Deep Drug Discovery
Unsupervised fragment-to-drug generation

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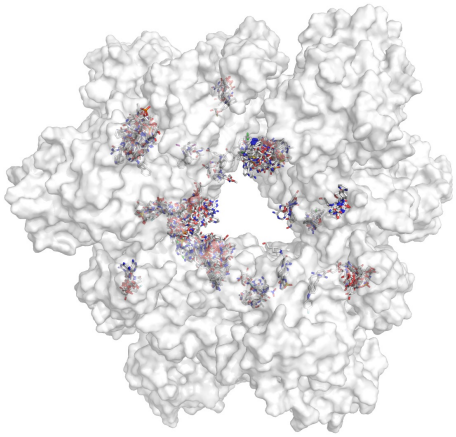
Chemotargets

Main components required to approach the dream

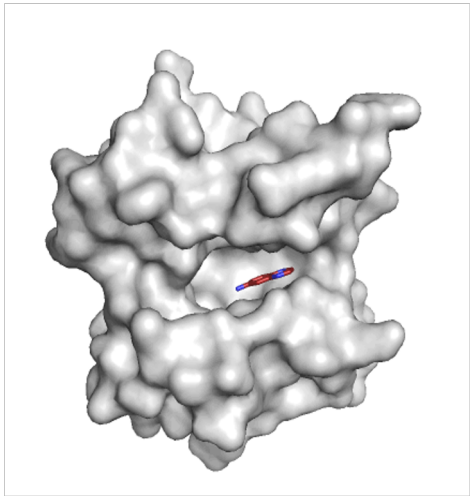
SurfScan

A method to perform fragment screening on complete protein surfaces



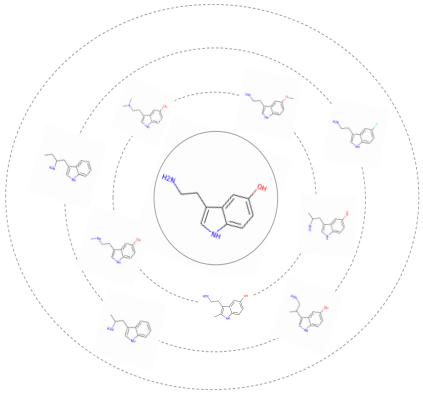
FragSteer

A method to differentiate stable from compatible interacting fragments



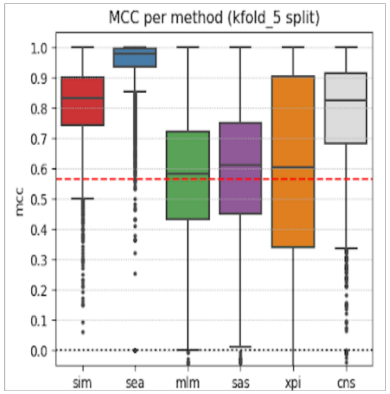
ChemBang

A method to expand the chemical space around stable fragments



PreCogs

A model suite to anticipate binding and safety of small molecules



SurfScan works

www.nature.com/scientificreports

scientific reports

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OPEN

Fragment-based virtual screening identifies a first-in-class preclinical drug candidate for Huntington's disease

Simon Marius Galyan[1]✉, Collin Y. Ewald[2], Xavier Jalencas[3,4], Shyam Masrani[5], Selin Meral[6] & Jordi Mestres[3,4]

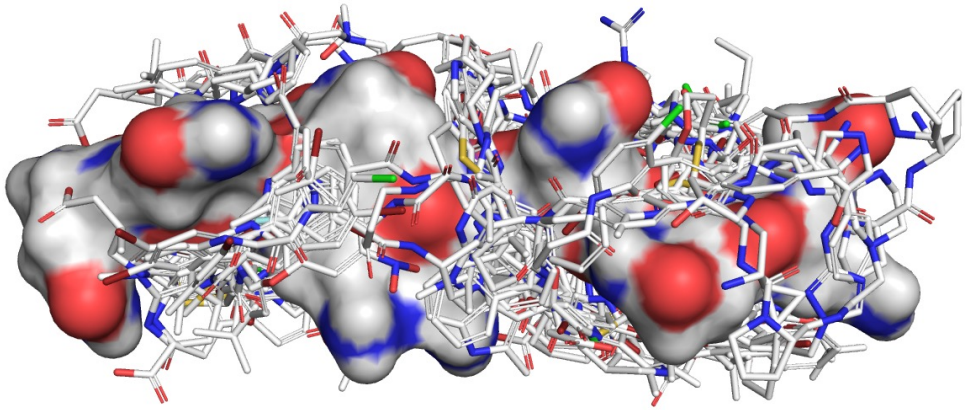


Figure 1. The selection of 67 small molecules docked on the surface of the polyQ tract peptide.

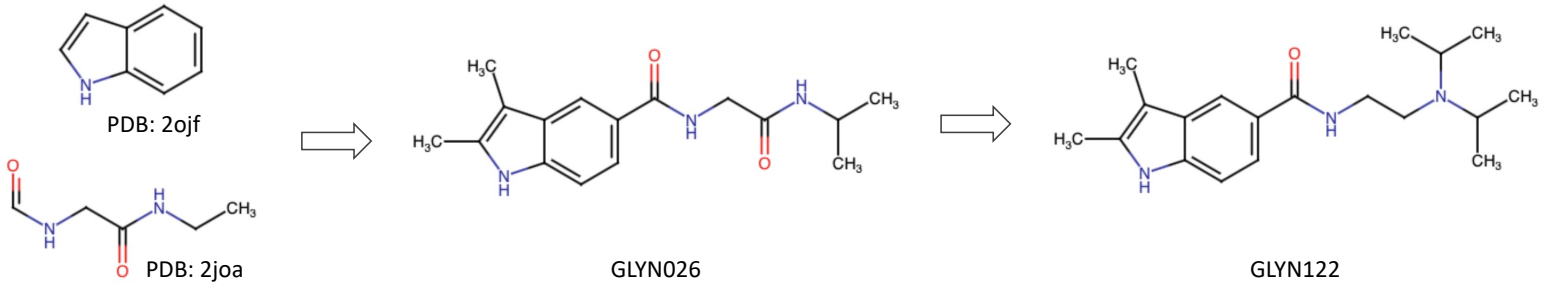


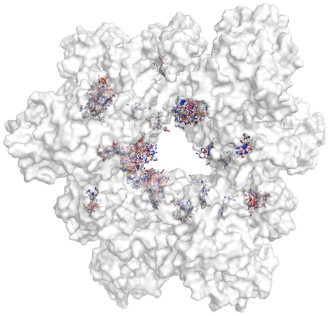
Figure 2. Selection of the preclinical candidate (GLYN122) from analogue expansion of a hit compound (GLYN026) derived from two adjacent chemical fragments obtained from virtual protein surface scanning.

Chemotargets' Deep Drug Discovery (D^3) platform

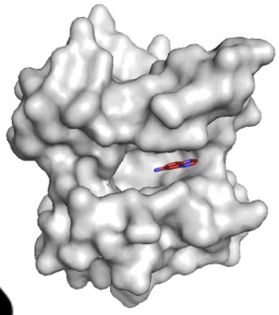
SurfScan

de novo design of bioactive small molecules based on full protein surface scan of chemical fragments

ML mapping of chemical fragments compatible with matching protein environments for agnostic design of small molecule ligands for difficult to treat targets



docked molecules



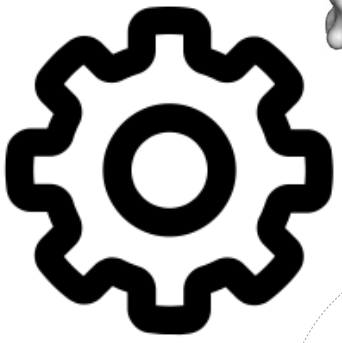
FragSteer

differentiating between stable and compatible interacting fragments

Steered molecular dynamics coupled with a differential evolution algorithm to find the optimal pulling directional to the unbound state

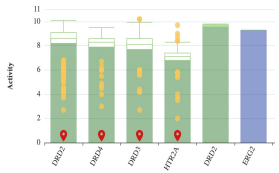
prioritised molecules

selected molecules

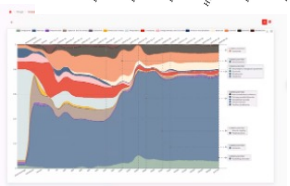


PreCogs

anticipating pharmacology and safety profiles



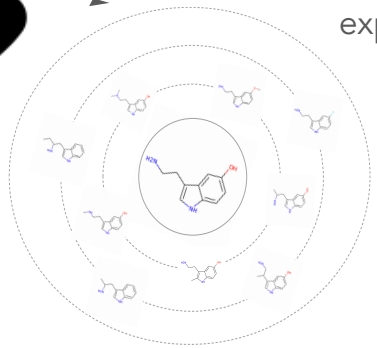
ML models for predicting on- and off-target pharmacology, preclinical ADME properties, metabolites, and postmarketing safety signals



expanded molecules

ChemBang

explosion of chemical space around seed molecules



ML library generator trained on known chemical transformations from commercial catalogues of synthesised molecules