Druggability Predictions of Ribonucleic Acid Crystal Structures

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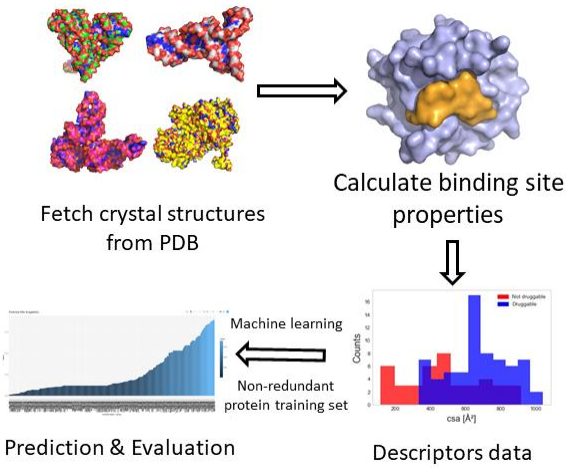

It is estimated that the intersection of genes which are disease-modifying and suited druggable targets constitutes about 0.02 to 0.05% of the human genome, limiting the amount of viable protein targets.[1, 2] Examples include riboswitches, which acts as 5'-UTR *cis*-regulating elements, which upon binding to small metabolites undergo a conformational change and thus switch on or off gene expression.[3-5]

A drug target needs to be relevant for a given disease and be able to be modulated by either biological or small molecules. In the latter case, the drug target needs to have a pocket that can bind drug-like ligands with high affinity, a property which is referred to as being "druggable". To identify such pockets in protein structures, we have previously derived a druggability predictor named DrugPred[6, 7], which we have in this work extended to also classify RNA binding sites. Due to the paucity of validated druggable RNA binding sites, we trained the predictor, DrugPred_RNA on protein binding sites described only by descriptors applicable for both protein and RNA structures. DrugPred_RNA, distinguishes druggable from less druggable binding sites with high accuracy. Further, known druggable RNA binding sites are classified correctly, making this a useful tool for RNA-based druggability predictions.

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