Supplementary Material

**Table S.1.** Comparison of the interactions at the binding pocket of all states between Mip-rapamycin and FKBP-rapamycin. The regions refer to the parts of protein as given in Figure 1(b) and (c). Hydrogen-bond index are given to each hydrogen-bond interactions. The residues, that occupy similar positions, are written in the same rows.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Region |  | Mip |  | FKBP12 |
| Residue | Interaction with rapamycin | Residue | Interaction with rapamycin |
| 3 | Y55 | 0 ps-VI : pipecolyl ring | Y26 | 0 ps-III : pipecolyl ring |
| 5 | F65 | 0 ps -VI : pyranosyl ring | F36 | 0 ps-III : pyranosyl ring |
|  | D66 | 0 ps -II : pyranosyl ring | D37 | 0 ps-III : side chain O--H-O cyclohexyl ring (1) |
|  |  | III-VI : side chain O--H-O cyclohexyl ring (7) |  |  |
| 6 | T76 | 0 ps -V : no interaction | R42 | 0 ps - II : cyclohexyl ring |
|  |  | VI : cyclohexyl ring |  | III-VI : no interaction |
| 7 | F77 | 0 ps-VI : pipecolyl ring | F46 | 0 ps-III : pipecolyl ring |
|  | Q78 | 0 ps-V : no interaction |  |  |
|  |  | VI : peptide H---O-H cyclohexyl ring (10) |  |  |
| 8 |  |  | Q53 | 0 ps-III : side chain O---HO cyclohexyl ring (2) |
|  | Q81 | 0 ps: C31-C32 | E54 | 0 ps : peptide O---HO cyclohexyl ring (3) |
|  |  | I : side chain O---HO-C28 (2) |  | I-III : cyclohexyl ring |
|  |  | II : side chain H---O=C32 (3) |  |  |
|  |  | III : side chain H---O=C26 (6) |  |  |
|  |  | IV : side chain H---OH-C28 (8) |  |  |
|  |  | V : side chain H---OH-C28 (8) |  |  |
|  |  |  : side chain H---O=C32(3) |  |  |
|  |  | VI : side chain O--HO cyclohexyl ring (11) |  |  |
|  | V82 | 0 ps : C31-C32 | V55 | 0 ps-III : cyclohexyl ring |
|  |  | I : cyclohexyl ring |  |  |
|  |  | II : pipecolyl ring |  |  |
|  |  | III-IV : C31-C32 |  |  |
|  |  | V : cyclohexyl ring |  |  |
|  |  | VI : pipecolyl ring |  |  |
|  | I83 | 0 ps-I : pipecolyl ring | I56 | 0 ps-III : peptide H---O=C1 (4) |
|  |  | II : side chain H---O=C8 (4) |  |  |
|  |  | III-VI : pipecolyl ring |  |  |
|  | P84 | 0 ps -II : cyclohexyl |  |  |
|  |  | III-VI : no interaction |  |  |
|  | W86 | 0 ps : no interaction | W59 | 0 ps-III : pipecolyl ring |
|  |  | I : pipecolyl ring |  |  |
|  |  | II : no interaction |  |  |
|  |  | III-VI : pipecolyl ring |  |  |
| 12 | G106 | 0 ps : no interaction |  |  |
|  |  | I : cyclohexyl ring |  |  |
|  |  | II-VI : no interaction |  |  |
|  | L107 | 0 ps : no interaction |  |  |
|  |  | I : cyclohexyl ring |  |  |
|  |  | II-VI : no interaction |  |  |
|  | A108 | 0 ps : peptide O---H-O cyclohexyl ring (1) |  |  |
|  |  | I -III : cyclohexyl ring |  |  |
|  |  | IV-VI : no interaction |  |  |
| 13 | Y109 | 0 ps : pyranosyl ring | Y82 | 0 ps-III : side chain OH---O=8 (5) |
|  |  | I-III : cyclohexyl ring |  |  |
|  |  | IV : cyclohexyl ring |  |  |
|  |  | V : no interaction |  |  |
|  |  | VI : pyranosyl ring |  |  |
|  | R112 | 0 ps-I : no interaction |  |  |
|  |  | II-V : cyclohexyl ring |  |  |
|  |  | VI: no interaction |  |  |
|  | S113 | 0 ps-I : no interaction |  |  |
|  |  | II-V : peptide O---H-O cyclohexyl ring (5) |  |  |
|  |  | IV : peptide H---O-H cyclohexyl ring (9) |  |  |
|  |  | VI : no interaction |  |  |
|  | V114 | 0 ps-I : pyranosyl ring |  |  |
|  |  | II-V : cyclohexyl ring and pyranosyl ring |  |  |
|  |  | VI : no interaction |  |  |
|  | G115 | 0 ps : pyranosyl ring |  |  |
|  |  | I-III : no interaction |  |  |
|  |  | IV-V : cyclohexyl ring |  |  |
|  |  | VI : no interaction |  |  |
|  | G116 | 0 ps-III : pyranosyl ring |  |  |
|  |  | IV-V : pyranosyl ring |  |  |
|  |  | VI : no interaction |  |  |
|  | P117 | 0 ps-III : no interaction | H87 | 0 ps-III : pyranosyl ring |
|  |  | IV : pyranosyl ring |  |  |
|  |  | V-VI : no interaction |  |  |
|  | I118 | 0 ps: pyranosyl ring | I90 | 0 ps-III : pyranosyl ring |
|  |  | I : pyranosyl ring |  |  |
|  |  | II : pyranosyl ring |  |  |
|  |  | III : no interaction |  |  |
|  |  | IV : pyranosyl ring |  |  |
|  |  | V : no interaction |  |  |
|  |  | VI : pyranosyl ring |  |  |
|  |  |  | I91 | 0 ps-III : pyranosyl ring |
| 14 | F126 | 0 ps-VI : pipecolyl ring | F99 | 0 ps-III : pipecolyl ring |