Transforming growth factor$\beta$and native human bone morphogenetic protein complex interact in a biphasic manner to modulate alkaline phosphatase, *Smad-1* and *Smad-2* synthesis in *in vitro* cultures of rat myoblast cells.

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Previous work has demonstrated that BMPs and TGF-βinteract synergistically in the primate (*Papio ursinus*, baboon) to induce rapid and exhuberant in vivo bone tissue. The present work demonstrates that addition of TGF-β to rat myoblast cells inhibits alkaline phosphatase activity induced by hBMP fraction at higher BMP doses only. At intermediate doses of BMP (150 μg/ml) alkaline phosphatase activity was not inhibited, and was in fact increased synergistically at the highest combined application of TGF-β1(5 ng/ml). TGF-β1 downregulated the expression of BMP-R1 mRNA, but less so at the intermediate doses of hBMP fraction (150 μg/ml series). *Smad-1* mRNA was also inhibited at high combinations of morphogens (300μg/ml BMP: 2.5 ng/ml TGF-β1), but strikingly, the maximum concentrations of *Smad-1* mRNA were found at the lower doses of hBMP fraction and higher doses of TGF-β1 (43μg/ml BMP: 4.3 ng/ml TGF-β1). *Smad-2* expression was high in control cultures and was strongly inhibited by moderate concentrations of TGF-β1 and hBMP fraction. This may indicate that rat myoblast cells may negatively control expression of *Smad-2*, the signaling protein of TGF-β1 , when exposed to TGF-β1 in *in vitro* cultures. Whether this may be correlated to the *in vivo* scenario will require additional work conducted with *in vivo* generated explants of tissue regenerates taken from the rodent heterotopic bioassay model.