β1 integrins mediate the BMP2 dependent transcriptional control of osteoblast differentiation and osteogenesis

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Résumé en anglais	Osteoblast differentiation is a highly regulated process that requires coordinated information from both soluble factors and the extracellular matrix. Among these extracellular stimuli, chemical and physical properties of the matrix are sensed through cell surface receptors such as integrins and transmitted into the nucleus to drive specific gene expression. Here, we showed that the conditional deletion of β1 integrins in the osteo-precursor population severely impacts bone formation and homeostasis both in vivo and in vitro. Mutant mice displayed a severe bone deficit characterized by bone fragility and reduced bone mass. We showed that β1 integrins are required for proper BMP2 dependent signaling at the pre-osteoblastic stage, by positively modulating Smad1/5-dependent transcriptional activity at the nuclear level. The lack of β1 integrins results in a transcription modulation that relies on a cooperative defect with other transcription factors rather than a plain blunted BMP2 response. Our results point to a nuclear modulation of Smad1/5 transcriptional activity by β1 integrins, allowing a tight control of osteoblast differentiation.
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