cGnRH-II by 10 times. These findings identify the S^{331} E^{332} P^{333} motif as the determinant of differential ligand selectivities between mammalian and non-mammalian GnRHRs and imply the existence of residues interacting with Arg^{8} of mGnRH and Trp^{7} and Tyr^{8} of cGnRH-II in non-mammalian GnRHRs within this motif.

D116 A Novel Protein, Src Homology Domain Binding Protein (SHOP), Suppresses a Platelet Derived Growth Factor (PDGF) BB induced Transformation in NIH3T3 cells

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The SHOP(Src Homolgy Domain Binding Protein) was initially isolated as a binding protein to the SH domain of Phospholipse Cg1 and later found to bind with adaptor proteins, Grb2 and p85a. The SHOP contains four PXXP sequence known as a SH3 domian binding motif and two YXXM sequence known as a p85a SH2 domain binding motif. In addition, SHOP contains several putative PKC phosphorylation sites. PLCg1, PI3 kinase p85a and Grb2 were all as Receptor tyrosine kinase (RTK) downstream members and have essential roles for cellular transformation upon PDGF BB stimulation. We have determined that SHOP is selectively associated with PLCg1, p85a and Grb2 upon stimulation with PDGF BB. Furthermore, constitutively overexpressed full length SHOP in NIH3T3 cells inhibits PDGF BB dependent cellular transformation (growth in soft agar). In addition, PXXP motifs of SHOP alone were able to inhibit the formation of colony in soft agar culture. Also, DT cells overexpressing SHOP underwent morphological changes resembling parental NIH3T3 cells. We also confirmed the changes in the level of PKA RIIb which induces reverse transformation in DT cells. We suggest that the inhibition of cellular transformation may be induced by reduction of JNK activity and increased p27Kip expression level. These findings show that the SHOP may have a role as a tumor suppressor protein.

D117 Ligand-Dependent Signal Transduction of Rat and Frog Gonadotropin-Releasing Hormone Receptors

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Recently, we have cloned three distinct types of GnRH receptors in the bullfrog (designated bfGnRHR-1, bfGnRHR-2, and bfGnRHR-3). In the present study, we elucidated the involvement of different signal transduction pathways mediated through these receptors in response to different ligands. With stimulation of variety GnRHs, all receptors could increase the inocitol phosphate production. Interestingly, bfGnRHR-2 induced cAMP production in response to cGnRH-II but not mGnRH while bfGnRHR-1 could induce cAMP production by mGnRH but not cGnRH-II. In consistence, either cGnRH-II/bfGnRHR-2 or mGnRH/bfGnRHR-1 mediated CRE-luc activities were inhibited by cotransfection of PKI, a PKA inhibitor, while PKI inhibited neither cGnRH-II/bfGnRHR-1 nor mGnRH/bfGnRHR-2 mediated CRE-luc activities. Taken together, these results indicate that different ligands may regulate the coupling of different G proteins with GnRHRs, which may in turn contribute to the activation of distinct second messenger systems.