Supporting Information

Molecular Dynamics Simulations for Human CAR Inverse Agonists

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Table S1. Cytotoxicity data from MTT tests for the studied ligands.

Ligand[a]	**Fold absorbance**[b] **(DMSO = 1)**
CITCO	1.09 ± 0.07
FL-82	0.97 ± 0.02
FL-81	0.92 ± 0.01
Permethrin	0.80 ± 0.11
Clotrimazole	1.02 ± 0.02
TPP	1.21 ± 0.04
Artemisin	1.08 ± 0.10
EE2*	0.93 ± 0.16
Androstanol	n.d.[c]
Androstenol*	0.75 ± 0.08
PK11195	1.03 ± 0.03
S07662	1.13 ± 0.09
Clomifene	n.d.[c]
Celecoxib	0.98 ± 0.02
Meclizine	1.26 ± 0.09
$HgCl_2$[d]	*0.04 ± <0.01*

[a]The concentration of ligand was 10 μM. For the ligands marked with "*" 50 μM concentration was used.

[b]Fold absorbance (vehicle control DMSO = 1) measured at 570 nm ± s.d.

[c]No data for MTT tests is available. No toxicity of these compounds was observed at 30 μM concentration when looking at the expression of β-galactosidase reporter gene which was used as a transfection control in M1H and M2H assays.

[d]Positive control (0.1 mM) for toxicity.

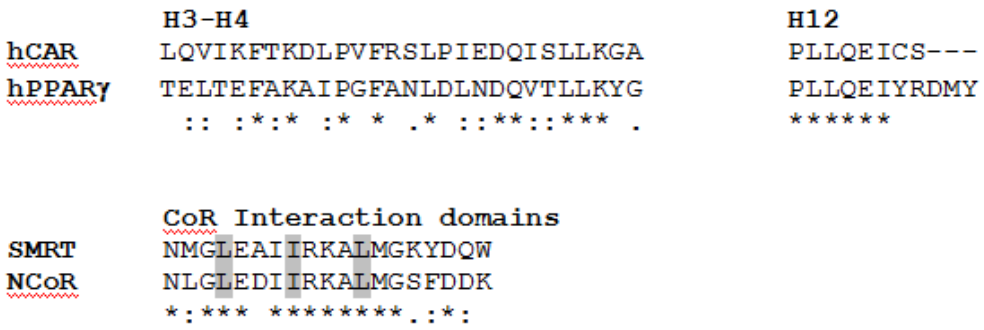

Figure S1. The alignment of co-regulator interacting regions (c-terminal part of H3, H4 and H12) of hCAR and PPARγ and the alignment of interaction domains of SMRT and NCoR. Identical residues have been identified with "*", conserved substitutions with ":" and semi-conserved substitutions with "." The most important and conserved residues in the NR interaction of SMRT and NCoR have been high-lighted with grey.

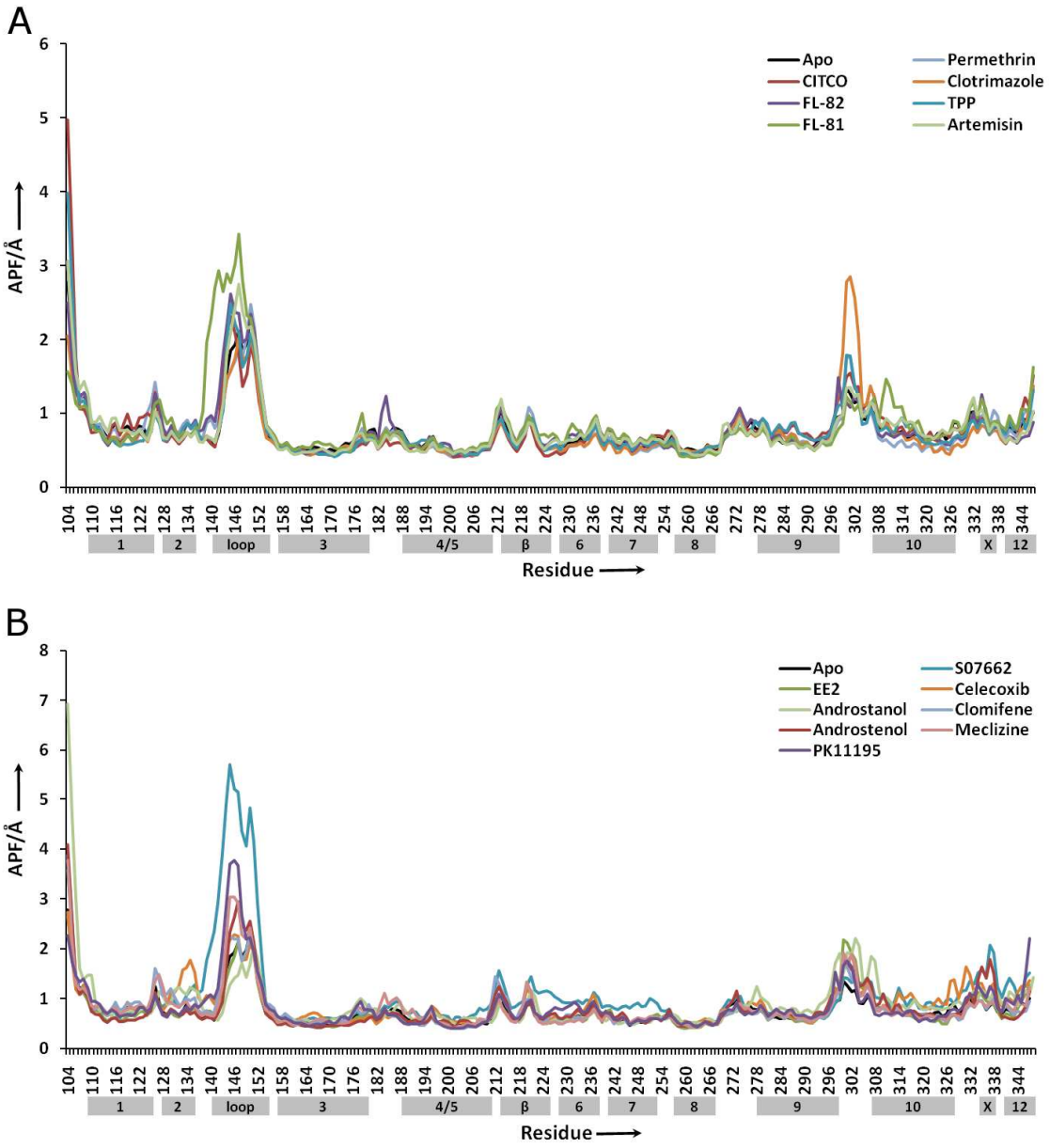

Figure S2. APFs of CAR LBD backbone during MDs with A) agonists and B) inverse agonists.

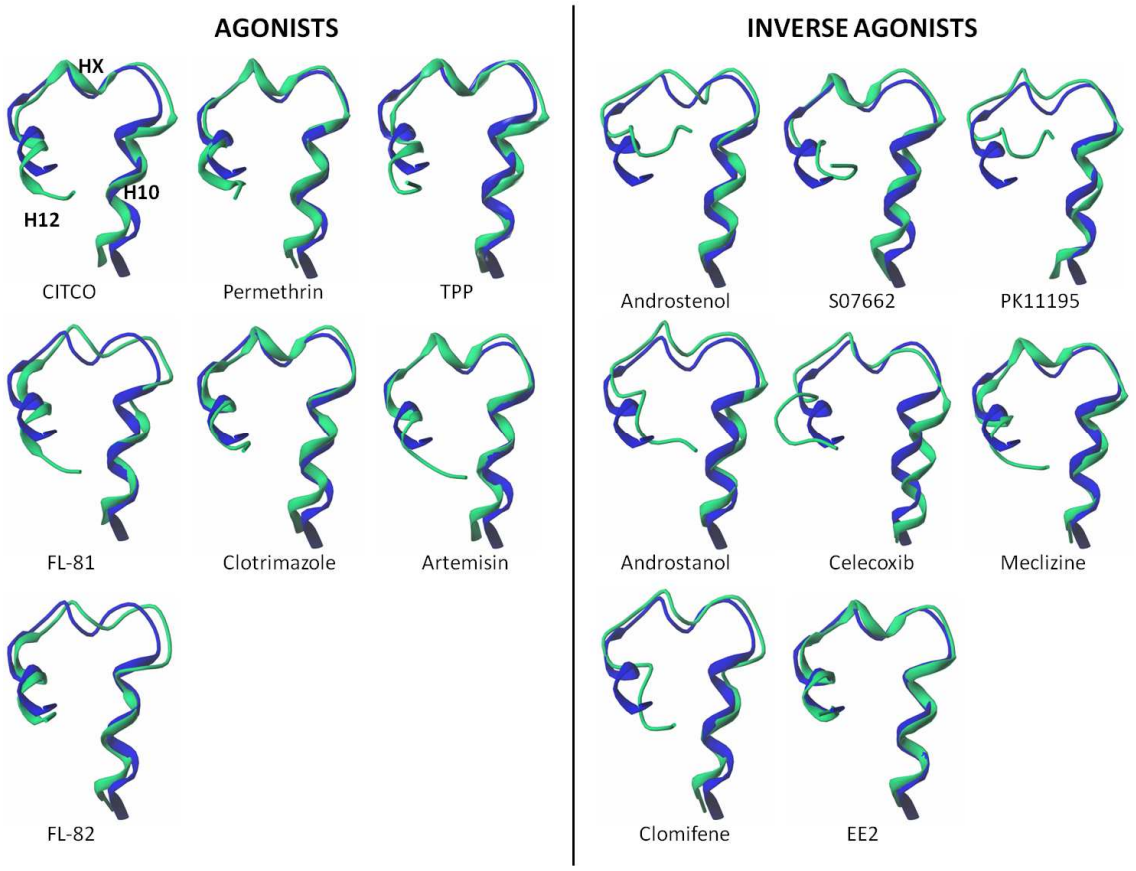

Figure S3. Position of H12 in the final structures of the MDs. Apo structure is shown in blue as a reference with each liganded structure (green).