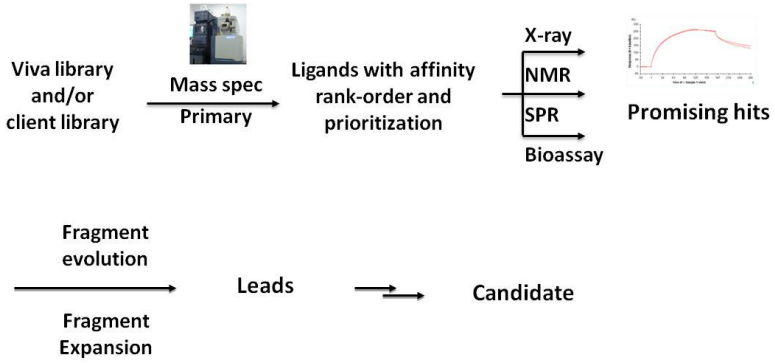
Case Study: Mass Spec Affinity Screening –

A high throughput ligand binding technology applicable to any soluble protein targets

A. Work Flow:

A spectrum of instrumental technologies in biophysics and biochemistry to confirm and validate hits from screening



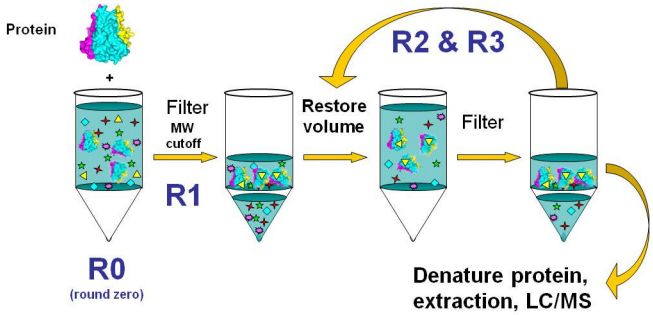
B. Affinity Based Ligand Binding:

Equilibrium binding at physiological relevant conditions

Driven by protein concentration

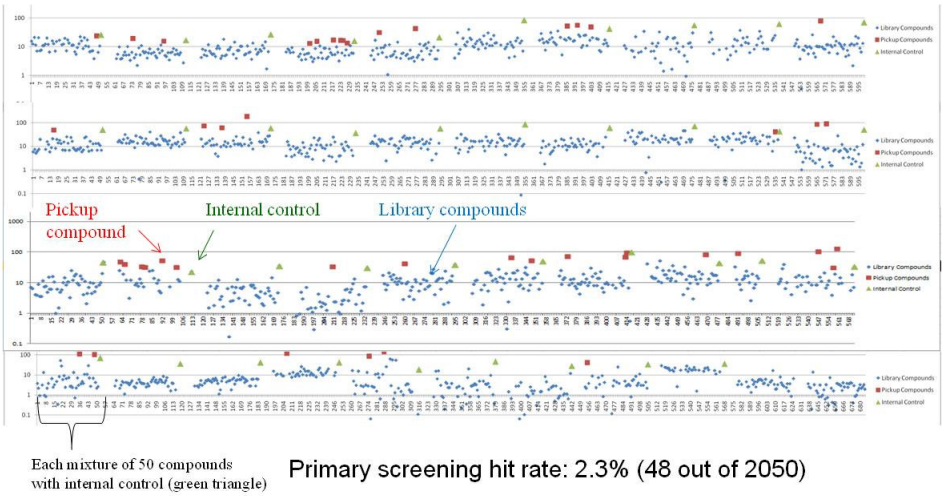
Non covalent binders

High throughput and quick turn around time in weeks



C. Screening of Viva Fragment Library:

Example: Screening of Viva Fragment Library identified many hits for a novel drug target of clients

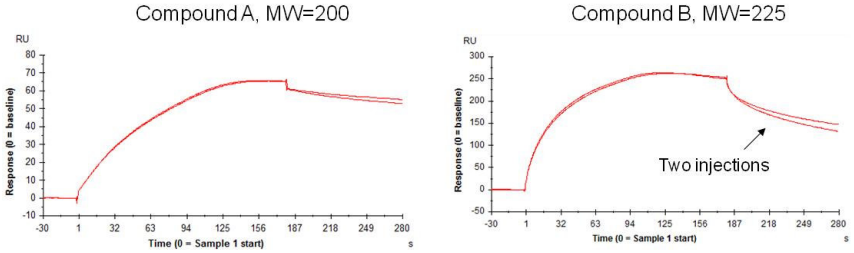


Primary screening hit rate: 2.3% (48 out of 2050)

D. Orthogonal Confirmation of Binding Activities by SPR, Thermostability assay X-ray, NMR, etc.:

Example: Fragment hits from Mass Spec affinity screening were confirmed by SPR

BIAcore confirmation of hits from Mass Spec based affinity screening

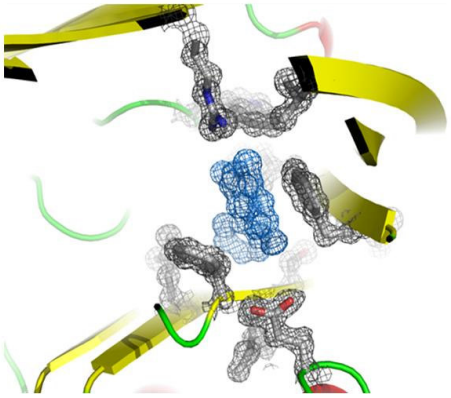


Duplicate samples were tested on BIAcore T200 at 100uM concentration

E. Turning Identified Fragments into Co-crystals with the Target:

Example:

Mass spec affinity screening hit rate: 1.5% (31 out of 2050)
BIAcore binding confirmation rate: 70% (21 out of 31)
Bioassay confirmation rate: 60% (18 out of 31)
High resolution X-ray co-crystallization structure obtained for 4 hits



F. Computational chemistry and structure based drug design to optimize binders from hits to leads, leads optimization to candidate compounds