Poster presentation

Glide XP fragment docking and structurebased pharmacophores

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In recent years, fragment-based drug design has become increasingly popular. Common computational approaches include building fragments up sequentially, or linking disparate fragments. However, the former approach can restrict the exploration of chemical space and may produce ligands that are not sufficiently drug-like, whereas the latter approach may result in difficulties when linking together the individual fragments.

Here, we describe a third approach that avoids these problems with the use of fragment-derived pharmacophore hypotheses. In our computational workflow a pharmacophore hypothesis is created using fragments docked and ranked by Glide XP, and virtual databases are screened against this hypothesis using Phase [1]. In an initial validation study on P38 Map Kinase, known active compounds were successfully retrieved and good enrichment factors were obtained.

References

1.   Dixon SL: J Comput Aided Mol Des 2006, 20:647-671.