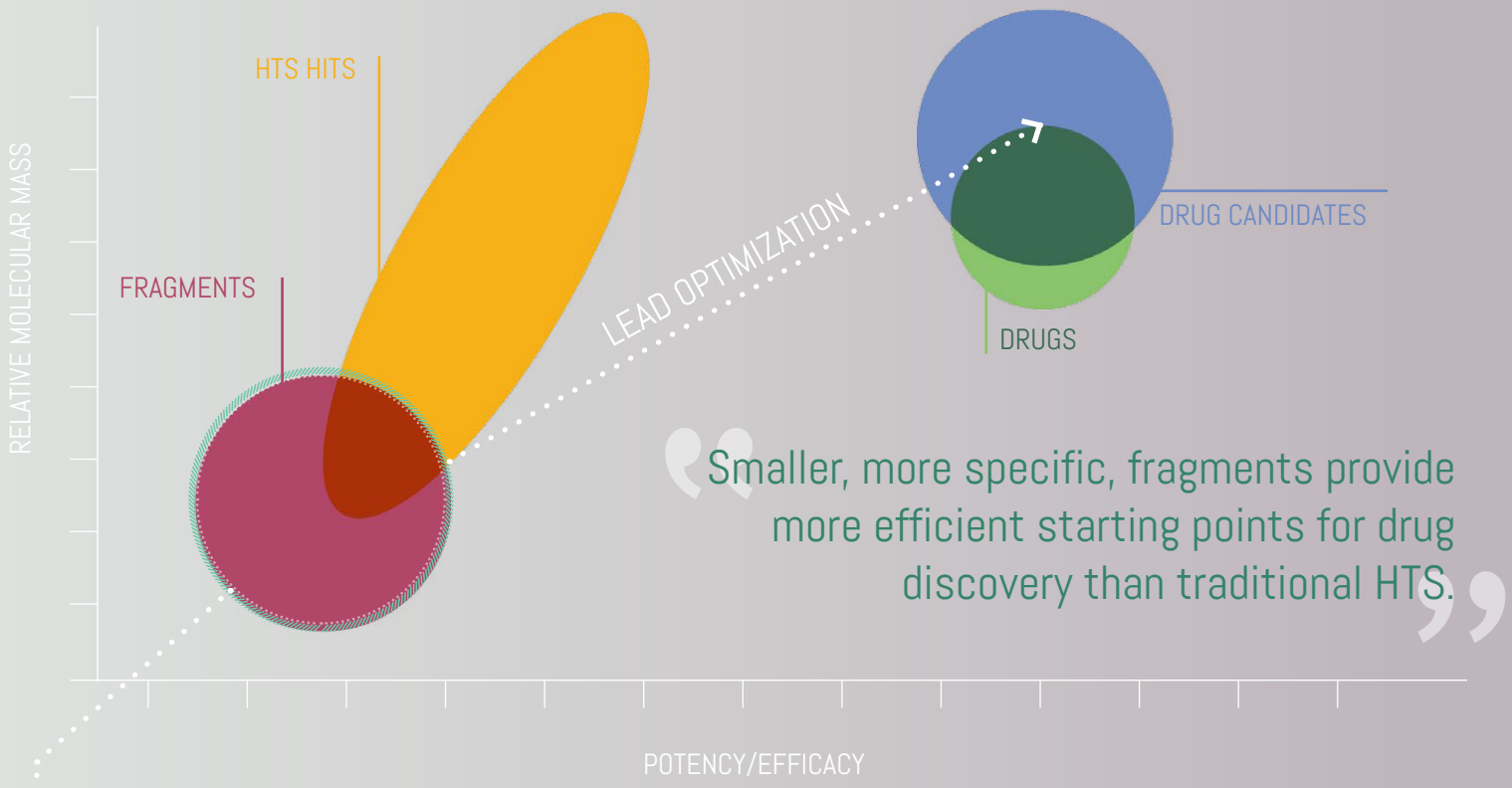
BERYLLIUM DISCOVERY

Your Preferred Discovery Partner

Premium Gene-To-Function Services

GENE TO PROTEIN → **STRUCTURE GUIDED LEAD DISCOVERY** → **FUNCTIONAL BIOLOGY**



"Smaller, more specific, fragments provide more efficient starting points for drug discovery than traditional HTS."

+ Fragment Screening

Efficiently sample target structure space

- Collection of over 5,000 fragments
- Smart pooled commercial and in-house libraries
- High resolution NMR and X-ray crystallography platforms

Obtain small molecule start points for your drug discovery program

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Working with Beryllium

- Target feasibility studies
- STD-NMR screening of fragment cocktails with instant deconvolution
- Hit validation by competition NMR screening
- X-ray crystallography of target plus fragment hits

1-6 MOS

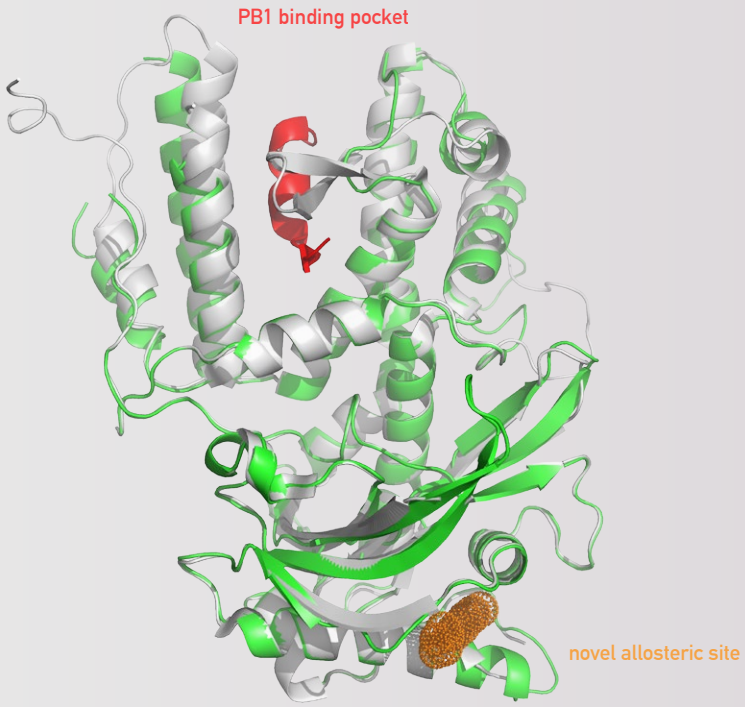
DELIVERABLE
List of hit fragments plus NMR data and publication-quality crystal structure

+ Orthogonal screening approaches: NMR, X-ray, SPR, DSF

SCIENTIFIC CASE STUDY

Collaboration with Seattle Structural Genomics Center for Infectious Diseases (SSGCID)

SSGCID wanted to use fragment based screening to identify starting points for novel anti flu drugs.



EXPERIENCE/INSIGHT:

Beryllium performed fragment screening against the polymerase acidic (PA) subunit of the heterotrimeric PA-PB1-PB2 by STD-NMR to identify fragments which bind to H1N1 PA-CTD and target a protein-protein interface:

- Screened the Fragments of Life library consisting of 1080 compounds
- 139 putative hits
- Top 50 hits were examined in singleton experiments yielding 39 confirmed hits
- 9 crystal structures of original and elaborated fragment hits

SOLUTION:

A number of fragments were identified by STD-NMR which were shown via x-ray crystallography to bind to a novel, distal yet highly conserved hydrophobic pocket on PA-CTD.

One chemical series bound a novel, conserved (in flu A) hydrophobic surface binding site near the vRNA loading site. Although we expected many of the hits to bind to the PB1 binding site which is a hot spot for in silico binding and conformational change, we obtained a series of chlorophenyl compounds which bound to a surface site distal to the PB1 binding site. Interestingly, this site is located in close proximity to the viral RNA (vRNA) loading site and a species specific differential loop.

These results have been published in Scientific Reports 4, Article number: 5944 (2014)