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Bone morphogenetic protein 3 negatively regulates bone tissue formation and regeneration

Viktorija Rumenovic[1,2], Slobodan Vukicevic[1,2], Igor Erjavec[1,2]

[1] Laboratory for Mineralized Tissues, School of Medicine, University of Zagreb, Zagreb, Croatia
[2] Scientific Centre of Excellence for Reproductive and Regenerative Medicine, School of Medicine, University of Zagreb, Zagreb, Croatia
E-mail: viktorija.rumenovic@mef.hr

INTRODUCTION: Bone morphogenetic protein 3 is the most abundant BMP in bone tissue, but its role is considered antagonistic to other members of the BMP protein family. Due to the limited research of BMP3, the exact mechanism on bone formation and maintenance is not sufficiently explored. With the use of Bmp3-/- mice, this research aims to explore the effect of BMP3 on bone formation in ectopic ossification assay and regeneration of long bone fracture, as well as characterize osteoblast progenitor markers in bone marrow mesenchymal stem cells (BMSC).

METHODS: BMSCs were isolated from murine long bones and osteoprogenitor lineage was analyzed using flow cytometry. To assess de novo bone formation, whole blood coagulum containing BMP6 was implanted in axillary region of WT and Bmp3-/- mice of both sexes. New bone formation was assessed using micro-CT, immunohistochemistry and gene expression analysis. To evaluate bone regeneration, a model of closed tibia fracture with intramedullary pin was established and analyzed using micro-CT and Goldner staining.

RESULTS: Flow cytometry revealed an increase in early osteoprogenitor cells in Bmp3-/- mice. Ectopically formed bone showed increased bone volume fraction in both Bmp3-/- males and females, compared to WT littermates. A prevalent bone phenotype was found in Bmp3-/- mice ectopic bone, with increased expression of Runx2 and a reduced expression of Sox9, as opposed to more chondrogenic phenotype in WT mice ectopic bone. A 3-fold increase in bone callus volume during tibial fracture healing was observed in Bmp3-/- males after 21 days.

CONCLUSION: BMP3 is shown to have an effect on early osteoprogenitor cells and its deficiency results in a higher level of new bone generation and a greater callus formation during fracture repair, thus augmenting the regulating effect of BMP3 on bone tissue growth and regeneration.