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Thesis Title:

BMP signaling controls postnatal muscle development.

Abstract:

Growth factors from several families of signaling molecules regulate muscle development and regeneration, and thereby determine correct muscle function. However, the regulatory mechanisms that coordinate the timing of muscle precursor generation, their differentiation and the subsequent formation of correct number and size of muscle fibers are still poorly understood. Bone Morphogenetic Proteins (BMPs), a subfamily of TGF-β growth factors, have been shown to be key signals that regulate embryonic and fetal muscle precursors during prenatal myogenesis, as well as the stem cells of adult muscle, termed 'satellite cells', when activated during muscle regeneration. The main aims of my thesis were to elucidate whether BMP signaling plays a role during postnatal/juvenile satellite cell-dependent muscle growth as well as for maintenance of adult muscle mass. I found that components of BMP signaling pathway are expressed in muscle satellite cells of neonatal, juvenile and adult mice. I used transgenic mouse lines to conditionally overexpress the BMP signaling cascade inhibitor Smad6 in muscle satellite cells and in differentiated skeletal muscle. I show that BMP signaling is required for correct proliferation of muscle satellite cells and their differentiation into myonuclei, thereby ensuring that the growing muscle fibers reach the correct final size. Moreover, I demonstrated that the final number of muscle stem cells is established during the postnatal/juvenile growth phase and this also depends on the BMP signaling cascade. Finally, I provide evidence that BMP signaling is a strong hypertrophic signal for the adult skeletal muscle and its presence is indispensable for muscle tissue maintenance. In summary, my findings demonstrate that BMPs are essential growth factors for postnatal skeletal muscle.