LECTURE SERIES 2025

INFECTION & IMMUNITY

LUXEMBOURG INSTITUTE OF HEALTH

22 April 2025

Tuesday

LECTURE 12:30 - 14:00

MEET * 14:30 - 16:00

Location and Signaling Biases; Exploring the Pluridimensionality of G Protein-Coupled Receptors' signaling

ABSTRACT

G protein-coupled receptors (GPCRs) represent the largest family of proteins involved in signal transduction across biological membranes. As such, they are the target of more than 30% of existing drugs and remain top targets for the development of new ones. It is now clear that are not unidimensional switches that turn 'on' or 'off' a single signaling pathway. Instead, each receptor can engage multiple signaling partners that can engage various downstream effector systems. Individual ligands can have differential efficacies toward specific subsets of the signaling effector repertoire engaged by a given receptor. In addition to this phenomenon, known as ligand-biased signaling, it was also found that in addition to signal from the plasma membrane, GPCRs can engage distinct signaling pathways from various subcellular organelles, leading to the concept of location bias. This pluridimensionality of GPCR Signaling opens new opportunities for the development of drugs targeting therapeutically relevant pathways while sparing those leading to undesirable effects. Yet, this pluri-dimensional nature of signaling efficacy presents a challenge to establish the complete signaling profile of drugs and to understand the structural basis of GPCR functional selectivity. Using a collection of bioluminescence resonance energy transfer (BRET)-based biosensors and imaging, we characterized the pluri-dimensional signaling profiles of many GPCRs and monitored the spatio-temporal signal propagation into distinct intracellular compartments. Computer-assisted analysis of the diverse signaling profiles observed allows the clustering of compounds into different groups permitting the association of specific signaling signatures with distinct functional outcomes. These studies open new avenues for the rational design of biased ligands with desired signaling properties.

SPEAKER

Prof. Dr. Michel Bouvier

Professor of Biochemistry and Molecular Medicine and Principal Investigator at the Institute for Research in Immunology and Cancer
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HOST:

Department of Infection and Immunity (LIH)

RESPONSIBLE SCIENTIST:

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* **Please note that registration is mandatory by sending an email to carole.weis@lih.lu or michelle.roderes@lih.lu**

Locations:

Lecture:
House of BioHealth
Conference Room
(ground floor 0)
29, rue Henri Koch,
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Meet:
House of BioHealth
Salle Françoise Barré Sinoussi
Registration mandatory

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