

A SYNTHETIC COLLAGEN-BINDING ARG-GLY-ASP (RGD) BIOMIMETIC PEPTIDE ENHANCES BONE CELL DIFFERENTIATION

Rick Visser^{1,2}, Pilar M Arrabal^{1,2}, Leonor Santos-Ruiz^{1,2}, Raúl Fernández-Barranco¹, Manuel Cifuentes^{1,2}, José Becerra^{1,2}

¹Andalusian Center for Nanomedicine and Biotechnology (BIONAND)-University of Málaga. Department of Cell Biology, Genetics and Physiology, Faculty of Sciences. Málaga, 29071, Spain. visser@uma.es

²CIBER-BBN (Networking Biomedical Research Center in Bioengineering, Biomaterials and Nanomedicine)

RGD (arginine-glycine-aspartic acid) peptides have shown some promising abilities to promote the attachment of cells to biomaterials and to direct their differentiation. However, anchoring these peptides to the biomaterial's surface is mandatory and usually implies several chemical linking steps. The aim of this work was to design and characterize a synthetic RGD biomimetic peptide that includes a collagen-binding domain for easy one-step functionalization of absorbable collagen sponges (ACSs), which are of frequent use in orthopaedic surgery.

The stable binding of biotinylated CBD-RGD peptide loaded onto ACSs was confirmed using chemiluminescence detection after washing of the sponges. Furthermore, the effect of the peptide on MC3T3-E1 mouse preosteoblasts and rat bone marrow-derived mesenchymal stem cells (MSCs) *in vitro* was characterized in terms of caspase activity, proliferation, alkaline phosphatase (ALP) activity, matrix mineralization and formation of focal adhesions. Finally, a rat ectopic osteogenesis model was used to determine if the co-administration of CBD-RGD could lower the dose of BMP-2 necessary to induce bone formation.

The CBD-RGD peptide was demonstrated to bind stable to ACSs, even after extensive washing. *In vitro*, the peptide did not induce apoptosis of the cells, but positively affected both cell growth and differentiation. It also seemed to affect the cytoskeleton arrangement of MC3T3-E1 cells, favoring the establishment of focal adhesions. At last, the *in vivo* experiments showed that ACSs functionalized with this peptide and loaded with a subfunctional dose of BMP-2 gave rise to ectopic bone.

In conclusion, the combination of CBD-RGD with the currently used collagen/BMP system might be a promising approach to improve osteogenesis and to reduce the doses of BMPs needed in clinical orthopaedics.

Visser R *et al.*, A collagen-targeted RGD biomimetic peptide to promote osteogenesis. *Tissue Eng Part A*. 2013 (in press). doi: 10.1089/ten.TEA.2012.0610. IF 2012: 4.065.