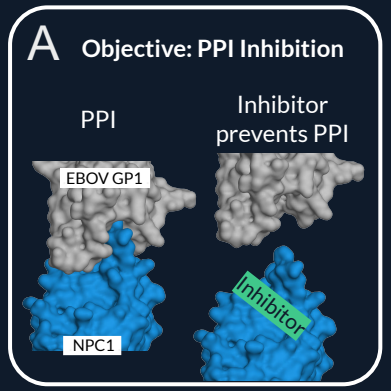
Sextant: A new tool for designing custom molecular templates for Protein-Protein Interaction Inhibitor Drug Design

PolarisQB



Introduction

Inhibiting Protein-Protein Interactions (PPIs) with small molecules is considered by many to be the most difficult area of drug discovery.
Here we developed a method for designing custom templates into empty binding pockets and designed a library of small molecules to inhibit interaction human NPC1 and Zaire Ebolavirus (EBOV) GP1 protein (Panel A).

Method

- The NPC1 pocket of interest without template molecule B) is the input for the Sextant process for building small molecule templates (C).
- QuADD returned a library of candidates, including 470 with dGs more favorable than the Sextant template (D, examples).

Conclusions

- The Sextant method designs templates into binding pockets.
- QuADD returns a strong candidate library
- This method can be applied to other protein pockets.
- This work is a part of a DARPA IMPAQT contract. More details here.
- To learn about our PPI wet lab results, contact us.