**Table S1** Effects on substrate-binding interaction of different Ssa1p mutations

| Mutation | RMSD (nm)[a] | Interaction energy (kJ mol$^{-1}$)[b] | Hydrogen bonds[c] | Hydrophobic interactions[c] | Distance of arch structure residues (nm)[d] | Number of hydrogen bonds between inner loops[d] |
|---|---|---|---|---|---|---|
| WT | 0.291 | -324.725 | 3.286 | 61.952 | 0.778 | 2.873 |
| L483W | 0.265 | -472.013 | 6.714 | 73.571 | 0.582 | 2.444 |
| L483A | 0.265 | -404.898 | 3.714 | 56.333 | 0.832 | 2.779 |
| L483H | 0.232 | -518.677 | 7.048 | 87.047 | 0.664 | 2.944 |

[a]RMSD of Cα atoms in the stabilized MD structure.
[b]Interaction energy calculated during the SMD
[c]Numbers of hydrogen bonds and hydrophobic interactions during the course of the SMD.
[d]Distance of arch structure residues and hydrogen bonds in between inner loops in stabilized MD structure.