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Sommario/riassunto	G protein-coupled receptor kinases (GRKs) and arrestins were initially identified as a pivotal player in the process of desensitization of agonist-activated G protein-coupled receptors (GPCRs). However, growing evidence suggests GRKs and arrestins fulfill a vital role in regulating a variety of cellular proteins involved in signal transduction independently of GPCRs. Thus, GRKs and arrestins can interact with non-GPCRs. GRKs and arrestins may directly affect functioning of non-GPCRs or indirectly regulate non-GPCR signaling. In addition, emerging evidence supports that changes in function and/or expression of GRKs and arrestins may be important in cardiovascular, inflammatory, metabolic, or cancer pathologies. A better understanding of the pathological roles of GRKs and arrestins would provide a basis for new therapeutic targets in different human diseases.