

## Supplementary Table S1

### Understanding TR binding to pMHC complexes: how does the TR scan many pMHC molecules yet preferentially bind to one

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#### Table S1. Grouping of TR proteins.

Mutations in MHC  $\alpha$  (I-ALPHA) chain and TR V $\beta$  domain (MHC-I; TR Cluster I.2 and I.3), TR mutant names and the degree of tilt or relative change (compared to the first structure with similar TR type, MHC allele and peptide sequence) in  $\theta$  are mentioned in parentheses (see Methods section for details).

| S.No.            | PDB code | Species | Peptide Sequence | MHC Allele | BE (kcal/mol) | Experimental binding affinity ( $K_d$ in $\mu$ M) | $\theta$ (°) | Diagonal TR docking angle (°) from literature | TR Type (TR name) | TR Cluster |
|------------------|----------|---------|------------------|------------|---------------|---|--------------|---|-------------------|------------|
| <b>TR/pMHC-I</b> |          |         |                  |            |               |   |              |   |                   |            |
| 1                | 2oi9     | Murine  | QLSPFPFDL        | H2-Ld      | -13.13        | -   | 47           | -   | 2C                | I.1        |
| 2                | 1g6r     | Murine  | SIYRYYGL         | H2-Kb      | -12.57        | -   | 52           | 44 [46]                                       | 2C                |            |
| 3                | 1mwa     | Murine  | EQYKFYSV         | H2-Kbm3    | -14.12        | -   | 43           | -   | 2C                |            |
| 4                | 2ckb     | Murine  | EQYKFYSV         | H2-Kb      | -11.78        | 10  | 62           | 22 [17]                                       | 2C                |            |
| 5                | 1fo0     | Murine  | INFDNTI          | H2-Kb      | -9.61         | 2.6   | 72           | 58 [46]                                       | BM3.3             |            |
| 6                | 1nam     | Murine  | RGYVYQGL         | H2-Kb      | -11.99        | 114   | 67           | -   | BM3.3             |            |
| 7                | 2ol3     | Murine  | SQYYNSL          | H2-Kb      | -11.47        | 112   | 71           | -   | BM3.3             |            |
| 8                | 2e7l     | Murine  | QLSPFPFDL        | H2-Ld      | -13.73        | 2 [23]  | 44           | 44  | M6                |            |
| 9                | 3e2h     | Murine  | QLSPFPFDL        | H2-Ld      | -12.16        | 4.6   | 60           | -   | M67               |            |
| 10               | 3e3q     | Murine  | QLSPFPFDL        | H2-Ld      | -12.76        | $11.6 \times 10^{-2}$                             | 50           | -   | M13               |            |
| 11               | 1kj2     | Murine  | KVITFIDL         | H2-Kb      | -15.30        | -   | 37           | -   | KB5-C20           |            |

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|------------------|----------|---------|------------------|----------------------------|---------------|--|-----------------------|--|----------------------|------------|
| <b>TR/pMHC-I</b> |          |         |                  |                            |               |  |                       |  |                      |            |
| 12               | 1w72     | Human   | EADPTGHSY        | A*0101                     | -9.26         | $1.4 \times 10^{-2}$                                     | 73                    | -  | FAB – HYB3           | I.2        |
| 13               | 1mi5     | Human   | FLRGRAYGL        | B*0801                     | -17.19        | -  | 32                    | -  | LC13                 |            |
| 14               | 3kpr     | Human   | EEYLKAWTF        | B*4405                     | -21.88        | 1.54   | 22                    | -  | LC13                 |            |
| 15               | 3kps     | Human   | EEYLQAFTY        | B*4405                     | -21.52        | 49   | 23                    | -  | LC13                 |            |
| 16               | 2esv     | Human   | VMAPRTLIL        | E*0101                     | -12.79        | 30.2   | 50                    | 50   | KK50.4               |            |
| 17               | 2nx5     | Human   | EPLPQGQLTAY      | B*3501                     | -14.76        | -  | 40                    | -  | ELS4                 |            |
| 18               | 2ak4     | Human   | LPEPLPQGQLTAY    | B*3508                     | -14.83        | 9.9  | 40                    | -  | SB27                 |            |
| 19               | 3kxf     | Human   | LPEPLPQGQLTAY    | B*3508 (Q65A, T69A, Q155A) | -18.70        | -  | 28                    | -  | SB27                 |            |
| 20               | 3ffc     | Human   | FLRGRAYGL        | B*0801                     | -18.60        | 8.9  | 30                    | 58   | CF34                 |            |
| 21               | 3dxa     | Human   | EENLLDFVRF       | B*4405                     | -18.10        | 0.3  | 31                    | 80   | DM1                  |            |
| 22               | 3mv7     | Human   | HPVGEADYFEY      | B*3501                     | -16.96        | -  | 33                    | -  | TK3                  |            |
| 23               | 3mv8     | Human   | HPVGEADYFEY      | B*3501                     | -16.68        | -  | 34                    | -  | TK3 (V $\beta$ Q55H) |            |
| 24               | 3mv9     | Human   | HPVGEADYFEY      | B*3501                     | -16.36        | -  | 35                    | -  | TK3 (V $\beta$ Q55A) |            |
| 25               | 1bd2     | Human   | LLFGYPVYV        | A*0201                     | -14.33        | -  | 45                    | 52 [17]  | B7                   |            |
| 26               | 1lp9     | Human   | ALWGFFPVL        | A*0201                     | -22.97        | 10   | 30                    | 89   | AHIII 12.2           |            |
| 27               | 2uwe     | Human   | ALWGFFPVL        | A*0201 (T163A)             | -22.44        | 4.7  | 21                    | -  | AHIII 12.2           |            |

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|------------------|-------------|---------|---|----------------|---------------|---|-----------------------|--|--------------------|-----------------|
| <b>TR/pMHC-I</b> |             |         |   |                |               |   |                       |  |                    |                 |
| 28               | 2j8u        | Human   | ALWGFFPVL                                 | A*0201 (K66A)  | -21.01        | 31.8  | 25                    | -  | AHIII 12.2         | I.3<br>(contd.) |
| 29               | 2jcc        | Human   | ALWGFFPVL                                 | A*0201 (W167A) | -22.74        | 15.4  | 20                    | -  | AHIII 12.2         |                 |
| 30               | 1ao7        | Human   | LLFGYPVYV                                 | A*0201         | -17.20        | -   | 32                    | 37 [17]  | A6                 |                 |
| 31               | 1qrm        | Human   | LLFGYAVYV                                 | A*0201         | -16.59        | 100   | 35                    | -  | A6                 |                 |
| 32               | 1qse        | Human   | LLFGYPRYV                                 | A*0201         | -17.28        | 8   | 31                    | -  | A6                 |                 |
| 33               | 1qsf        | Human   | LLFGYPVAV                                 | A*0201         | -14.99        | -   | 39                    | -  | A6                 |                 |
| 34               | 2gj6        | Human   | LLFGKPVYV                                 | A*0201         | -15.49        | 160   | 37                    | -  | A6                 |                 |
| 35               | 3d39        | Human   | LLFGFPVYV (Y5{4-fluoroPhenylalanine})     | A*0201         | -15.16        | 0.64  | 38.5                  | -  | A6                 |                 |
| 36               | 3d3v        | Human   | LLFGFPVYV (Y5{3,4-difluoroPhenylalanine}) | A*0201         | -15.40        | 0.46  | 37                    | -  | A6                 |                 |
| 37               | 3h9s        | Human   | MLWGYLQYV                                 | A*0201         | -14.91        | -   | 39                    | -  | A6                 |                 |
| 38               | <b>2bnr</b> | Human   | SLLMWITQC                                 | A*0201         | -14.93        | 13.3  | 39                    | 69   | 1G4                |                 |
| 39               | <b>2f54</b> | Human   | SLLMWITQC                                 | A*0201         | -15.59        | 15  | 36                    | -  | 1G4 (-3 $^\circ$ ) |                 |
| 40               | 2f53        | Human   | SLLMWITQC                                 | A*0201         | -16.06        | $1 \times 10^{-3}$                                | 36                    | -  | 1G4 (c49c50)       |                 |
| 41               | 2p5e        | Human   | SLLMWITQC                                 | A*0201         | -16.08        | $48 \times 10^{-6}$                               | 36                    | -  | 1G4 (c58c61)       |                 |
| 42               | 2p5w        | Human   | SLLMWITQC                                 | A*0201         | -16.69        | -   | 34                    | -  | 1G4 (c58c62)       |                 |
| 43               | 2pye        | Human   | SLLMWITQC                                 | A*0201         | -15.21        | $8.16 \times 10^{-2}$                             | 38                    | -  | 1G4 (c5c1)         |                 |
| 44               | 2bnq        | Human   | SLLMWITQV                                 | A*0201         | -15.23        | 5   | 38                    | 68.1   | 1G4                |                 |

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|-------------------|-------------|---------|--------------------|------------|---------------|--|-----------------------|--|---|-----------------|
| <b>TR/pMHC-I</b>  |             |         |                    |            |               |  |                       |  |   |                 |
| 45                | <i>loga</i> | Human   | GILGFVFTL          | A*0201     | -11.99        | -  | 69                    | 69   | V $\beta$ 17 V $\alpha$ 10.2                  | I.3<br>(contd.) |
| 46                | <i>2vlj</i> | Human   | GILGFVFTL          | A*0201     | -11.77        | 5.2  | 70                    | -  | V $\beta$ 17 V $\alpha$ 10.2 (+5 $^\circ$ )   |                 |
| 47                | <i>2vll</i> | Human   | GILGFVFTL          | A*0201     | -11.48        | 5.2  | 70.5                  | -  | V $\beta$ 17 V $\alpha$ 10.2 (+10 $^\circ$ )  |                 |
| 48                | 2vlr        | Human   | GILGFVFTL          | A*0201     | -11.88        | 4.9  | 70                    | -  | V $\beta$ 17 V $\alpha$ 10.2 (V $\beta$ S99A) |                 |
| 49                | 3gsn        | Human   | NLVPMVATV          | A*0201     | -16.66        | 27.7   | 34.5                  | 35   | RA14  |                 |
| 50                | 3hgl        | Human   | ELAGIGILTV         | A*0201     | -17.58        | 18   | 30                    | 35   | MEL5  |                 |
| <b>TR/pMHC-II</b> |             |         |                    |            |               |  |                       |  |   |                 |
| 1                 | 1u3h        | Murine  | SRGGASQYRPSQ       | I-Au       | -15.06        | -  | 73                    | -  | 172.10 V $\beta$ 8.2                          | II.1            |
| 2                 | 2z3l        | Murine  | RGGASQYRPSQ        | I-Au       | -13.01        | 25.3   | 87                    | -  | cl 19 V $\beta$ 8.2                           |                 |
| 3                 | 2pxy        | Murine  | RGGASQYRPSQ        | I-Au       | -14.47        | 25.4   | 77                    | -  | 1934.4 V $\beta$ 8.2                          |                 |
| 4                 | 3mbe        | Murine  | GAMKRHGLDNYRGYSLGN | I-Ag7      | -22.42        | $16.2 \times 10^{-2}$                                    | 38                    | 48   | 21.30   |                 |
| 5                 | 1d9k        | Murine  | GNSHRGAIEWEGIESG   | I-Ak       | -15.42        | -  | 71                    | 80   | D10   |                 |
| 6                 | 1j8h        | Human   | PKYVKQNTLKLAT      | DRB1*0401  | -16.76        | -  | 56                    | -  | HA1.7   | II.2            |
| 7                 | 1fyt        | Human   | PKYVKQNTLKLAT      | DRB1*0101  | -15.87        | -  | 60                    | 70   | HA1.7   |                 |
| 8                 | 1zgl        | Human   | VHFFKNIVTPRTPG     | DRA*0101   | -15.59        | -  | 61                    | 47   | 3A6   |                 |
| 9                 | 2iam        | Human   | GELIGILNAAKVPAD    | DRB1*0101  | -13.72        | -  | 79                    | 71   | E8  |                 |
| 10                | 2ian        | Human   | GELIGTLNAAKVPAD    | DRB1*0101  | -14.96        | -  | 75                    | 71   | E8  |                 |
| 11                | 1ymm        | Human   | ENPVVHFFKNIVTP     | DRB1*1501  | -11.76        | -  | 112                   | 110  | Ob.1A12                                       |                 |