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Insilico study of Tyrosine Kinase active site and Angiogenic Inhibitors.

ABSTRACT

The tyrosine kinases are the key targets for the reason that; they play a key role in the modulation of growth factor signaling. The small inhibitor molecules of tyrosine kinase contend with the ATP binding site of the catalytic domain of various oncogenic tyrosine kinases. These are small orally active molecules that are having a favorable safety profile and can be easily mixed with the other forms of chemotherapy or radiation therapy, many tyrosine kinase inhibitors have been found to have effective antitumor activity and have been approved and some these are in clinical trials.

The tyrosine kinases are the key intermediators for the signaling cascade, which determining the important roles in different biological processes like apoptosis, differentiation, metabolism and growth in response to external and internal stimuli.

The key role of tyrosine kinases in the pathophysiology of cancer are recently going on progresses. Although their specific activity is tightly modulated in normal cells, they can adopt transforming functions due to autocrine paracrine stimulation, overexpression, mutation and leading to malignancy.

The essential oncogenic activation in cancer cells can be choked up by selective tyrosine kinase inhibitors. The ways of oncogenic activation and the different kind of comings for tyrosine kinase inhibition are like antisense, heat shock proteins, monoclonal antibodies, immunoconjugates, small molecule inhibitors and peptide drugs are brushed up in light of the significant molecules.

The angiogenesis is a key event for cancer cell proliferation and growth, tyrosine kinase inhibitors are the effective targets for anti-angiogenesis that can be well applied as a new mode of cancer therapy.

In the process of angiogenesis the new blood vessels are formed from pre-existing ones through the proliferation of vascular endothelial cells. It is an important physiological process in the growth of cancer cells still it play an important role in the progression of human diseases such as atherosclerosis,diabetic-retinopathy&cancer.

The events of the most cogent angiogenic inhibitors that counteract the effects of vascular endothelial growth factor and basic fibroblast growth factor have recently been known.

Angiogenic inhibitors are intermediated through cell surface receptors that are having integral protein tyrosine kinase activity. However, the mechanism by which these different angiogenesis inhibitors put to use their common effects remains largely unidentified. A variety of well characterized angiogenesis inhibitors (including angiostatin, thalidomide, 2-methoxy estradiol, transforming growth factor-, and fumagillin) effectively blocked vascular endothelial growth factor. PD173074 (PDB code 2FGI) is a specific inhibitor of mitogen-activated protein kinase and it is a known angiogenesis inhibitor, it also blocked the observed vascular endothelial growth factor.