
Preface

The signaling by most G protein-coupled receptors (GPCRs) is regulated by a conserved two-step mechanism: phosphorylation of active receptor by G protein-coupled receptor kinases (GRKs) followed by specific binding of an arrestin protein to the active phosphoreceptor. Arrestin binding blocks further coupling of the receptor to G proteins, promotes the recruitment of the complex to coated pits for internalization, and initiates a second, G protein-independent round of signaling. Whereas GPCRs, G proteins, and arrestins are getting a lot of attention, GRKs remain underestimated and under-investigated players in the regulation of GPCR signaling. For example, in recent years, biased GPCR signaling, i.e., differential signaling via G protein- and arrestin-dependent pathways, has been extensively investigated in the hope of designing GPCR-targeting drugs with fewer side effects. However, for a ligand to be biased toward arrestins, it must be biased toward GRKs first due to the fact that GRK phosphorylation in most cases is necessary for high-affinity arrestin binding. GRKs have numerous other functions in addition to phosphorylating GPCRs, some of which do and some do not require kinase activity. In this book, we include up-to-date descriptions of known GRK-dependent mechanisms, both associated with GPCR functions and receptor-independent. The chapters cover a wide range of studies from invertebrates to humans. Comprehensive mechanistic elucidation of GRK functions and their regulation in cells is necessary for a better understanding of cell biology, as well as for devising novel research approaches and therapeutic strategies.

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