

Preface

The first arrestin was discovered in the visual system as a key player in the shutoff of prototypical G protein-coupled receptor (GPCR) rhodopsin. Cloning and functional characterization of its homologues revealed that specific binding of arrestin to the active phosphorylated forms of the great majority of GPCRs stops their G protein-mediated signaling. Arrestins are average sized ~45 kDa proteins with the fold shared with (and probably inherited from) proteins involved in vesicle trafficking. Arrestin family is fairly small: vertebrates express four subtypes, whereas other branches of the animal kingdom have even fewer different arrestins. Yet these few arrestins not only bind hundreds of GPCR subtypes expressed in virtually all animals but also interact with dozens of non-receptor-signaling proteins. Some of these interactions occur regardless of receptor binding, some are promoted by it, while others are precluded or suppressed by GPCR interaction. This places arrestins at an important intersection of signaling pathways in the cell where external and internal inputs are integrated into coherent behavior. This volume describes our current understanding of the biological role of visual and nonvisual arrestins in different cells and tissues, focusing on the mechanisms of arrestin-mediated regulation of GPCRs and non-receptor-signaling proteins in health and disease. This book covers a wide range of arrestin functions, emphasizing therapeutic potential of targeting arrestin interactions with individual partners. Arrestins are ultimate scaffolds: they organize multiprotein signaling complexes and localize them to particular cellular compartments. Everything arrestins do is mediated by protein–protein interactions. Since highly regulated protein–protein interactions underlie most vital cell functions, arrestins are a perfect proving ground for designing novel protein-based therapeutic tools to channel cell signaling in the desired direction.

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