Investigating Protein Kinase A binding interactions during growth factor mediated signaling

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Stimulation of cells with growth factors has been shown to induce growth and proliferation in vascular smooth muscle cells and fibroblasts in a pathway regulated by cyclic AMP-dependent protein kinase A (PKA). When the catalytic subunit of PKA (PKA-C) is phosphorylated at the tyrosine 330 (Y330) residue in response to stimulation of a receptor tyrosine kinase (RTK) with growth factor, PKA-C may act as a regulator of a molecular pathway to propagate a signal. Preliminary data revealed that a phosphopeptide corresponding to the region of PKA encompassing Y330 interacts with several Src homology 2 domain-containing proteins *in vitro*, including the regulatory subunit (p85) of phosphatidylinositol 3- kinase (PI3K) and several Src family kinases. This suggests that phosphorylation of PKA-C on Y330 induces one or more protein-protein interactions. The interaction of the full length catalytic subunit of PKA with the regulatory subunit of PI3K was investigated in cell lines. Results demonstrated that indeed, PKA-C, the RTK specific for the growth factor, and p85 co-immunoprecipitate in response to stimulation of cells with growth factors. Additionally, our data indicates that the interaction can be induced in the absence of growth factor using forskolin to activate PKA. Our recent data do not suggest that these interactions are regulated by phosphorylation at the Y330 site, however. These findings are relevant to our understanding of the PKA pathway and its connection to growth factor mediated signaling, and they may contribute to our knowledge of mechanisms underlying pathological responses.