|  |  |  |  |
| --- | --- | --- | --- |
| Binding site | *PS polar groups* | *CTI amino acid residues* | *Bond type and orientation* |
| **Binding site 1**  Affinity (kcal/mol)  ‒3.7 | **PO4–** | **K+18**(N+H3), **C38**(NHpb σ+), **Y22**(OHσ+) | ionic, 2 ion-hydrogen, i.s. |
| **COO–** | **L6**(NHpb σ+), **K+35**(N+H3) | ion-hydrogen, ionic, i.s. |
| **1CO**σ**–C** | **K12**(NHpbσ+) | hydrogen |
| **1C=O**σ− | **K+12**(N+H3) | ion-polar |
| **2C=O**σ− | **K+12**(N+H3) | ion-polar |
| **N+H3** | **R36**(C=Opbσ−) | ion-polar |
| **Binding site 2**  Affinity (kcal/mol)  ‒3.7 | **PO4–** | **K+23**(N+H3), **R+36**(=N+H2) | 2 ionic |
| **COO–** | **None** | into solution |
| **2****C=O**σ− | **R+36**(=N+H2) | ion-polar |
| **N+H3** | **D−29**(C=Opbσ−), **T31**(C=Opbσ−) | 2 ion-polar |
| **Binding site 3**  Affinity (kcal/mol)  ‒3.7 | **PO4–** | **C38**(NHpbσ+), **Y22**(OH σ+) | 2 ion-hydrogen, into solution |
| **COO–** | **K12**(NHpbσ+) | ion-hydrogen |
| **1CO**σ**–C** | **K+35**(N+H3) | ion-polar |
| **1C=O** σ− | **K+35**(N+H3) | ion-polar |
| **2COC**σ**–** | **K+35**(N+H3) | ion-polar |
| **2C=O** σ− | **L6**(OHσ+) | hydrogen |
| **N+H3** | **T13**(C=Opbσ−) | ion-polar |
| **Binding site 4**  Affinity (kcal/mol)  ‒3.7 | **PO4–** | **K+12**(N+H3) | ionic, |
| **1C=O** σ− | **C38**(NHpbσ+) | hydrogen |
| **N+H3** | **K12**(NHpb σ+), **K12**(C=Opbσ−) | ion-hydrogen repulsion, ion-polar |
| **Binding site 5**  Affinity (kcal/mol)  ‒3.6 | **PO4–** | **K12**(NHpb σ+), **N60**(-NH2 σ+) | 2 ion-hydrogen |
| **COO–** | **L6**(**O**Hσ+), **K+35**(N+H3) | ion-hydrogen, ionic |
| **1C=O** σ− | **K+12**( N+H3) | ion-polar |
| **2C=O** σ− | **Y22**(OHσ+) | hydrogen |
| **N+H3** | **Y22**(Oσ−H) | ion-polar |
| **Binding site 6**  Affinity (kcal/mol)  ‒3.6 | **PO4–** | **None** | into solution |
| **COO–** | **K12**(NHpbσ+) | ion-hydrogen |
| **1CO**σ**–C** | **Y22**(OHσ+) | hydrogen |
| **2CO**σ**–C** | **Y22**(OHσ+) | hydrogen |
| **2C=O** σ− | **K+18**(N+H3) | ion-polar |
| **N+H3** | **T13**(C=Opbσ−) | ion-polar |
| **Binding site 7**  Affinity (kcal/mol)  ‒3.5 | **PO4–** | **K12**(NHpbσ+), **C38**(NHpbσ+) | 2 ion-hydrogen |
| **COO–** | **L6**(**O**Hσ+), **K+35**(N+H3) | ion-hydrogen, ionic |
| **1CO**σ**–C** | **C38**(NHpbσ+) | ion-hydrogen |
| **1C=O** σ− | **Y22**(OHσ+) | hydrogen |
| **2C=O** σ− | **K+12**(N+H3), **K12**(NHpbσ+) | ion-polar, hydrogen |
| **N+H3** | **R36**(C=Opbσ−) | ion-polar |
| **Binding site 8**  Affinity (kcal/mol)  ‒3.5 | **PO4–** | **Y22**(OHσ+) | ion-hydrogen, into solution |
| **COO–** | **L6**(**O**Hσ+), **K+35**(N+H3) | ion-hydrogen, ionic |
| **2C=O** σ− | **C38**(NHpbσ+) | hydrogen |
| **N+H3** | **K+35**(N+H3) | ionic repulsion, into solution |
| **Binding site 9**  Affinity (kcal/mol)  ‒3.4 | **PO4–** | **K+5**(N+H3) | ionic, into solution |
| **COO–** | **Y22**(OH σ+), **K+35**(N+H3) | ion-polar, ionic |
| **N+H3** | **R36**(C=Opbσ−) | ion-polar |

**S5 Table. Summary of amino acid residues in CTI that interact with PS.**

Hypothetical binding sites in CTI that bind to the phospholipid headgroup of PS as determined by AutoDock modeling. The table shows a complete list of amino acid residues in CTI that interact with the PS charged and polar groups for various binding sites. Pb in C=Opbσ− or in NHpbσ+ denotes a peptide bond.