BEACTICA™
Interactions understood. Leads improved.

Kinetic & mechanistic characterization

Control the kinetics to increase chances of clinical efficacy

Benefits

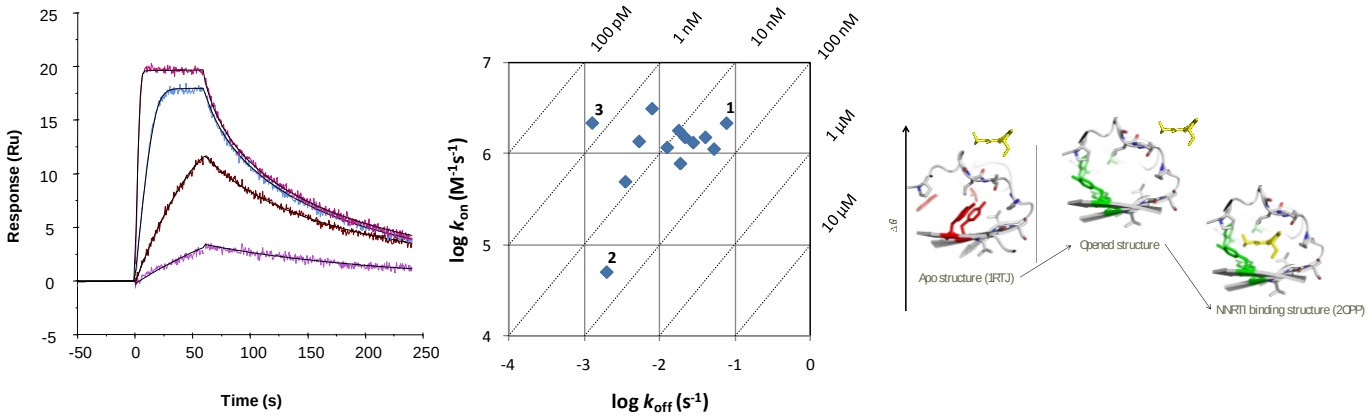
The efficacy of inhibiting a target is dependent on the rate of target inactivation and the residence time of the ligand. Therefore, two different ligands with identical affinity can differ significantly in clinical efficacy due to differences in kinetics. Gaining control over the association and dissociation rate of your ligand can provide a competitive advantage. In addition, the discovery of ligands with unexpected kinetics can provide an inventive step, making your compounds patentable.

Deliverables

- Mechanism and complexity of the interaction
- Kinetic constants (k_{on}, k_{off} and other parameters for more complex mechanisms)
- Superior determination of K_D values
- Comparative data for competitor compounds

Technical details

The analysis of protein-ligand interactions are performed by SPR biosensor-based experiments. This entails the immobilization of the target protein onto a sensor chip followed by injection of a concentration series of reference and test compounds. Analysis of the response with respect to injection time allows for the assignment of the interaction mechanism and the determination of the corresponding rate constants as well as dissociation constants.



Examples of kinetic traces of a kinase inhibitor binding via a simple direct fit mechanism (left). Kinetic data can be shown in k_{on}/k_{off} plots (middle). Compounds **1** and **2** are equipotent in terms of affinity but show differences in kinetics. By increasing on-rate for **2** or by decreasing off-rate for **1**, the potency of **3** could be reached. Scheme to the right shows a more complex mechanistic mechanism (selected fit) illustrated by structures of HIV-1 RT.

Beactica *– Interactions understood. Leads improved.*

Beactica represents scientific excellence in Surface Plasmon Resonance (SPR) biosensor-based interaction analysis for small molecule drug discovery programmes. We offer expertise and services in the area of lead discovery and optimization using our proprietary drug discovery platform.

Contact

Per Källblad *Ph.D.*
CEO

T: +46 18 56 08 80
E: per.kallblad@beactica.com

Beactica AB
Virdings allé 2
SE-754 50 Uppsala
Sweden

www.beactica.com