Human Urotensin-II (h-UII) and Urotensin II-related peptide (h-URP) are agonists of the Urotensin Receptor (UT), a G-protein coupled receptor. They are implicated in numerous pathological disorders such as metabolic syndrome, psychological and neurological disorders\(^1\). A few years ago, our team designed several pharmacophores by considering agonists and antagonists of UT and compared them to the 3D structure of h-UII\(^3\). From these pharmacophores, a virtual screening of the CERMN chemical library was carried out and led to the discovery of a first set of UT antagonists. New data concerning the notion of biased ligands\(^2\) encouraged us to extend this study by considering more recent binding and pharmacological data for non peptide, pseudo peptide and natural peptide ligands of UT. From a new set of non-peptide ligands, various pharmacophores were generated. These pharmacophores were analyzed and aligned to h-URP and U-II conformations resulting from long molecular dynamic simulations and free energy calculations (Figure 1). To complete this work, a docking study was carried out on UT.

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Figure 1. Alignment of one conformation of h-URP with one pharmacophore.