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Distribution and Characterization of Specific Cellular Binding Proteins for Bone Morphogenetic Protein-2.

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To elucidate the precise physiological function as well as the action mechanism of BMPs, we have examined the distribution of the specific cellular binding proteins for BMP-2 on a wide variety of cell types. A single class of high affinity-specific binding sites for BMP-2 were identified not only on osteoblastic cells but also on major types of non-hematopoietic cells in a rather ubiquitous fashion (1,200-60,000 receptors/cell, Kd = 35-230 pM). Affinity cross-linking of radiolabeled BMP showed five components with apparent molecular masses of 170,105,90,80,and 70 kDa. These results suggest that major types of cells may be potential targets for BMP-2 action.

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Cell Type-specific Modulation of Cell Growth by Transforming Growth Factor β 1 Does Not Correlate with Mitogen-activated Protein Kinase Activation.

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Although TGF-β 1 stimulated the growth of quiescent mouse fibroblasts, it failed to detectably stimulate the activation of MAPKs at any time point up to the reinitiation of DNA replication. TGF-β 1 also failed to stimulate the expression of the c-*fos* gene. Furthermore, TGF-β 1 synergistically enhanced the mitogenic action of epidermal growth factor (EGF) without affecting EGF-induced MAPK activation in these fibroblasts. Thus, the ability of TGF-β 1 to modulate cell proliferation is apparently not associated with the activation of MAPKs.

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Constitutive Activation of Mitogen-activated Protein (MAP) Kinases in Human Renal Cell Carcinoma.

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In this study, we examined whether constitutive activation of the MAPK cascade was associated with the carcinogenesis of human renal cell carcinomas (RCCs) in a series of 25 tumors and in corresponding normal kidneys. Constitutive activation of MAPKs in tumor tissues was found in 12 cases (48%). The activation of MAPKs was correlated with MEK and Raf-1 activation. No mutations were noted in H-,K-, or N-ras genes in any of the 25 tumor samples. Our results suggest that constitutive activation of MAPKs may be associated with the carcinogenesis of human RCCs.