Department of Pharmacology
2023 - 2024 Seminar Series

“Structural consequences of receptor barcoding by GRK2 and GRK5”

Atypical chemokine receptor 3 (ACKR3) is an arrestin-biased 7TM receptor involved in neutrophil migration that is uniquely phosphorylated by GRK2 and GRK5. These phosphorylation "barcodes" are proposed to lead to distinct outcomes downstream of GPCRs, but to date no molecular mechanism is known. We now show that barcoding leads to either ACKR3-adjacent complexes or more heterogeneous "tail only" assemblies with arrestin, respectively. Surprisingly, arrestin2/3 do not interact within the cytoplasmic cleft of ACKR3, and instead bind at profoundly different angles to the micelle surface. Thus, both barcode and arrestin isoform can markedly affect the configuration of a receptor-arresting complex, which in turn can drive unique downstream events.

John J. G. Tesmer, Ph.D., FAAAS, FASPET

Purdue University

February 20th, 2024
4:00 PM
214 Light Hall

Host: Seva Gurevich

VANDERBILT
School of Medicine
Basic Sciences