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Ptk's and signal transduction: The role of luteolin

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Signal transduction usually involves the binding of small extracellular signaling molecules to receptors that face outwards from the plasma membrane and trigger events inside the cell.

The role of cytoplasmic signal transduction pathways contributing to cell transformation and cancer is a generally accepted concept. The involvement of tyrosine kinase-encoded growth factor receptors and Ras in many cancers is unequivocal. Oncogenic conversion of receptor protein tyrosine kinases (RTK) is a frequent feature of malignant cells. Hyper expression and/or mutation of the EGF receptor (erbB1) and Neu (erbB2) in combination with the establishment of autocrine/paracrine loops from their ligand (EGF, TGF, heregulin, etc.) have been found in many cancers of epithelial origin. Frequent Ras mutations in some of these malignancies also contribute to a host of signal transduction pathways involving Ras, phosphatidylinositol 3-kinase, phospholipase C, protein tyrosine phosphatases, and Src tyrosine kinases. Ras, the activation of which is controlled by tyrosine kinases, in turn regulates signal transduction pathways including the mitogen-activated protein kinase (MAPK) pathway. The multiple varieties of signaling by secreted molecules are frequently divided into three general categories based on the distance over which signals are transmitted. Regulatory proteins and peptides that are signaling molecules involved in this process are generally considered factors that are expressed by one cell and are responded to by receptors on another nearby cell.

A number of botanical compounds inhibit protein kinase C (PKC). This protein is involved in receptor desensitization, in modulating membrane structure events, in regulating transcription, in mediating immune responses, in regulating cell growth and in learning and memory. These functions are achieved by PKC mediated phosphorylation of other proteins. Some flavonoids provide valuable bases for the design of analogues that could be used to specifically block particular isoforms of PI 3-kinase or PKC and their downstream-dependent cellular responses.

Luteolin has been shown significant inhibitory effects against PKC ϵ and c-Src kinase. In several studies, luteolin inhibited PI kinase at low micromolar concentrations (<20mM). PI kinase is elevated up to fourfold in some type of cancers. Luteolin pluripotent activity is not surprising. PKC and other kinases all require ATP to donate phosphorous atoms for energy. If ATP is prevented from interacting with the enzyme, the enzyme cannot function. Luteolin has been shown to inhibit ATP-enzyme interaction.

Biography

Manuela Malaguti-Boyle, PhD, MHN is a passionate Integrative Medicine Practitioner with many years of Clinical Experience in treating patients affected by cancer both nationally and internationally. She is the Director of Clinician Solutions, an advisory service for other health care Practitioners treating cancer patients. Manuela consults as the Senior Scientific Advisor for evidence-based research of complementary medicine. She has published more than 20 papers in peer-reviewed journals in Australia and United Kingdom and is a very well know educational speaker to the Medical Oncology Community in Australia.

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