

Oral Abstract

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The osteogenic potential and contribution of muscle stem cells to bone formation and repair

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Bone morphogenetic proteins (BMPs) are able to potently stimulate osteogenic (bone cell) differentiation. Our research has found that when treated with BMP-2, bone marrow stromal cells and myoblasts express comparable levels of early and late bone markers. In contrast, fibroblasts respond considerably less to BMP-2. Bioinformatics analysis revealed several myogenic responsive elements in the 2kB upstream promoter of mouse and human BMP receptor 1A (*Bmpr-1a*) gene. Quantitative PCR showed that *Bmpr-1a* is robustly expressed by osteoprogenitors and myoblasts, but not in fibroblasts. When MyoD was expressed in fibroblasts using a lentiviral vector, *Bmpr-1a* expression was upregulated. This is consistent with previous studies showing that forced MyoD expression can increase the sensitivity of fibroblasts to BMP treatment.

While these studies indicate a strong potential for muscle progenitors to respond to osteogenic stimulation, more sophisticated models are needed to determine the capacity of muscle progenitors to form bone *in vivo*. To track the fate of MyoD+ progenitors, we are utilizing the MyoD-Cre × ROSA26R (MyoD+/LacZ) reporter mice and the MyoD-Cre × Z/AP (MyoD+/AP) reporter mice. In these lines, MyoD+ progenitors undergo a recombination event that causes permanent expression of a LacZ or alkaline phosphatase (AP) transgene. Pilot *ex vivo* culture experiments confirm that muscle progenitors maintain strong reporter expression, even after an osteogenic gene profile has been induced by BMP-2 treatment. Studies using these mouse models to mimic heterotopic bone formation and fracture repair are currently in progress. These models will provide a versatile means of cell fate tracking in orthopaedic models.