

FRAGMENT-BASED LEAD GENERATION

Capabilities Overview

Screening

- Ligand observe NMR methods: STD, wLOGSY, CPMG

Library Preparation

- Identity, solubility, purity
- Automated smart pooling

Follow-up Analysis

- Validation (follow-up singletons)
- Rank-order; cluster

Target Generation

- Protein generation and purification

Target Preparation

- Screen design; sample optimization; experimental conditions optimization

Complimentary Capabilities

- Orthogonal methods (SPR)
- X-Ray Crystallography
- Computational Chemistry
- Chemical elaboration to support optimization
- Biological assay design and support

Library Screening Options

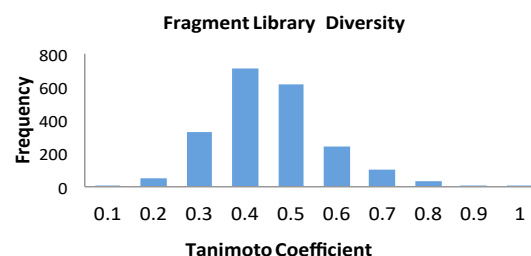
Fragment Library

Commercial and Proprietary

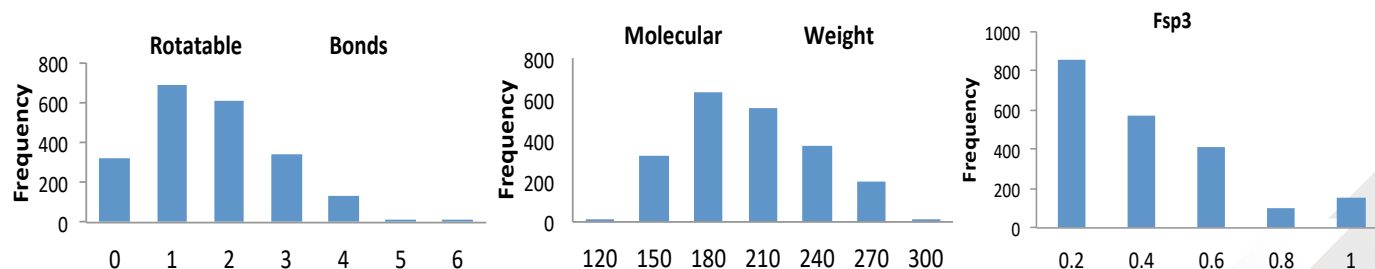
- Fragment sets from internal small molecule collections
- Fragment sets designed from FDA approved drugs
- ¹⁹F- containing fragments
- Covalent fragments
- Commercial fragments

External libraries

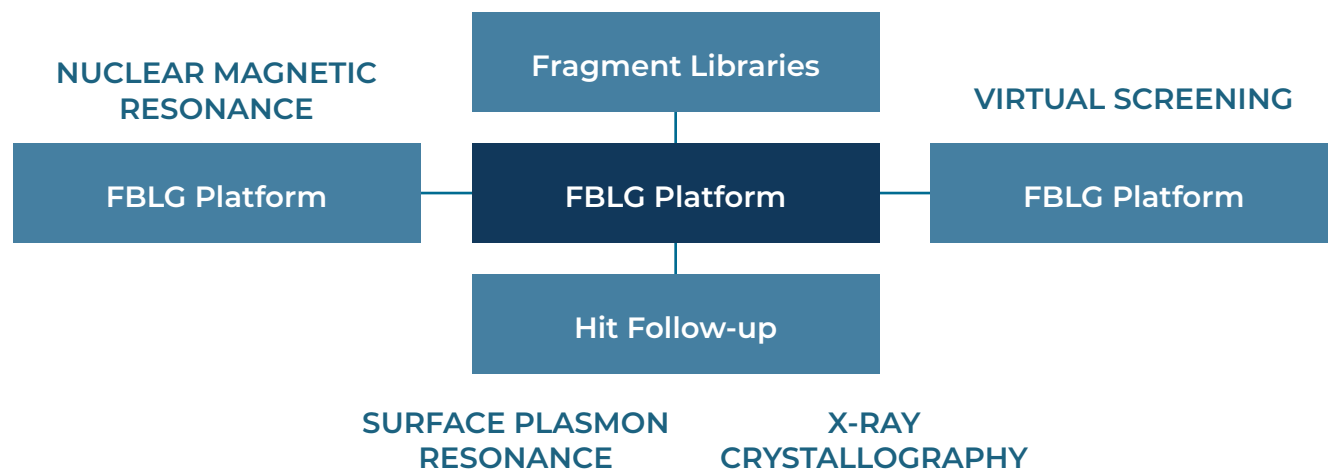
- Client-provided
- Client-selected commercial libraries
- Custom commercial libraries



Select Fragment Library Properties

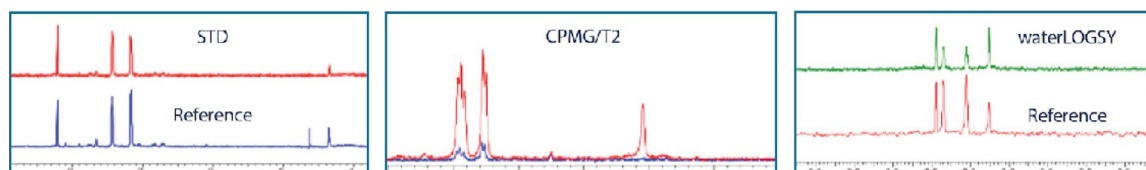


Cutting Edge Screening Platform



Versatile Biophysical Screening Methods

Primary Screening via Ligand Observe NMR: STD, wLOGSY and CPMG



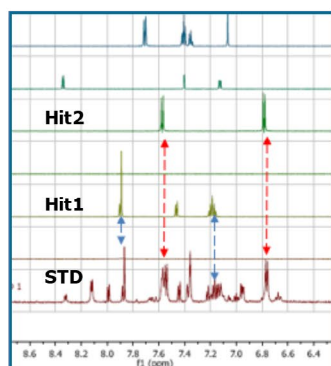
Additional Screening Methods

- ^{19}F NMR
- TSA
- SPR

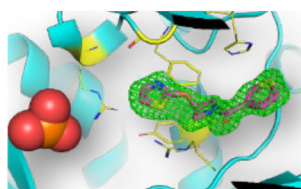
CASE STUDY: Fragment-Based Drug Design Of Novel Nampt Scaffolds

NAMPT (nicotinamide phosphoribosyltransferase): An oncology target in the cellular metabolism pathway.

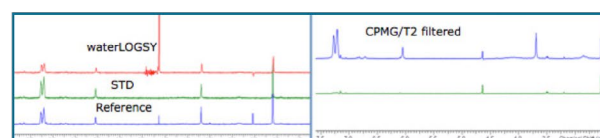
Primary Screening: STD NMR of 1000 fragments in 100 pools. Hits were selected based on structural diversity, virtual screening and the strength of the STD signals from the primary screen



Validation: X-ray co-crystal structures confirm multiple screening hits as true binders to NAMPT



Confirmation: The top hits from the primary screen were screened as singletons and confirmed via STD NMR, waterLOGSY and CPMG experiments



Orthogonal Methods: SPR and biochemical assays to confirm binding and functional enzyme inhibition

**Validated Novel Scaffold
for NAMPT**