Supporting Information

Structural basis for the accommodation of bis- and tris-aromatic derivatives in Vitamin D Nuclear Receptor

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Supplementary Figures 1, 2, 3 and 4.

Supplementary Table 1

Supp. Figure 1: Superimposition of the overall of structures VDR/ $1\alpha,25(\text{OH})_2\text{VD}_3$ (green) with those of VDR/ CD4802 (red), CD4742 (orange), CD4720 (light orange) and CD4849 (yellow).

Supp. Figure 2: Schematic representation of the VDR ligand binding pocket bound to CD3938 where only residues closer than 4.0 Å to the ligand are shown. Protein side chains forming hydrogen bonds with the ligand are shown labeled in red. Residues in van der Waals contact with the ligand are drawn schematically. The three letter code corresponds to the zVDR. The interactions lost in the non-secosteroidal VDR complexes are shown green and those gained in yellow.

a.

b.

Supp. Figure 3: Schematic representation of the VDR ligand binding pocket bound to CD4528 where only residues closer than 4.0 Å to the ligand are shown. Protein side chains forming hydrogen bonds with the ligand are shown labeled in red. Residues in van der Waals contact with the ligand are drawn schematically. The three letter code corresponds to the hVDR. The interactions lost in the non-secosteroidal VDR complexes are shown green and those gained in yellow.

a.

b.

Supp. Figure 4: Schematic representation of the VDR ligand binding pocket bound to CD4820 where only residues closer than 4.0 Å to the ligand are shown. Protein side chains forming hydrogen bonds with the ligand are shown labeled in red. Residues in van der Waals contact with the ligand are drawn schematically. The three letter code corresponds to the zVDR. The interactions lost in the non-secosteroidal VDR complexes are shown green and those gained in yellow.

Supp. Table 1: Volumes of the ligands and of the zVDR LBP in the zVDR complexes.

Complexes	Volume of zVDR LBP (Å³)	Volume of ligand (Å³)
zVDR/calcitriol	687	367
zVDR/CD3938	670	362
zVDR/CD4528	680	359
zVDR/CD4742	758	403
zVDR/CD4720	762	406
zVDR/CD4849	723	404
zVDR/CD4802	765	418