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## **The activation mechanisms of G protein-coupled receptors : the case of the adenosine A2B and HCA2/3 receptors**

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# Stellingen

Bij het proefschrift

## The activation mechanisms of G protein-coupled receptors

The case of the adenosine A<sub>2B</sub> and HCA<sub>2/3</sub> receptors

1. 'A single-GPCR-one-G protein yeast system' is an easy, fast, and robust method to test the importance of each receptor residue in agonist and antagonist binding and in expression level in combination with mutagenesis studies, molecular modeling and bio-informatics.

*This thesis*

2. Key residues have their own reasons for existing.

*This thesis, chapter 3 and 4*

3. Even mutation of a single residue may lead to receptor silencing, demonstrating its critical role in G protein coupling and receptor activation.

*Zhu, S., et al. Cell. Signalling. 2015, 27, 2371-2379.*

*This thesis*

4. GPCRs resemble a complex social system, and subfamily members look like brothers and sisters. Although they share high sequence identity, they also have their own personalities.

*Fredriksson, R., et al. Mol. Pharmacol. 2005, 67, 1414-1425.*

*This thesis, chapter 5*

5. Key regions for GPCR/G-protein coupling are located at the interface between transmembrane helices and intracellular loops, as evidenced from the structural features of the G protein/GPCR interaction.

*Moreira, I.S. BBA-Gen. Subjects. 2014, 1840, 16-33.*

6. Discovering and understanding the G protein activation/G protein selectivity profile of GPCRs can substantially contribute to further drug discovery and development.

*Deupi, X., and Kobilka, B. Adv. Protein Chem. 2007, 74, 137-166.*

*Eglen, R. M., and Reisine, T. Pharmaceuticals. 2011, 4, 244-272.*

7. Residence time of ligands on their target receptors should be considered during lead optimization to potentially make the drug discovery process more efficient.  
*Tummino, P. J., and Copeland, R. A. Biochemistry. 2008, 47, 5481-5492.*
8. Antagonists think they are the protagonists, which sometimes can be true.  
*Pinna, A. CNS drugs. 2014, 28, 455-474.*
9. Your ability is beyond what you know.
10. Difficulties in your mind are much more scary than they are in real life.
11. Life itself is a very challenging experiment and being a mom is the hardest, most enjoyable and happiest experiment.
12. "Nothing in life is to be feared, it is only to be understood. Now is the time to understand more, so that we may fear less."  
*Marie Curie*