

## **Supplementary method**

### **Antibody structure modeling**

Antibody structure modeling of 176 Fv was generated using Discovery Studio® Software 2017 R2(DS). Homology template structures of the top hits predicted by the Identify Framework Templates protocol were selected. These structures were used as input structures, becoming the foundation on which the Model Antibody Framework protocol built a chimeric antibody Fab structure. The Model Antibody Loops protocol identifies templates and manufactures models for CDRs using Hidden Markov Models(HMM). We used this protocol to rebuild the CDR loops. Finally, the homology model of 176 Fv was subject to energy minimization using the CHARMM force field. In this way, we developed a lowest energy structure for docking and further analysis.

### **Antibody Docking**

The structure of the LILRB1 (PDB ID:5KNM) was retrieved from the Protein Data Bank (PDB) and subject to energy minimization by using CHARMM force field for the structure preparation. Rigid body docking of 176 and LILRB1 was performed using the ZDock algorithm as described <sup>1</sup>. Next, hierarchical sets of clusters with different docked poses were generated according to antibody position. Rescoring of the poses was done using the ZRank scoring function based on the electrostatics, van der Waals, and desolvation energy terms.

Docked poses were filtered based on the ligand binding sites we identified, Arg-84 and Tyr-76. Next, 56 ranked poses with the ZRank scores lower than -55 were selected from the largest ten clusters. These were input into the RDock procedure. Input docked structures were refined by eliminating small clashes and optimizing polar and charge interactions, then re-ranked according to the electrostatics and solvation energy terms <sup>2</sup>. All 56 docked poses were performed by RDock with default parameters.

### **Binding interaction analysis**

The objective of using RDock was to identify the residues at the interface of antibody-antigen and calculate the binding energy between the 176 antibody and LILBR1. The interaction analysis was performed using DS and PyMOL. The nonpolar interaction energy was computed through the Calculate Interaction Energy protocol implemented in DS. Complexes with higher binding affinity between Tyr-76 and Arg-84 of LILBR1 and 176 Fv were considered to present favorable docking conformation.

The structure of h176 was predicted using DS. Docking of LILRB1-D1D2 with h176 Fab was performed using the ZDOCKpro module of the Insight II package. The general protocol for running ZDOCK includes two consecutive steps of calculation described as geometry search in ZDOCK and energy search in RDOCK. The crystal structure of LILRB1-D1D2 was obtained from the PDB database. RDOCK was used to

refine the top ZDOCK poses. Poses with high scores in both ZDOCK and RDOCK were selected as candidate complexes.

### Sequence alignment and phylogenetic analysis

D1 and D2 amino acid sequences of all LILRA and LILRB family members were analyzed. An exception was LILRB4, for which D1 domain was analyzed. The accession numbers of proteins in GenBank are as follows: LILRB1, Q8NHL6; LILRB2, Q8N423; LILRB3, O75022; LILRB4, Q8NHJ6; LILRB5, O75023; LILRA1, O75019; LILRA2, Q8N149; LILRA3, Q8N6C8; LILRA4, P59901; LILRA5, A6NI73; LILRA6, Q6PI73. The D1 region was defined as position 27 to position 115 and D2 as position 116 to position 221. Multiple alignments were performed using ClustalX (Version 2.1) with all the D1D2 sequences. MEGA (Version 7.0) was used to generate the phylogenetic tree.

### Reference

1. Chen R, Weng ZP. Docking unbound proteins using shape complementarity, desolvation, and electrostatics. *Proteins* 2002;**47**:281-94. doi: 10.1002/prot.10092 pmid:<http://www.ncbi.nlm.nih.gov/pubmed/11948782/>
2. Chen R, Li L, Weng ZP. ZDOCK: An initial-stage protein-docking algorithm. *Proteins* 2003;**52**:80-87. doi: 10.1002/prot.10389 pmid:<http://www.ncbi.nlm.nih.gov/pubmed/12784371/>