

(OP 82) Dexamethasone-Loaded Carboxymethylchitosan/Poly(Amidoamine) Dendrimer Nanoparticles Enhances Bone Formation *In Vivo*

J.M. Oliveira^{1,2,3}, R.A. Sousa^{1,2}, N. Kotobuki³, P.B. Malafaya^{1,2}, M. Tadokoro³, M. Hirose³, J.F. Mano^{1,2}, R.L. Reis^{1,2}, H. Ohgushi³

¹3B's Research Group–Biomaterials, Biodegradables and Biomimetics, Department of Polymer Engineering, University of Minho, Campus de Gualtar, 4710-057 Braga, Portugal

²IBB–Institute for Biotechnology and Bioengineering, PT Government Associated Laboratory, Braga, Portugal;

³Research Institute for Cell Engineering (RICE), National Institute of Advanced Industrial Science and Technology (AIST), Nakoji 3-11-46, Amagasaki, 661-0974 Hyogo, Japan

Dexamethasone-loaded carboxymethylchitosan/poly(amidoamine) dendrimer nanoparticles, CMC/PAMAM-Dex were successfully synthesized to find applications as a controlled system of relevant molecules in Bone Tissue Engineering. These are aimed at modulating the proliferation and differentiation of stem cells, both *in vitro* and *in vivo*. In previous work, we have demonstrated that CMC/PAMAM-Dex nanoparticles are internalized with high efficiency by different cell types, namely osteoblastic-cells, SaOs-2 and rat bone marrow stromal cells, RBMSCs. The biocompatibility of HA and SPCL scaffolds was also assessed by means of seeding RBMSCs onto the materials and performing a luminescent cell viability assay, after 24 and 72 hrs.

In this work, the ability of the nanoparticles to induce the osteogenic differentiation of RBMSCs and bone formation was investigated by exposing the nanoparticles (dispersed in culture media) to RBMSCs during expansion period, then cells were trypsinized and seeded (cell number of 1×10^6 per scaffold) overnight onto the hydroxyapatite, HA and starch-polycaprolactone, SPCL scaffolds. Afterwards, the constructs were implanted subcutaneously on the back of F344 rats for the period of 4 weeks. After the implantation period, the animals were sacrificed and constructs retrieved. Micro-Computed Tomography (μ -CT) analysis, ALP activity, osteocalcin content (ELISA), and calcium content were performed to investigate new bone formation. For routine examination of undecalcified constructs, Haematoxylin & Eosin (H&E) and Toluidine blue staining were also carried out. Results have shown that CMC/PAMAM-Dex nanoparticles are biocompatible and enhanced new bone formation as compared to controls (RBMSCs/scaffolds that were not exposed to nanoparticles), *in vivo*.