The handle http://hdl.handle.net/1887/19781 holds various files of this Leiden University dissertation.

**Author:** Farenc, Carine  
**Title:** Discovery of small molecules inhibitors of EphA4  
**Date:** 2012-09-13
Stellingen

Behorende bij het proefschrift:

Discovery of small molecules inhibitors of EphA4

1) The JMS in EphA4 is not responsible for the change in the relative position of the αC-helix, contrary to earlier suggestions.

   \textit{This thesis Chapter 4}
   
   \textit{Wiesner et al. 2006, 25, 4686-4696}

2) As only 20\% of the eukaryotic protein kinases have a threonine residue as a gatekeeper, specifically addressing interactions with this residue will be beneficial in terms of selectivity.

   \textit{This thesis Chapter 5}
   
   \textit{Zucotto et al. 2009, 53, 2681-2694}

3) Competition binding experiments allow one to differentiate artifactual ligand binding from real binding and can provide insight into the binding site of the target.

   \textit{This thesis Chapter 6}

4) As a biological assay is an important tool in a drug discovery project, it is important to carefully develop and select a relevant methodology.

   \textit{This thesis Chapter 7}

5) The most striking consequence of the development of fragment-based lead discovery has been the intense application of orthogonal biophysical methods to characterize binding modes and interactions as compounds are optimized.


6) Selectivity is a critical issue for small-molecule kinase inhibitors, thus the relationship between selectivity, kinome interaction patterns and biological activity needs to be explored and more clearly defined.


7) Nowadays, kinase inhibitor discovery takes place through rational drug design rather than through high throughput screening and empirical optimization on the basis of structure–activity relationships.

8) The emergence mutations in the ATP-binding domains of tyrosine kinases and the activation of downstream and parallel signaling pathways in drug-resistant tumors emphasize the need to develop novel targeted therapies.


9) The drug discovery process is less of a series of hard and fast rules than a loose system of guidelines and hunches. This lack of predictability is part of what makes the process so frustrating and fascinating.

    *Daniel Erlanson- Practical fragment blogspot*

10) A drug is a substance, which, when injected into a rabbit, produces a paper.

    *Otto Loewi- German pharmacologist (1873-1961)*