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mTORC1 hyperactivation causes skeletal defects during embryogenesis

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The mechanistic/mammalian target of rapamycin complex-1 (mTORC1) orchestrates various signaling pathways and controls different cellular functions. Tuberous sclerosis complex 1 (*Tsc1*) and complex 2 (*Tsc2*) negatively regulate mTORC1 activity. Mouse genetic studies, including our own work, have demonstrated that inactivation of mTORC1 in undifferentiated mesenchymal cells and chondrocytes causes drastic skeletal abnormalities. Here we revealed that sustained overactivation of mTORC1 leads to abnormal skeletogenesis through its expression in undifferentiated mesenchymal cells during embryogenesis. Disruption of *Tsc1* in undifferentiated mesenchymal cells by paired-related homeobox 1 (*Prx1*)-*Cre*-mediated recombination causes skeletal defects in appendicular skeletons. Meanwhile, inactivation of *Tsc1* in chondrocytes via collagen type II $\alpha 1$ (*Col2a1*)-*Cre* or in osteoprogenitors via *Osterix* (*Osx*)-*Cre* did not lead to skeletal abnormalities in either appendicular or axial skeletons. These findings provide a better insight into the molecular mechanism of skeletal development at the embryonic stage.