Development of new chemical tools to study the cannabinoid receptor type 2

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Propositions

Part of the Thesis

Development of New Chemical Tools to Study the Cannabinoid Receptor Type 2

1. The complexity of the endocannabinoid system is becoming better understood and new details of endocannabinoid system signalling are emerging which raise the possibility of new treatment modalities.
   This thesis, Chapters 1 and 5, Maccarrone, M. Expert review of clinical pharmacology, ***2017****, 10 (4), 443-455*

2. The endocannabinoid system is a complex system of interconnected parts, and clinical efficacy will benefit from synergy between multiple therapeutic agents.
   Russo, E., Guy, G.W. Medical Hypotheses, 66 (2), ***2006****, 234-246*

3. X-ray crystallography or cryo-EM are not necessary to design selective ligands. High homology between CB_1R and CB_2R has made it difficult to discover how ligands can be selective, yet, many CB_2R selective ligands already exist.
   This thesis, Chapter 2. Li, X., Chang, H. et al. Nature Communications, 2023, 14 (1)

4. Selective small molecules are the future in cannabinoid research as cannabinoid antibodies are highly unreliable, just look at the controversy of whether CB_2R is expressed in neuron or not.
   Manzanares J., Cabañero D. Biochem Pharmacol. ***2018****, 157, 108-121*

5. The unnaturally high concentrations of receptor in *in vitro* overexpression systems can cause artifacts such as spontaneous activity.
   Khilnani G, Khilnani A. Indian J Pharmacol. 2011, 43 (5), 492-501

6. A reference compound should always be included as control when testing new molecules *in vitro*.
   This thesis, Chapter 6

7. *In silico* data should always be substantiated with *in vitro/in vivo* studies.
   This thesis, Chapter 2. Jean-Quartier, C., Jeanquartier, F., Jurisica, I. et al. BMC Cancer, ***2018****, 18, 408*

8. Fully profiled chemical probes are necessary for proper target validation.
   Bunnage M.E., Chekler E.L.P. Nat Chem Biol. 2013, 9 (4), 195-199

9. Structure-activity relationship data remain valuable not only for optimizing potency and selectivity of a ligand, but also for discovering novel and non-classical structures with improved pharmacological parameters.
   This thesis, Chapter 3, Bow E.W., Rimoldi J.M. Perspectives in Medical Chemistry, ***2016****, 8.*

10. Propositions are an archaic element of promotions that require more time than they are worth in their occasional mentioning during a defence.

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