Electronic Supplementary Material (ESI) for Soft Matter

Supporting information

Drug promiscuity of P-glycoprotein and its mechanism of interaction with paclitaxel and doxorubicin

Junqiao Zhang, Tianyang Sun, Lijun Liang, Tao Wu, Qi Wang*

Soft Matter Research Center and Department of Chemistry, Zhejiang University, Hangzhou, 310027, P. R. China

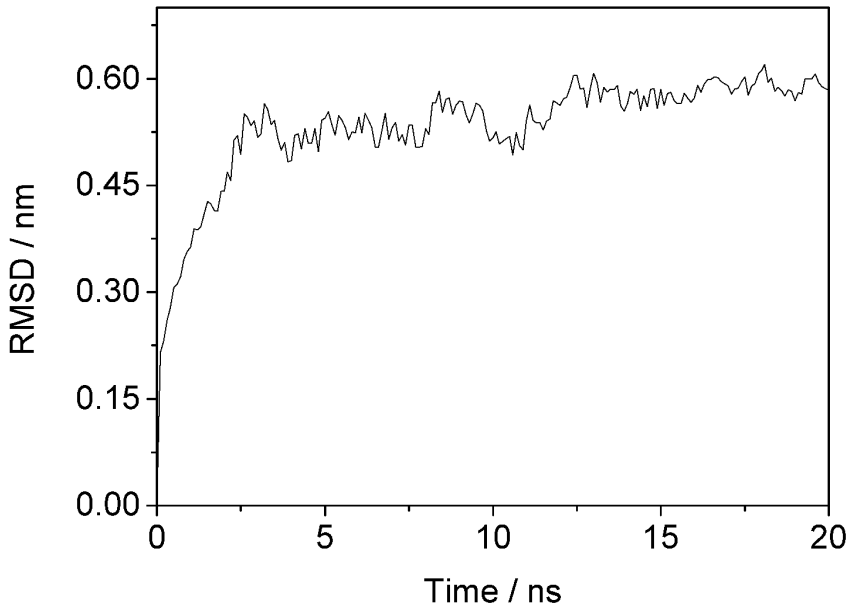

Figure S1. RMSD of P-gp (alpha-C).

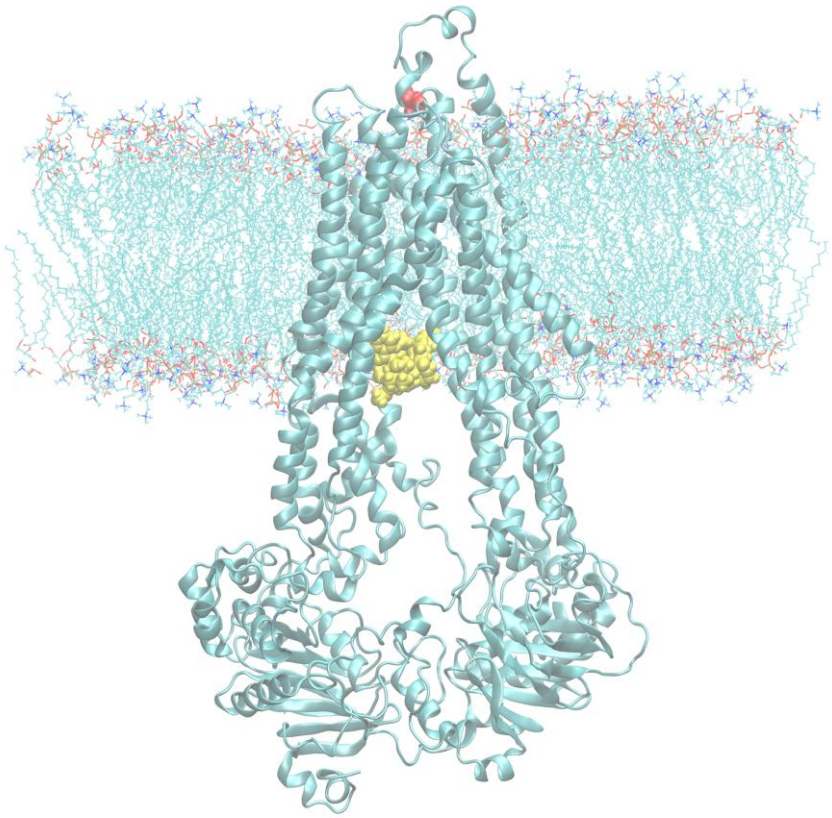

Figure S2. Initial structure of the production run. Paclitaxel are colored yellow and Ala82 are colored red. P-gp is rendered as main chain new cartoons and the POPC membrane is rendered line. Doxorubicin in MD_2 was manually placed the same place with paclitaxel.

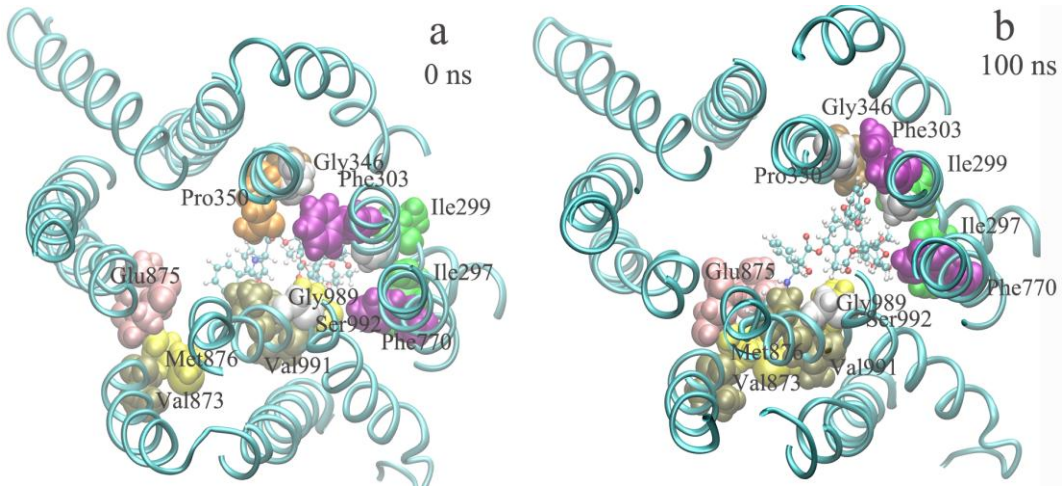

Figure S3. Important inner residues in paclitaxel's movement in MD_1.

Paclitaxel is rendered as CPK spheres and P-gp is rendered as main chain new cartoons. Important inner residues are rendered as vdW models. Phe303 is very noticeable. **(a)** The first snapshot from the top view. **(b)** The last snapshot from the top view.

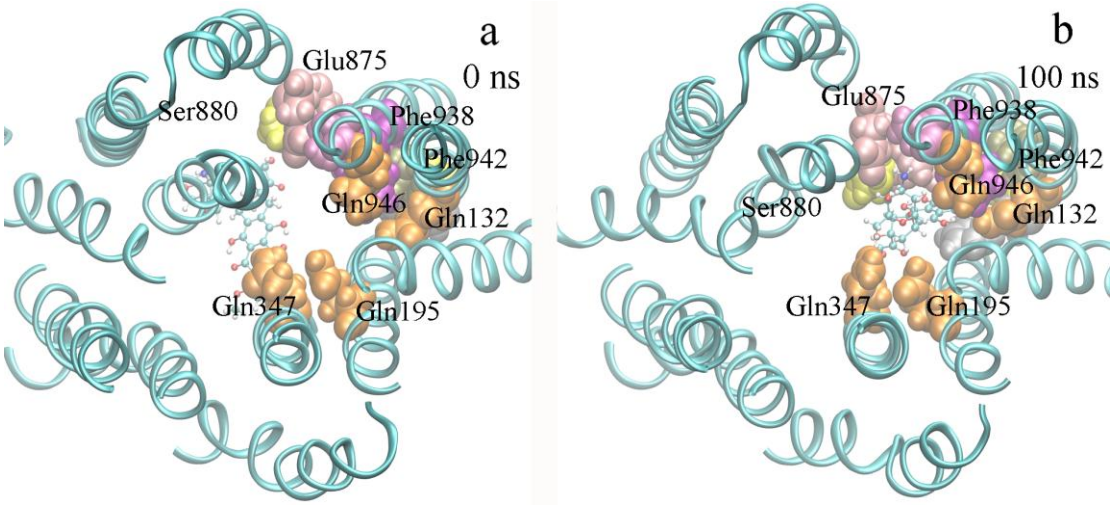

Figure S4. Important inner residues in doxorubicin's movement in MD_2.

Doxorubicin is rendered as CPK spheres and P-gp are rendered as main chain new cartoons. Important inner residues are rendered as vdW models. **(a)** The first snapshot from the top view. **(b)** The last snapshot from the top view.

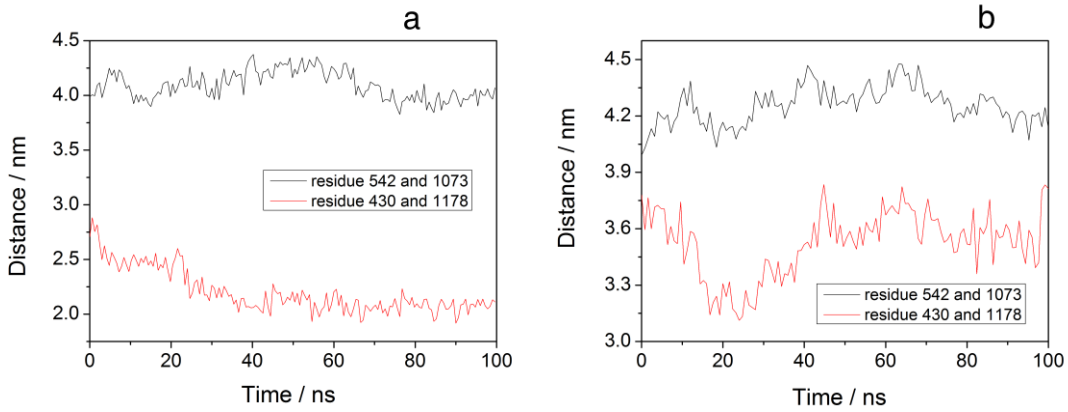

Figure S5. Distance between motif A and motif C. For human P-gp, Motif A is GNSGCGKS (residues 1070 to 1077), and its motif C is LSGGQ (residues 540 to 544). For another pair, Motif A is GSSGCGKS (residues 427 to 434), and its motif C is LSGGQ (residues 1176 to 1180). We use the distance between the fourth residue in motif A (G) and the third residue in motif C (G) to measure the NBD distance changes. **(a)** The distance curve of distance of motif A and motif C in MD_1. **(b)** The distance curve of distance of motif A and motif C in MD_2.

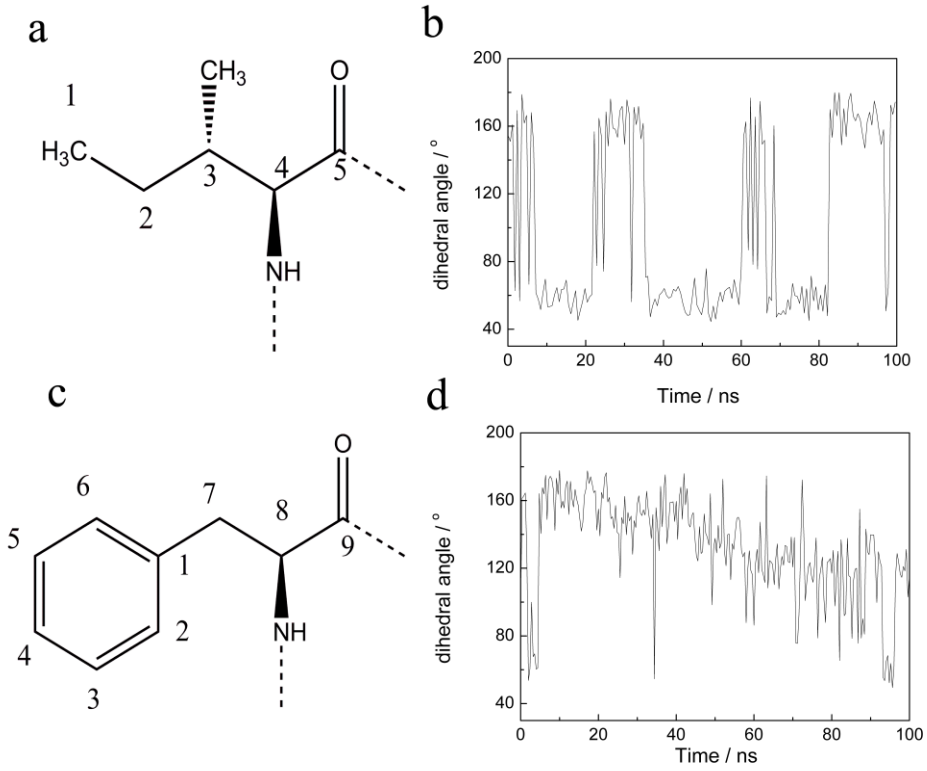

Figure S6. Some obviously flexible side chains of inner residues. (a) Ile297 residue. **(b)** The dihedral angle of Ile297 atoms 1, 2, 3, 4 in MD_1. **(c)** Phe938 residue. **(d)** The dihedral angle of Phe938 atoms 8, 7, 1, 2 in MD_2.

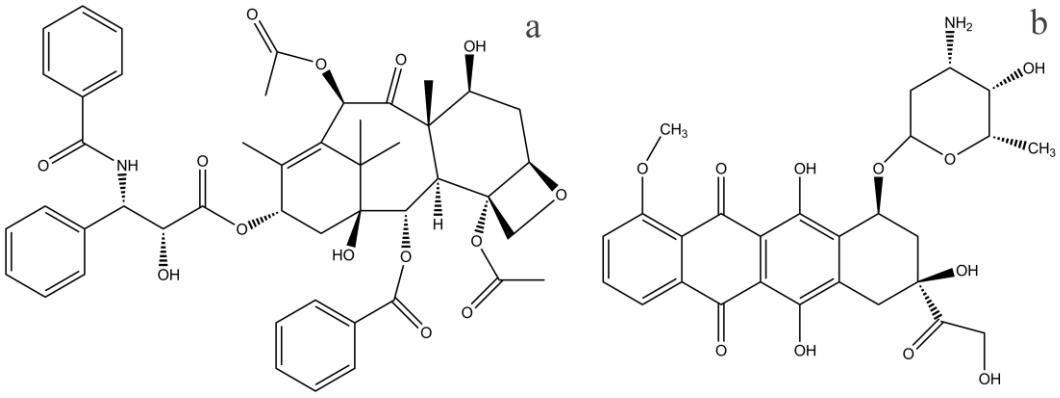

Figure S7. Chemical structures of paclitaxel (a) and doxorubicin (b).