Protein kinase A

Protein kinase A (PKA), also known as cAMP-dependent protein kinase, is an enzyme that plays a vital role in regulating various cellular processes in eukaryotic organisms, including humans. PKA is a member of the protein kinase family, which consists of enzymes responsible for adding phosphate groups to other proteins, a process known as phosphorylation. Phosphorylation is a critical mechanism in cell signaling, controlling various aspects of cellular activity.

Here are some key features and functions of protein kinase A:

Structure: PKA is a holoenzyme consisting of two catalytic subunits (C subunits) and two regulatory subunits (R subunits). The enzyme's activity is regulated by the binding of cyclic adenosine monophosphate (cAMP) to the regulatory subunits.

Activation: PKA is activated when the intracellular concentration of cAMP increases. This typically occurs in response to the activation of G protein-coupled receptors (GPCRs) by extracellular signals such as hormones or neurotransmitters. When cAMP binds to the R subunits, it causes a conformational change that releases the catalytic subunits, allowing them to phosphorylate target proteins.

Phosphorylation: Once activated, PKA catalytic subunits phosphorylate serine or threonine residues on target proteins. These target proteins can include enzymes, transcription factors, ion channels, and other signaling molecules. Phosphorylation by PKA can either activate or inhibit the function of these target proteins, depending on the specific context.

Cellular Functions: PKA is involved in the regulation of a wide range of cellular processes, including:

Metabolism: PKA regulates glycogen metabolism, lipid metabolism, and glucose homeostasis by phosphorylating enzymes involved in these pathways. Gene Expression: PKA can phosphorylate transcription factors and co-regulators, influencing gene expression in response to extracellular signals. Ion Channels: PKA phosphorylation of ion channels can modulate their activity, affecting processes like neurotransmission and muscle contraction. Cell Growth and Differentiation: PKA is implicated in cell proliferation, differentiation, and apoptosis. Disease Associations: Dysregulation of PKA signaling has been linked to various diseases, including cancer, diabetes, and neurodegenerative disorders. Mutations in genes encoding PKA subunits can result in rare genetic conditions known as “protein kinase A-related disorders.”

Research Tool: PKA is a valuable tool in cell and molecular biology research. Researchers use PKA and cAMP analogs to manipulate cellular signaling pathways and study the effects of PKA activation on specific cellular processes.

Protein kinase A is just one of many protein kinases that play crucial roles in cellular signaling. Its importance lies in its ability to integrate extracellular signals and convey them to intracellular targets through phosphorylation events, thus allowing cells to respond appropriately to their environment.

Mitigation of cardiac autonomic dysregulation by neuromodulation technologies is emerging as a new therapeutic modality of heart failure (HF). This progress has necessitated the identification of a biomarker for the quantification of sympathovagal balance, the potential target of 'neuromodulation' strategies. The currently available autonomic nervous system assessment parameters do not truly reflect the sympathovagal balance of the ventricle. Protein kinase A (PKA) is an intracellular enzyme that plays a major role in the pathophysiology of functional and structural ventricular remodeling in HF. Interestingly, sympathetic and parasympathetic activations exert reciprocal influence on the activity of PKA [1)].

1)

Chakraborty P, Po SS, Yabluchanskiy A, Dasari TW. Protein kinase A: A potential marker of sympathovagal imbalance in heart failure. Life Sci. 2023 Sep 2:122069. doi: 10.1016/j.lfs.2023.122069. Epub ahead of print. PMID: 37666387.