The effect of combining bone morphogenetic proteins-2 and -6 on osteoblastic differentiation and bone formation

Gustavo Rico-Llanos[1], Kristina Bodnárová[2], Pilar M. Arrabal[1], Manuel Cifuentes[1], José Becerra[1], Rick Visser[1]

1. Dept. Cell Biology, Genetics & Physiology; Faculty of Science; University of Málaga, Spain. Networking Research Centre on Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN). Andalusian Centre for Nanomedicine and Biotechnology (BIONAND).

2. Dept. of Genetics. Comenius University, Bratislava, Slovakia

Abstract

Bone morphogenetic proteins-2 and -7 (BMP-2 and -7) are the only two members of the BMP subfamily approved to date to be used in combination with collagen type I in orthopedic surgery, although other BMPs have proven to also be highly osteoinductive. All the osteogenic BMPs signal through Smad-1/-5/-8 phosphorylation, but they have different preferences for the BMP receptors they use.

Very high supraphysiological doses of BMPs have been used in the clinics for the treatment of non-union fractures and spinal fusions. Besides the high cost of these treatments, safety concerns have been recently raised. Hence there is an active field in finding alternatives to the most classical collagen + BMP-2 system.

The aim of this work was to study the effect of combining two osteogenic BMPs (-2 and -6) belonging to different groups within the subfamily, and with different affinities to the existing BMP receptors. Both the growth and osteoblastic differentiation of MC3T3-E1 mouse preosteoblasts and rat bone marrow-derived mesenchymal stem cells (MSCs) under these conditions were studied, as well as *in vivo* ectopic bone formation when the BMPs were combined with collagen type I sponges. We show that the effect of these two growth factors is additive and that their combination might be helpful to accelerate *in vivo* osteogenesis while reducing the amount of each individual BMP used.