Target X Model: Reliable Protein Pocket Ligandability Prediction for Smarter Target Prioritization

David LeBard and Neha Vithani

OpenEye, Cadence Molecular Sciences, 9 Bisbee Court Suite D, Santa Fe, NM 87508

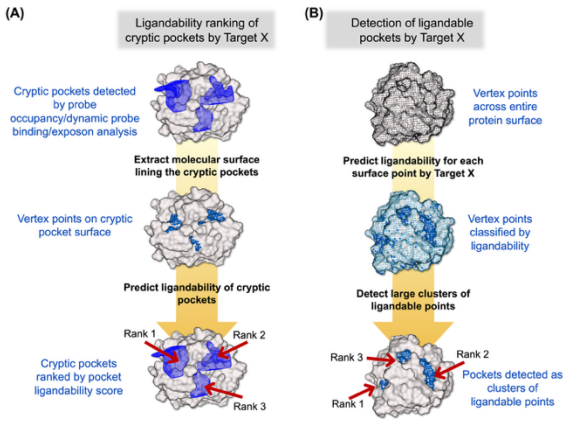
Summary:

- Target X model is trained on 1,847 non-redundant ligand-binding pockets curated using 3D pocket similarity, ensuring minimal bias and data leakage.
- The model reaches 91% accuracy and 97% precision in distinguishing ligandable from non-ligandable surfaces.
- Target X model correctly identifies 81% of FDA-approved drug binding sites and enables reliable early-stage pocket prioritization.

Product Keywords: Target X, Pocket Detection, Cryptic Pocket, Ligandability, Groovy, SiteHopper, Orion®

Abstract:

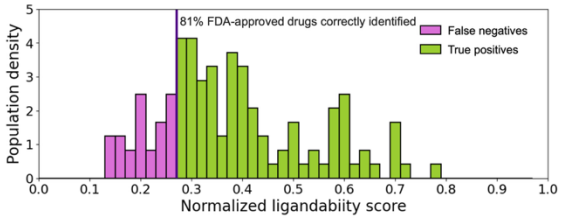
Accurately identifying ligandable pockets remains a bottleneck in early drug discovery. Many existing models suffer from use of global protein similarity metrics to define pocket redundancy, rather than pocket similarity, hence introducing bias and data leakage.



Target X ligandability assessment model can be used to rank pockets identified from (A). molecular dynamics simulations, such as from Target X pocket detection, or (B). applied directly on static protein structures.

OpenEye's Target X ligandability assessment model was trained on 1,847 high-quality, non-redundant ligand-binding pockets (Groovy) curated using 3D pocket similarity (SiteHopper) instead of sequence or fold similarity. Removing similar pockets at the binding-site level reduces hidden bias and improves performance on new, unrelated targets.

On an independent validation set, Target X differentiates ligandable from non-ligandable surfaces with 91% accuracy and 97% precision. When evaluated on 121 protein complexes bound to FDA-approved drugs, it correctly identified 81% of drug-binding sites as ligandable.



Target X correctly identifies 81% of FDA-approved drug binding sites.

Using the Target X ligandability approach, scientists can more confidently assess and prioritize protein pockets at the onset of a structure-based drug discovery program.

Reference: Vithani et. al. Preprints. Research Square. Feb 12, 2026. DOI: https://doi.org/10.21203/rs.3.rs-8833408/v1

info@eyesopen.com