DEPARTMENT OF CHEMICAL & PHYSICAL SCIENCES
COLLOQUIUM SERIES

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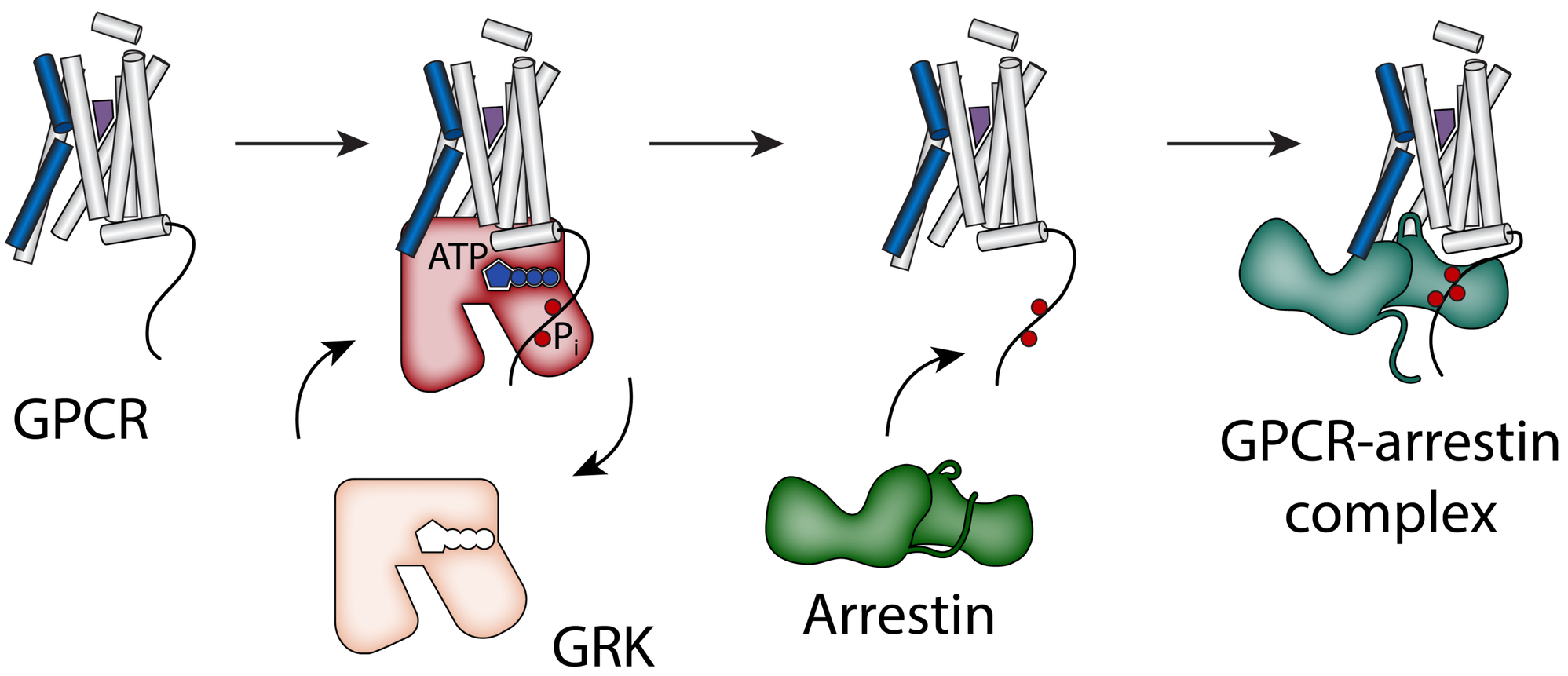
DR. JOHN JANETZKO

DEPARTMENT OF MOLECULAR AND CELLULAR PHYSIOLOGY
STANFORD UNIVERSITY

Understanding the molecular mechanisms of GPCR recognition by β-arrestin



G protein-coupled receptors (GPCRs) are a family of seven transmembrane proteins whose functions are to transduce extracellular signals, often in the form of hormones and neurotransmitters, to intracellular signals that are propagated through one of two signal transduction routes: G protein-mediated signaling or β-arrestin-mediated signaling. In order for the receptor to engage β-arrestin it must first be phosphorylated. Today, while there is a wealth of structural information pertaining to the basis of G protein-receptor interactions, there exists no structure of a non-rhodopsin GPCR in complex with arrestin. Using cryo-electron microscopy we have obtained a structure of the neurotensin type I receptor (NTSR1) in complex with β-arrestin-1. This structure reveals how the receptor is engaged by β-arrestin, how phosphorylation of the receptor might regulate arrestin recruitment and activation and how the plasticity of the interactions formed between the two enable only two isoforms of β-arrestin to recognize a large number of diverse GPCRs.