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2007 Best Basic Abstract

Winner: Dr Hong Zhou *et al.*

Abstract:

Osteoblast-targeted disruption of glucocorticoid signalling delays intramembranous bone development *in vivo*

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Transgenic expression of 11beta-hydroxysteroid dehydrogenase type 2, driven by a 2.3kb collagen type I promoter (Col2.3-HSD2), abrogates intracellular glucocorticoid signalling in mature osteoblasts. To investigate the effects of osteoblast-targeted disruption of glucocorticoid signalling on early intramembranous and endochondral skeletal development, we analysed calvaria and long bones of wild-type (WT) and Col2.3-HSD2 transgenic (tg) mice aged 0, 1, 7, 10 and 14 days.

HSD2 mRNA and protein expression was present in all tested bones of transgenic mice but absent in those of WT mice. In marked contrast to WT littermates, tg mice had poorly-formed parietal bones with substantial cranial cartilage present at day 0. The cranial cartilage plate was present in all tg mice but absent in WT mice at day 1. By day 7, the cranial cartilage plate was reduced in size but still present in tg animals. Transgenic calvaria appeared normal by day 14. TUNEL staining indicated reduced chondrocyte apoptosis and immunohistochemical analyses showed reduced protein expression of MT1-MMP, an enzyme essential for calvarial cartilage removal, in the cranial cartilage of tg mice. In contrast, no phenotype was observed in the long bones of tg mice.

Our results indicate that osteoblast-targeted disruption of glucocorticoid signalling results in delayed intramembranous bone development without affecting endochondral bone. These findings further suggest that osteoblasts regulate cranial cartilage removal in neonatal mice, a function that appears to be glucocorticoid-dependent and mediated through activation of chondrocytic MT1-MMP expression. Our studies point to a novel role for both glucocorticoid and osteoblasts in intramembranous bone development.