Predicting Ligand-Receptor Interactions of Promiscuous Proteins by PhE/SVM: The Nuclear Receptor PXR

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The nuclear receptor pregnane X receptor (PXR) plays a critical role in Phase I or II metabolism and excretion because it can increase induction levels of metabolism enzymes upon activation by a wide range of endogenous and xenobiotic molecules. In this study, an *in silico* model was developed to predict the activation of hPXR using the newly invented pharmacophore ensemble/support vector machine (PhE/SVM) scheme, which can fully take into account the promiscuous nature of hPXR, namely flexible protein conformation and multiple ligand orientations. The predictions are in good experimental observations and the calculated results are consistent with the published hPXR-ligand co-complex structure. Furthermore, the derived model not only showed highly statistical significance but completely met with various validation criteria. Therefore, this accurate PhE/SVM model can be utilized for predicting the activation of hPXR to facilitate drug discovery and drug development.