XtalPi

Combination of DEL Screening and Computational Platform

Accelerating Results with Precision and Efficiency

XtalPi Application Note

While DEL screening offers significant advantages, many users prefer virtual screening in the early stages of drug discovery due to speed and cost

DEL Screening

Massive Library Size

Enables simultaneous screening of billions of compounds, increasing the chances of finding novel hits

Minimal Protein and Assay Requirements

Requires minimal target protein and assay development, making highly efficient and accessible for early-stage drug discovery

Reduced False Positives

Yields more reliable results, reducing false positives compared to virtual screening

Virtual Screening

Speed

Conducted quickly without needing physical samples

Cost-Effectiveness

Narrows compound candidates with low cost before moving to more resource-intensive methods

XtalPi Combines DEL Library Screening with its Proprietary Computational Platform to Accelerate the Screening Process, Maximize Efficiency & Lower Cost

DEL Screening

- **Screens** massive compound libraries **simultaneously**
- Requires **minimal** target protein
- **Reduces** false positive

The XtalPi Difference

Computational Platform

- **Lowers** the number of compounds to be synthesized
- Serves an **additional validation** step for accuracy

Accelerates the screening process
Maximizes resource efficiency
Lowers synthesis costs

DEL Screening Combined with the Computational Platform Reduces Time and Resources Without Compromising Accuracy

Approximate Timeline

~7 Weeks In Total

2 Weeks

Confirmation of DEL affinity selection conditions

3 Weeks

Sequencing results analysis and selection of enriched DEL compounds from building blocks

2 Weeks

Computational binding pose analysis and affinity predictions to recommend fewer but better compounds for synthesis

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2 Weeks
Confirmation of DEL affinity selection conditions

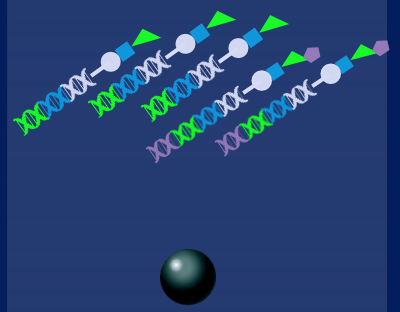
3 Weeks
Sequencing results analysis and selection of positive binders

2 Weeks
Compound selection by docking pose analysis and FEP calculations

Project-Specific Assessments to Confirm DEL Affinity Selection Conditions

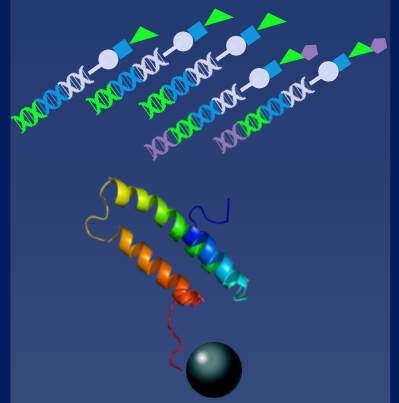
Non-targeting control

DEL compounds were incubated with beads without the immobilized target.



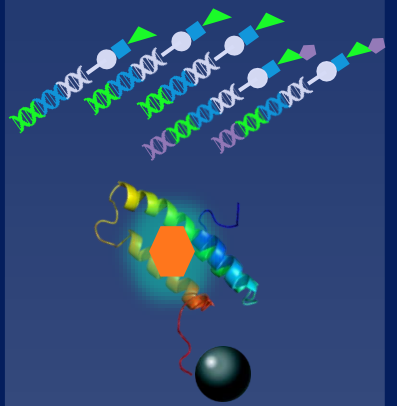
Target only

DEL molecules were incubated with the target immobilized on beads.



Target with ligand

A known ligand binds to the immobilized PPI target on beads before incubation with DEL compounds.



- Beads
- DEL molecules
- Protein of interest
- Known ligand of the protein

Other selection conditions can also be tailored and designed to best identify potential target binders

Submitted in Parallel to Next-Generation Sequencing

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3 Weeks
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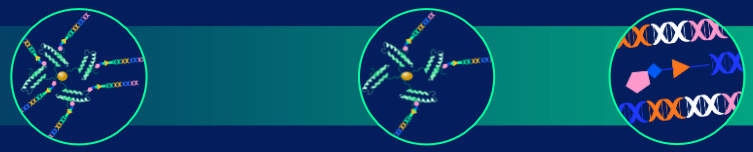
Compound selection by docking pose analysis and FEP calculations

Hit Screening via DEL Affinity Selection and NGS Identified Active Compounds with High Speed and Throughput

Several Rounds of DEL Affinity Selection



a. Library Incubation **b. Wash** **c. Elution**

Incubate the PPI-like target with XtalPi's exclusive 3- and 4-cycle DEL, containing over 100 billion DNA-encoded compounds

Next Generation Sequencing

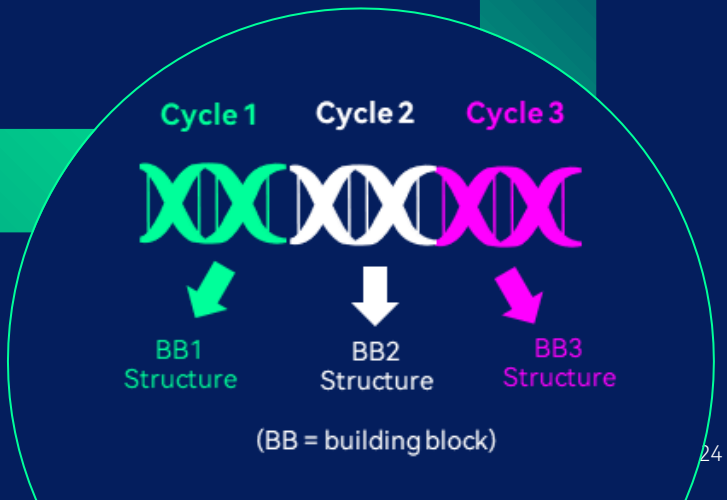
Send for next-generation sequencing (NGS) of their DNA tags

Identifying Building Block Structures and Selecting Potential Positive Binders

Positive Binders

Ready for XtalPi Computational Platform

NGS data deconvoluted to identify building blocks and select potential positive binders for computational screening based on enrichment patterns, suggesting high target affinity



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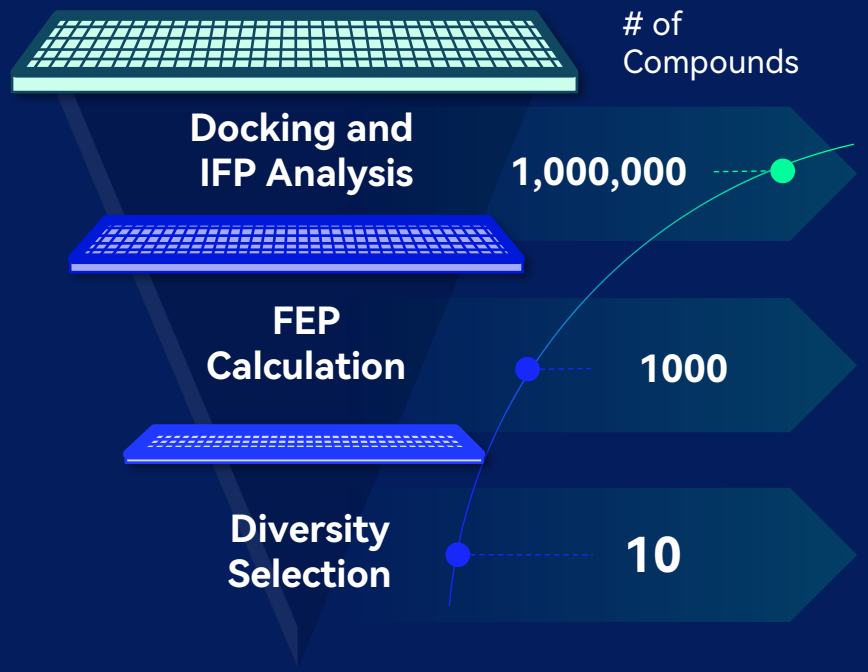
Computational Platform Reduces the Time and Cost of Potent Hit Identification by Recommending Optimal Compounds

Docking Pose Analysis and Free Energy Perturbation (FEP) Calculations



XPose
Receptor-ligand binding pose prediction software analyzes docking poses of selected DEL screening compounds using interaction fingerprints (IFP).

XFEP
Click **here** to learn more about XFEP application in drug discovery
FEP calculation software employs a proprietary force field to predict FEP for compounds with the best binding poses.

Calculated binding free energies identify compounds with the highest predicted target affinity for automated off-DNA synthesis and validation.

The XtalPi Computational Platform **reduces** time to **~ 2 weeks,** narrowing the selection to a **few compounds for synthesis.**

Combination of DEL Screening with XtalPi's Computational Platform Accelerates the Screening Process, Maximizes Efficiency, and Ensures Accuracy

Approximate Timeline

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~7 Weeks In Total

- Combination of DEL and Computational Platform **reduces** the **number of synthesized compounds** and **time** while **ensuring accuracy** and **quality**

Cost-Effective Screening

Leverages DEL technology to rapidly screen billions of compounds at a **fraction of the cost** of physical screening

Efficient Selection by Computation-Driven Prediction

Facilitates the synthesis of only handful compounds to reduce time and resources

Also offer Automated Synthesis and In-house Biology Assay Platform to streamline and accelerate drug discovery process.

Please click here if you want to learn more about our automated synthesis and in-house biology platform

Contact Us for More Information

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