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The Use of Shape and Pharmacophore in High Throughput Crystallography Refinements and Lead Hopping: An Application Study. Samuel Toba, Zeljko Dzakula, Daniel Berard, Jon Sutter, Al Maynard. Accelrys Inc, San Diego, CA.

We report here shape and pharmacophore hypotheses derived from protein binding sites. The hypotheses generated augment the electron density information in the search for bound ligand as part of the crystal refinement process. The hypotheses can further be applied for lead-hopping to discover novel molecules. Our use of shape, pharmacophore, and excluded volumes features protocol provides one step approach to reduce false positives in ligand search and helps identify novel leads from virtual screening of databases.