Séminaire

CONFÉRENCIER INVITÉ

Vendredi 26 Janvier 2018 à 11h

Salle des séminaires

Institut de biologie structurale - 71 avenue des Martyrs CS 10090 38044 Grenoble Cedex 9 - T.+33 (0)4 57 42 85 00

www.ibs.fr

par **Guillaume Lebon**

Institut de Génomique Fonctionnelle

Montpellier

Structural and molecular basis of Class C GCPRs signalling

G protein-coupled receptors (GPCRs) are complex allosteric machineries regulated by endogenous ligands and drugs, as well as exogenous natural compounds. Class C GPCRs that include metabotropic glutamate receptors (mGlu), taste receptors, GABAB receptors and Calcium-sensing receptors, are unusual in terms of their molecular architecture and allosteric regulation. They all form obligate dimers and dimerization is fundamental for their function. Development of innovative methodologies has resulted in the solution of a large number of class A receptor structures that shed light on their molecular activation mechanism. However, there is no structure of an intact full-length class C receptor dimer to date. As a first step toward structure determination, we have thermostabilised the mGlu5 receptor bound to a negative allosteric modular (NAM). Thermostabilised mGlu5 receptor is fully functional and displays an increased thermal stability compared to the WT mGlu5 receptor. Using single-particle electron cryomicroscopy (cryoEM) we obtained high-quality images of mGlu5 receptor dimers in ice that allowed us to visualise isolated single particles of the receptor dimer. The class averages revealed the presence of dimeric single particles of the receptor. Understanding the structural basis of mGlu receptor dimer signalling will represent a landmark achievement and pave the way for structural investigation of GPCR dimer signalling in general.

Hôte : Michel Vivaudou (IBS/Channels)