

Scientists reveal how tendons shape developing bones

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Bones, muscles and tendons work together to provide the perfect balance between stability and movement in the skeleton. Now, Weizmann Institute scientists show that this partnership begins in the embryo, when the bones are still taking shape. The study, published in a recent issue of *Developmental Cell*, describes a previously unrecognized interaction between tendons and bones that drives the development of a strong skeletal system.

'Our [skeleton](#), with its bones, joints and muscle connections serves us so well in our daily lives that we hardly pay attention to this extraordinary system,' says Dr. Elazar Zelzer of the Weizmann Institute's Molecular Genetics Department. 'Although previous research has uncovered mechanisms that contribute to the development and growth of each component of this complex and wonderfully adaptable organ system, specific interactions between bones, muscles and tendons that drive the assembly of the musculoskeletal system are not fully understood.'

Zelzer, research student Einat Blitz, Sergey Viukov and colleagues, were interested in uncovering the molecular mechanisms that regulate the formation of [bone](#) ridges - bony protuberances that provide a stable anchoring point for the tendons that connect muscles with bones. Bone ridges are critical for the skeleton's ability to cope with the considerable mechanical stresses exerted by the muscles. The researchers used embryonic mouse skeletons to study a bone ridge called the deltoid tuberosity, located on the humerus bone in the arm.

They discovered, to their surprise, that rather than being shaped by processes within the skeleton, bone-ridge formation was directly regulated by tendons and muscles in a two-phase procedure. First, the embryonic tendons initiated bone-ridge formation by attaching to the skeleton. This interaction induced the tendon cells to express a specific protein called scleraxis, which in turn, led to the production of another protein, BMP4 - a molecule involved in the onset of [bone formation](#). Blocking BMP4 production in tendon cells prevented deltoid tuberosity bone ridge formation. In the second phase, the subsequent growth and ultimate size of the deltoid tuberosity was directly regulated by muscle activity.

The results demonstrate that tendons play an active role in initiating bone ridge patterning. Zelzer: 'These findings provide a new perspective on the regulation of skeletogenesis in the context of the musculoskeletal system, and they shed light on an important mechanism that underlies the assembly of this system.'

Provided by Weizmann Institute of Science

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