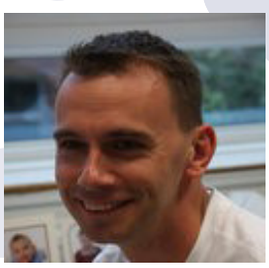
07. September 2022
Time: 16:30 h

Institute of Biochemistry and Molecular Medicine (IBMM)
Seminar Room ground floor,
Gertrud-Woker Str. 5,
3012 Bern

Everybody is welcome

Follow the NCCR TransCure lectures:
http://www.nccr-transcure.ch/events
Twitter: @NCCR_TransCure



Dr. Graham Ladds is Professorship in Receptor Pharmacology, Univ. of Cambridge, and fellow of St John's College (UK).

This lecture is hosted by Prof. Martin Lochner (IBMM).

NCCR TransCure Lecture in Biology
by Graham Ladds

Agonist bias at Class A/B GPCRs: Therapeutic potential at last?

G protein-coupled receptors (GPCRs) are the largest family of cell surface receptors (>800 members) and remain one of the major targets for therapeutic intervention (~30% of marketed drugs target these receptors). GPCRs have been grouped into different classes based upon their homology with Class A being the largest family and Class B1 contain receptors that respond to peptides which modulate many key physiological functions. GPCR signalling is initiated through agonist binding, typically at the orthosteric site, promoting activation of a heterotrimeric G protein complex. Mammalian cells express upward of 15 different Gα subunits (grouped into 4 main families) with some GPCRs being promiscuous (pleiotropic) activating a wide array of different Gα subunits depending on the agonist (referred to as biased agonism). The therapeutic promise of biased agonists is obvious - it allows the design of ligands that actively engage with one beneficial signalling outcome whilst reducing the contribution from those that mediate more undesirable effects. However, it is not without controversy. In the first half of this presentation, I will describe our studies look at agonist bias for the Class A GPCR – the adenosine A1 receptor by document our investigations into a novel agonist BnOCPA which we think has significant therapeutic potential. In the second half, I will describe our studies of agonist bias at Class B1 GPCRs, specifically the calcitonin-like receptor (CLR) and the gastric inhibitory polypeptide receptor (GIPR). I will describe how a family of molecular chaperones (the receptor-activity modifying proteins - RAMPs) influences agonist bias at these two GPCRs.

NCCR TransCure
Excellence in Membrane Transport Research
Swiss National Science Foundation
UNIVERSITÄT BERN