 13 | L-Methionine | -4.60 |
| ASCT2 outward-open | | |
| 1 | L-DAP (neutral beta) (Figure 1F) | -5.78 |
| 2 | L-DAP (positively charged) (Figure 1G) | -5.59 |
| 3 | L-DAP (negatively charged) (Figure 1D) | -5.58 |
| 4 | L-DAB | -5.49 |
| 5 | L-DAP (neutral alpha) (Figure 1E) | -5.24 |
| 6 | L-Asparagine | -4.84 |
| 7 | L-Glutamine | -4.62 |
| 8 | L-Methionine | -4.52 |
| 9 | L-Leucine | -4.48 |
| 10 | L-Threonine | -4.34 |
| 11 | L-Cysteine | -4.17 |
| 12 | L-Serine | -3.80 |
| 13 | L-Alanine | -3.26 |

**Supplementary Table 1.** Glide docking scores for ligands docked to ASCT2 homology models in 2 conformations.




**Supplementary Figure 1.** Docking pose of L-DAB and L-DAP. **(A)** Side view of the ASCT2 homology model in the outward-open conformation (gray ribbon) with docked L-DAP (green sticks). The substrate binding site is highlighted with dark gray shadow; HP1 is shown in teal and HP2 in salmon. Broken lines indicate the approximate location of the membrane. **(B)** Docking pose of L-DAB and **(C)** L-DAP. Residues predicted to make hydrogen bonds (dark gray dashes) are labeled. Oxygen, nitrogen and sulfur atoms are represented in red, blue, and yellow, respectively.