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Titolo The Structural Basis of Arrestin Functions [[electronic resource] /] /

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Nota di contenuto Arrestins: discovery of the family and functional role of conformational

flexibility -- Overview of arrestin-mediated signaling with receptors and non-receptor binding partners -- Initial crystallographic studies of visual arrestin: insights and perspectives -- Structural basis for barrestins in GPCR trafficking -- Arrestin-3: the structural basis of lower receptor selectivity -- Phosphate sensor and construction of phosphorylation-independent arrestins -- Comprehensive analysis of the role of arrestin residues in receptor binding -- How arrestin recognizes and binds active GPCRs -- Localization of conformational dynamics of arrestins by HDX-MS -- GPCR footprint on arrestins and manipulation of receptor specificity -- The structure of the polar core mutant R175E and its functional implications -- Active conformations of arrestins: expected and unexpected changes -- The arrestinreceptor complex: exciting answers and new questions -- Scaffolding c-Jun N-terminal kinase cascades: mechanistic insights from the reconstituted arrestin-JNK cascades -- Arrestin-dependent ERK activation and its disruption -- The functional role of the

conformational changes in arrestin upon activation -- Is signaling

specificity encoded in arrestin conformation? -- Monofunctional elements of multi-functional arrestin proteins -- Arrestins in cell death.

Sommario/riassunto

This volume summarizes our current understanding of the structural basis of the functions of arrestin family of proteins. Arrestins were first discovered as key players in the desensitization of G protein-coupled receptors (GPCRs). Recent studies showed that arrestins are important signal transducers in their own right, organizing multi-protein complexes and scaffolding numerous signaling cascades that regulate cell proliferation, differentiation, and apoptotic death. Here arrestin functions are described primarily from the structural prospective. The book covers basal structure of arrestin proteins, receptor bindinginduced conformational changes in arrestins, as well as the structure of "pre-activated" mutants. Particular focus is on the arrestin elements interacting with numerous binding partners, GPCRs and cytoplasmic signaling proteins. We expect that this information and insights will help to understand and exploit the phenomenon of signaling bias, which is a new promising direction in drug discovery. The chapters are written by the world-class specialists in the field, mostly the people who actually contributed the data discussed. The book gives coherent historical prospective and describes the most recent findings. The book would be particularly useful for scientists in academia and industry working in the fields of pharmacology, cell biology, structural biology, and drug discovery. We expect that the focus on the molecular basis of protein-protein interactions would help to develop novel tools for engaging this important type of targets for research and therapeutic purposes.