LXRβ: FRET-based compound-CoF peptide profiling, peptide gradient

These pix now show the apparent affinities of individual cofactor peptides in the presence of constant saturating concentrations of ligands to LXRβ. In the absence of ligand, the recruitment of corepressor peptides from NCoR and SMRT can be nicely seen. Whereas Ref Cpd 1 and Ref Cpd 2 show about the same relative affinities to coactivator peptides from NCoA3, SRC-1 and TRAP220; Ref Cpd 2 induces a much higher apparent affinity to the NCoR corepressor peptide than Ref Cpd 1. NCoA3 and TRAP220 peptide affinity is substantially reduced with Px Cpd 2 whereas affinity to NCoR even increases compared to Ref Cpd 2.

These data can be used to deduce individual ligand cofactor peptide signatures in terms of CoF peptide EC50s. This allows to compare relative agonistic (coactivator recrutiment) to antagonistic (corepressor recruitment) behaviour of compounds in absolute quantitative terms. In addition, the peptide gradient mode allows the direct comparison independent from the ligand´s potency since the compound is added at saturating concentrations.