# NMR structural studies of protein-small molecule interactions

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**Stellingen**

Behorende bij het proefschrift:

**NMR structural studies of protein small molecule interactions**

1. The presence of high concentrations of fragments in the gel retardation assay disrupts the DNA binding capability of $TEL_{ETS}$ domain.
   *This thesis, Chapter 2*

2. The inhibitor stabilizes the Rit1-GDP complex by a novel mechanism, which is steric inhibition of GDP release.
   *This thesis, Chapter 3*

3. The first documented case of a small molecule exchanging between multiple binding poses is observed in the Rit1-inhibitor complex in which the inhibitor does not bind in one preferred orientation or even within a single binding site.
   *This thesis, Chapter* 3

4. The NMR costructure of Hsp90-small molecule complex shows the most physiologically relevant orientation of the small molecule compared with multiple orientations observed in the crystal structures.
   *This thesis, Chapter 4*

   *Brough, P.A., et al, J Med Chem,* ***2009****, 52(15),4794-4809.*

5. Structural biology methods show how and where a fragment binds in the protein target binding site and more importantly tells you what to do next.

6. NMR-based techniques can provide structural information when other biophysical approaches to obtain binding site information are unsuccessful.

7. NMR methods are preferable over X-ray crystallography for detecting very weak protein-ligand interactions.

8. For selection and optimization of fragments the use of specialized methods and instruments is as important as the application of concepts, such as the idea of ligand efficiency.

*Monya Baker, Nature Reviews in Drug Discovery, **2013**,12, 5-7*

9. The progress of science will benefit from the publication in journals or shared on-line resources of confirmed negative results.

10. One of the critical elements to solve a complex problem is starting with a positive outlook.

11. Half of the problem is solved when the problem itself is identified.

12. Mistakes are often silly when looked upon retrospectively.