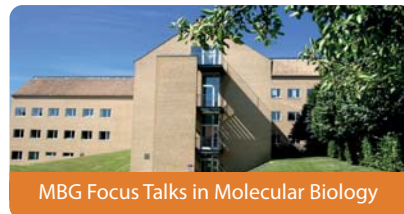


# MBG FOCUS TALK

hosted by Section for Structural Biology



**Tuesday 17th July 2018 from 10:15-11:00**

MBG conference room (3130-303), Gustav Wieds Vej 10C, 8000 Aarhus C

## By Xiangyu Liu

Beijing Advanced Innovation Center for Structural Biology  
School of Medicine, Tsinghua University  
Beijing, China



## Structural insights into G protein activation

The crystal structure of beta2 adrenergic receptor ( $\beta 2AR$ ) – Gs complex provided the first high-resolution snapshot of how agonist bound GPCR activates a heterotrimeric G protein. In this nucleotide-free complex ( $R^*-G^{empty}$ ), the C-terminal  $\alpha$ -5 helix of Gs undergoes a large structural change to penetrate the core of the  $\beta 2AR$ , into a space created by the outward movement of TM6. Recent single molecule experiments provide evidence for the existence of a transient complex between the  $\beta 2AR$  and GDP bound Gs protein ( $R^*-G^{GDP}$ ) that involves a smaller outward movement of TM6 and may represent an intermediate on the way to the formation of  $R^*-G^{empty}$ .  $R^*-G^{GDP}$  is not amenable to characterization by crystallography, as it appears to be a transient intermediate complex that is less stable than  $R^*-G^{empty}$ . However, we have been able to crystallize the  $\beta 2AR$  fused to the carboxyl terminal 14 amino acids from Gs  $\alpha 5$  helix (GsCT). Unexpectedly, we obtained a structure of GsCT interacting with active  $\beta 2AR$  in a different mode compare to  $\beta 2AR$ -Gs complex. The binding mode involves interactions between conserved E392 and R389 of Gs and the D and R of the conserved DRY sequence of the  $\beta 2AR$ . Of interest, in GDP-bound Gs, E392 and R389 are solvent exposed and accessible to the cytoplasmic surface of the  $\beta 2AR$ . Moreover, mutations of E392 and R389 alter interactions with Gs. These observations suggest that the structure presented here may represent an intermediate state in the formation of  $R^*-G^{empty}$ .

**Host: Professor Poul Nissen**