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The ins and outs of ligand binding to CCR2

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Stellingen

behorend bij het proefschrift

The INS and OUTS of ligand binding to CCR2

1. G protein-coupled receptors contain ligand binding sites throughout their entire
This thesis
2. The concept of biased signaling forces us to put agonism and antagonism into new perspective, and to consider the environment within their definition.
This thesis
3. Structure-kinetics relationships should be incorporated in early stages of hit-to-lead optimization in order to identify ligands with appropriate residence times.
This thesis
4. Chemists, pharmacologists and computational biologists should join forces and study the influence of drug binding kinetics on drug action at a molecular as well as a systems level in order to unravel the determinants for clinical success per target and disease.
This thesis
5. The expression of a certain chemokine receptor does not always imply a pro-inflammatory contribution to the disease state, which should be considered before proposing therapeutic receptor blockade.
This thesis, Cardona, A.E., et al., Blood 2008, 112 (2), 256-263
6. A target-centric approach for first-in-class drugs, without consideration of an optimal molecular mechanism of action, may contribute to the current high attrition rates and low productivity in pharmaceutical research and development.
Swinney, D.C and Anthony, J. Nature Reviews Drug Discovery 2011, 10, 507-519
7. Illuminating the dynamic nature of GPCRs offers a key to understanding the molecular mechanisms of biased and nonbiased signaling.
Vardy, E., Roth, B. Cell 2013, 152, 385-386
8. Polypharmacology across several disease-relevant targets can improve therapeutic efficacy, prevent drug resistance, or reduce therapeutic-target-related adverse effects.
Peters, J.U. Journal of Medicinal Chemistry 2013, 56 (22), 8955-8971
9. Een promotor is net als een Volkswagenbusje; hij sputtert regelmatig (tegen), maar brengt je altijd vooruit.
10. Een golf pakken is een piece of cake, maar een golf surfen is andere koek.