OS03-2 Application of compound database in virtual drug screening

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We have developed software for computer-aided drug development (myPresto) and a chemical compound library (LigandBox). The software has been applied to 13 target proteins and the hit ratio has been several% to 50% except one target. As the result, over 200 active compounds were found. In general, in-silico screening succeeds in providing good database enrichment in approximately half of the cases and fails in hit compound prediction in the other half, since the protein structure is flexible. One approach is so-called ensemble docking in which many protein structures are prepared and many in-silico screening results are generated. In ensemble docking, how to select the most reliable result among many results is serious problem. We proposed a concept of a set of "universal active probes" (UAPs), which is a set of small active compounds those bind to different kinds of proteins. The hit ratio of the true active compounds in in-silico screening showed positive correlation to that of the UAPs. Thus, if the UAPs were added to the compound library, the screening result that shows a high hit ratio of the UAPs could give reliable actual hit compounds for the target protein. In addition, compound library could be used for protein-ligand pocket prediction and prediction of druggability of the ligand-binding pocket.