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LETTER TO THE EDITOR

Is ceramics an appropriate bone morphogenetic protein delivery system for clinical use?

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Kuroiwa et al. [1] recently published in International Orthopaedics an experimental scientific article titled "Escherichia coli-derived BMP-2-absorbed β-TCP granules induce bone regeneration in rabbit critical-sized femoral segmental defects" presenting the results in bone regeneration of femoral segmental defects in rabbits. They used *E. coli*-derived BMP-2 absorbed on β-TCP granules to induce bone in rabbit femoral segmental defects; however, the healing was very slow (at 12 weeks 40% and at 24 weeks 90% healed), as compared to an autologous BMP carrier which induced healing of critical ulnar defects in rabbits within only few weeks [2, 3]. In the article, the authors quote in support of the use of β-TCP as a BMP delivery system earlier reported work in rats, minipigs, rabbits, and two patients for alveolar bone regeneration [1]. A report using ceramics and BMP in a porcine spine vertebral model has also been previously published [4]. This suggests that a combination of β-TCP and a BMP, regardless whether produced in *E. coli* or CHO cells, has currently no clear perspective of a clinically meaningful effect. CHO cell-derived BMP could also be produced equally cheap as *E. coli*-derived BMP.

In addition, the selection of articles describing the preclinical and clinical use of BMPs missed original clinical studies with new indications [5–10]. Surprisingly, authors refer to preclinical studies with BMP scaffolds unrelated to those superseding to randomized clinical trials used for marketing approval of rhBMP-2- and rhBMP-7-based products; for example, they quote the collagen-chondroitin sulfate-based PLLA-SAIB-coated rhBMP-2 delivery system which has never been translated to clinical testing [11].

To demonstrate the clinical use of BMPs, authors refer to published work on rhBMP-7 and platelet-rich plasma (PRP) in patients with long bone non-unions, while new indications like the randomized controlled clinical trial in children with neurofibromatosis type I and a congenital non-union of the tibia [12], as well as results in patients with a non-union of the scaphoid bone [5], were omitted. The BMP data source has therefore been inappropriately selected, transferring a limited presentation of the possible use of BMPs.

Compliance with ethical standards

Conflict of interest MP and NS declare no conflict of interest. SV is the founder of Genera Research, a Croatian biotechnology company conducting clinical trials with Osteogrow, a novel bone graft substitute.

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