The 224th
Institute of Life Science Seminar

Date & Time November 19 (Thu), 2026, 16:00 – 17:30

Venue Building 3, 3rd Floor, Room 315A

Title Mechanism and Manipulation of Metabotropic Glutamate Receptor 5 Allostery

Speaker Dr. Kaavya Krishna Kumar (Weill Cornell Medicine)

Abstract

Metabotropic glutamate receptor 5 (mGlu5) is a class C G protein-coupled receptor (GPCR) that plays critical roles in synaptic plasticity, learning, memory, and neuropsychiatric disease. mGlu5 functions as an obligate dimer, with approximately 120 Å separating the extracellular glutamate-binding site from the transmembrane core that engages downstream G proteins. Activation requires large-scale conformational rearrangements that propagate across this extended architecture. To elucidate the molecular basis of mGlu5 activation, we combine conformation-selective nanobodies, cryo-electron microscopy, and single-molecule biophysics to resolve discrete activation states and define the receptor's activation pathway. These findings provide mechanistic insight into how ligand binding reshapes receptor architecture to control signaling and establish a framework for the rational design of conformation-selective modulators targeting neurological disorders.

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