FBDD Case Studies

- We have pioneered the use of off-rate screening (ORS) to kinetically sample hit-to-lead chemical space, combining our expertise in cheminformatics, compound library synthesis and use of surface plasmon resonance (SPR), to enable screening of unpurified reaction products. This has been applied to the rapid generation of lead compounds from fragment hits without purification of compound libraries or the use of protein structure (Murray, J. B. et al., J. Med. Chem. 2014).
- By combining structural, thermodynamic and kinetic information from the wide range of ligand hits, we are able to design novel potent drug-like molecules. Our successes include generation of lead compounds that inhibit protein-protein interactions, ATPases and kinases, leading to clinical candidates for Mcl-1, Bcl-2, Hsp90 and Chk1. Published examples of our novel technologies and approach include use of our ORS technology in the identification of novel inhibitors of PDHK, and using our expertise in protein engineering, expression and crystallography to generate Chk1-derived surrogates of LRRK2.