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EAI-TupletScore, a pharmacophore and shape driven ligand-based de-novo design algorithm

KM Smith*, BB Masek, RD Clark, T Mansley, E Abrahamian and S Nagy

Address: Tripos Intl., Inc., 1699 S. Hanley Rd, St Louis, Missouri 63144, USA
* Corresponding author

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We describe a ligand-based de-novo design algorithm EAI-TupletScore and studies that demonstrate its ability to successfully generate lead hops between different classes of active ligands from the DUD dataset [1]. EAI-TupletScore uses the de-novo design engine EA-Inventor with a Pareto-Borda [2][3] scoring method that employs pharmacophore and steric tuplets [4], as well as UNITY fingerprint similarities to a set of lead compounds to design novel ligands that maximize pharmacophore and shape similarity, while maintaining a certain level of structural dissimilarity, to these lead compounds. EAI-TupletScore, can be used to design novel ligand scaffolds (lead generation or lead hopping) or to optimize attachments on a fixed scaffold (lead optimization).

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