BiophysTO Lunchtime Seminar Series

Date
Tuesday, May 22 2018
10:30 am

Location
CCBR
Red Seminar Room

Anthony Watts

Biomembrane Structure Unit, Department of Biochemistry, University of Oxford

Multiscale spectroscopies for understanding GPCR mediated cell signalling

G protein-coupled receptors (GPCRs) play a pivotal role in cellular signalling, highlighted by the fact that they form the target for ~40% of marketed pharmaceuticals. While evidence has been accumulating for the existence and functional significance of GPCR oligomers, the matter is still under debate, in part due to lack of consensus on morphological aspects, such as the receptor interfaces involved in oligomerisation, and their possible dynamic nature [1]. Neurotensin receptor 1 (NTS1) is one of few GPCRs that can be produced in *E. coli* in an active state, and has been implicated in a variety of conditions including schizophrenia and various cancers. NTS1 has been demonstrated by us to show lipid dependent functionality [2-5] and dimerise in lipid bilayers [6], however, there is still no structural or dynamic information on the receptor dimer. Here, we combine ensemble FRET [6], DEER, single molecule methods and *in silico* approaches [7] to probe NTS1 dimerization. The results support the presence of a concentration-dependent dynamic equilibrium between monomers and dimers, which could provide a means of regulation of receptor signalling and biased coupling in vivo.

[1] Ferré et al. (2014) Pharmacol Rev 66;
[2] Oates et al., (2012) BBA – Biomembranes, 1818:2228-2233.
[3] Adamson & Watts (2014) FEBS Letts, 588(24):4701–4707
[4] Dijkman & Watts A. (2015) BBA – Biomembranes,1848(11);2889-2897
[5] Bolivar et al. (2016), BBA – Biomembranes, 1858(6):1278–1287
[6] Harding et al. (2009) Biophys J 96:964-973
[7]. Dijkman et al., (2018) Nature Comms DOI: 10.1038/s41467-018-03727-6

Host: Dr. Oliver Ernst

Seminar Sponsors

UTM
Chemical and Physical Sciences
VP Research Vice-Dean Graduate

UTSG
Biochemistry IBBME Medical Biophysics
Physics Chemistry