PI3K/Akt pathway

The PI3K/Akt pathway, also known as the phosphoinositide 3-kinase/protein kinase B pathway, is a crucial intracellular signaling pathway that plays a central role in regulating various cellular processes, including cell growth, cell survival, and cell metabolism. Dysregulation of this pathway has been implicated in various diseases, including cancer, diabetes, and cardiovascular disorders. Here's an overview of the PI3K/Akt pathway:

Ligand Binding and Receptor Activation: The PI3K/Akt pathway is often initiated by the binding of extracellular signaling molecules, such as growth factors (e.g., insulin, epidermal growth factor, insulin-like growth factor), to their cell surface receptors. This binding leads to the activation of receptor tyrosine kinases (RTKs) or other receptors.

Activation of PI3K: Upon receptor activation, the enzyme phosphoinositide 3-kinase (PI3K) is recruited to the receptor complex. PI3K phosphorylates the lipid molecule phosphatidylinositol 4,5-bisphosphate (PIP2) to generate phosphatidylinositol 3,4,5-trisphosphate (PIP3).

Recruitment of Akt: PIP3 serves as a secondary messenger and recruits the serine/threonine kinase protein kinase B (Akt or PKB) to the cell membrane, where Akt is phosphorylated at two critical residues: threonine 308 and serine 473.

Akt Activation: The phosphorylation of Akt at these sites by phosphoinositide-dependent kinase 1 (PDK1) and the mammalian target of rapamycin complex 2 (mTORC2), respectively, leads to the activation of Akt.

Akt-Mediated Signaling: Activated Akt phosphorylates a wide range of downstream target proteins, influencing various cellular processes. Some of the key functions of Akt in the PI3K/Akt pathway include:

Promoting cell survival by inhibiting pro-apoptotic factors. Regulating cell growth and protein synthesis by activating mTORC1. Influencing glucose metabolism by modulating the translocation of glucose transporters (e.g., GLUT4). Regulating cell proliferation and cell cycle progression. Promoting angiogenesis and influencing vascular function. Cellular Responses: The collective actions of Akt and its downstream targets result in various cellular responses, depending on the context. These responses can include cell survival, growth, proliferation, metabolism, and differentiation.

Negative Feedback Loops: The PI3K/Akt pathway is tightly regulated by negative feedback loops, which serve to prevent excessive activation. These feedback mechanisms can involve the activation of phosphatases that dephosphorylate pathway components.

The PI3K/Akt pathway is a key player in the regulation of cell homeostasis and is frequently hyperactivated in cancer, contributing to uncontrolled cell growth and survival. As a result, this pathway has become an attractive target for cancer therapy, and several drugs that inhibit components of the pathway have been developed.

In addition to its role in cancer, the PI3K/Akt pathway also plays a critical role in insulin signaling and glucose metabolism, making it relevant to conditions such as diabetes and obesity. Understanding the intricate regulation and functions of this pathway is of great importance for both basic biology and therapeutic development.