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[Lab. of Biology]

**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,  $K_d = 35-230$  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  $\beta$  1 Does Not Correlate with Mitogen-activated  
Protein Kinase Activation.**

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Although TGF- $\beta$  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- $\beta$  1 also failed to stimulate the expression of the *c-fos* gene. Furthermore, TGF- $\beta$  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- $\beta$  1 to modulate cell proliferation is apparently not associated with the activation of MAPKs.

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[Lab. of Biology]

**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.