

Cover Page



Universiteit Leiden



The handle <http://hdl.handle.net/1887/65384> holds various files of this Leiden University dissertation.

**Author:** Doornbos, M.L.J.

**Title:** Towards improved drug action : target binding kinetics and functional efficacy at the mGlu2 receptor

**Issue Date:** 2018-09-12

# STELLINGEN

behorende bij het proefschrift

## Towards improved drug action

### Target binding kinetics and functional efficacy at the mGlu<sub>2</sub> receptor

1. Kinetic parameters should be assessed in the early phases of drug discovery to avoid overlooking promising drug candidates.  
*This thesis, chapters 3 and 4*
2. Improved understanding of the structural, conformational and thermodynamic determinants of residence time is needed so that medicinal chemists can prospectively design this feature into a molecular series.  
*This thesis, chapter 4; Copeland RA. Nat Rev Drug Discov. 2016; 15: 87–95.*
3. Covalent allosteric modulators are very useful tool compounds, and promising future medicines too.  
*This thesis, chapter 5*
4. Label-free assays provide a powerful addition to existing traditional endpoint-assays.  
*This thesis, chapter 6*
5. Understanding the modes of action for individual allosteric modulators is important since they vary between allosteric modulators and could influence *in vivo* pharmacological properties.  
*O'Brien et al. Mol. Pharm. 2018; 93: 526-540.*
6. More advanced mathematical models are needed that incorporate residence time — along with pharmacokinetic parameters — to predict the required dose and dosing interval for humans that will provide the greatest opportunity for drug efficacy across a range of therapeutic areas.  
*Copeland RA. Nat Rev Drug Discov. 2016; 15: 87–95.*
7. Label-free assays should be incorporated in clinical diagnostics, since they enable evaluation of drug potency using patient-derived cells, thereby contributing to precision medicine.  
*Hillger et al. Drug Discov. Today. 2017; 22: 1808-1815.*
8. The general focus on publishing only positive results is wrong - it is useful and important to also publish well documented failures.  
*Pfeffer, C. & Olsen, B. R. J. Negat. Results Biomed. 2002; 1: 2.*
9. Science is not just 'a matter of opinion'.
10. Research performed in collaborations provides stronger outcomes.
11. Simplicity is the hallmark of truth.  
*Herman Boerhaave*
12. The pessimist complains about the wind; the optimist expects it to change; the realist adjusts the sails.