Supplementary material

S1. RMSD values obtained for the alignment of C1 cluster from AA-MDS for different sites of WT-MRP4, G187W and Y556C

Alignment	RMSD value	Significant or not significant
WT-MRP4 (TMDs)/G187W (TMDs)	3.927 Å	Significant
WT-MRP4 (TMDs)/Y556C (TMDs)	4.139 Å	Significant
G187W (TMDs)/ Y556C (TMDs)	4.485 Å	Significant
WT-MRP4 (r85-248)/ G187W (r85-248)	3.323 Å	Significant
WT-MRP4 (r85-248)/ Y556C (r85-248)	3.801 Å	Significant
G187W (r85-248)/ Y556C (r85-248)	5.027 Å	Significant
WT-MRP4 (r715-866)/ G187W(r715-866)	4.485 Å	Significant
WT-MRP4 (r715-866)/ Y556C (r715-866)	4.555 Å	Significant
G187W (r715-866)/ Y556C (r715-866)	4.528 Å	Significant

Ligand binding diagram interactions



S2. Binding site and intermolecular interaction of cholic acid in WT-MRP4 (**A**), G187W (**B**) and Y556C (**C**). **D** Nomenclature of LIDs.

*Nomenclature for the LIDs is presented in S2 only.



S3. Binding site and intermolecular interaction of taurocholic acid in WT-MRP4 (**A**), G187W (**B**) and Y556C (**C**).



S4. Binding site and intermolecular interactions of cefazoline in WT-MRP4 (A), G187W (B) and Y556C (C).



S5. Binding site and intermolecular interaction of ceefourin-1 in WT-MRP4 (**A**), G187W (**B**) and Y556C (**C**).



S6. WT-MRP4-FA complex at T0 in AA-MDS



S7. WT-MRP4-FA complex at 5 ns in AA-MDS



S8. WT-MRP4-FA complex at 10 ns in AA-MDS



S9. WT-MRP4-FA complex at 15 ns in AA-MDS



S10. WT-MRP4-FA complex at 20 ns in AA-MDS



S11. WT-MRP4-FA complex at 25 ns in AA-MDS



S12. G187W-FA complex at T0 in AA-MDS



S13. G187W-FA complex at 5 ns in AA-MDS



S14. G187W-FA complex at 10 ns in AA-MDS



S15. G187W-FA complex at 15 ns in AA-MDS



S16. G187W-FA complex at 20 ns in AA-MDS



S17. G187W-FA complex at 25 ns in AA-MDS



S18. Y556C-FA complex at T0 in AA-MDS



S19. Y556C-FA complex at 5 ns in AA-MDS



S20. Y556C-FA complex at 10 ns in AA-MDS



S21. Y556C-FA complex at 15 ns in AA-MDS



S22. Y556C-FA complex at 20 ns in AA-MDS



S23. Y556C-FA complex at 25 ns in AA-MDS