CBMN seminar by Marina CASIRAGHI

13th October at 2PM at IECB

Title: Structural and dynamic insights into G protein–coupled receptor signaling

Abstract:

G protein coupled receptors (GPCRs) form the largest family of membrane proteins. They mediate most responses to hormones and neurotransmitters and underlie the senses of sight, smell and taste. Nearly half of all approved drugs act on GPCRs, which are also implicated in conditions such as drug addiction, including opioid dependence. Despite their structural diversity (~800 members) GPCRs couple to only four G protein subfamilies. The molecular determinants underlying GPCR selectivity remain poorly understood, yet such knowledge is essential for developing drugs that preferentially activate selected signaling pathway, a paradigm known as biased agonism. The β_2-adrenergic receptor (β_2AR), a prototypical class A GPCR, has been used to characterize GPCR selectivity and biased agonism through a combination of complementary structural (cryo-EM), biochemical and biophysical methods (EPR, fluorescence spectroscopy, single-molecule FRET). Our data provide mechanistic insights into G-protein subtype selectivity at the β_2AR and the molecular basis of GPCR activation and signaling in response to biased ligands.

Biography:

Dr. Casiraghi received her master's degree in molecular biology from University of Milano Bicocca, Italy. She conducted her PhD at the Institut de biologie physico-chimique (IBPC) in Paris under the supervision of Dr. Laurent Catoire, focusing on the investigation of G-protein coupled receptors (GPCRs) conformational landscape by solution-state NMR. For her postdoctoral work, she joined the laboratory of Prof. Brian K. Kobilka at Stanford University, USA. At Stanford, she bridged structural determination by cryo-EM and biophysical investigations to address the molecular determinants of GPCR activation and signaling. While at Stanford, Dr. Casiraghi was the recipient of the Marie Sklodowska-Curie postdoctoral fellowship and American Heart Association (AHA) postdoctoral fellowship. Currently, she is a Young Researchers Marie Sklodowska-Curie fellow at University of Milan, Italy, where her research focuses on novel therapeutic strategies to target GPCRs implicated in addiction.