Tenocytic induction of stem cells from bone marrow on polymeric microparticles for a new concept of tendon regenerative prosthesis

Silvia Claros,[1,3] Mª Carmen Araque-Monrós,[1,2] Noela Rodríguez-Losada,[4] Luis Gil-Santos,[2,5] Manuel Monleón-Pradas,[1,2] Jorge Más-Estellés,[2] José Antonio Andrades,[1,3] José Becerra[1,3,6]

Email: becerra@uma.es

[1]*Laboratory of Bioengineering and Tissue Regeneration (LABRET), Department of Cell Biology, Genetics and Physiology, Faculty of Sciences, University of Málaga. IBIMA, Málaga, 29071, Spain*

[2]*Centro de Biomateriales e Ingeniería Tisular, Universitat. Politècnica de València, Valencia, 46022, Spain*

[3]*Networking Biomedical Research Center in Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN), Madrid, 28029, Spain*

[4]*Department of Human Physiology, Faculty of Medicine, University of Málaga, Biomedicine Research Institute of Malaga (IBIMA C07), Málaga, 29071, Spain*

[5]*Centro de Recuperación y Rehabilitación de Levante, Km 11,7 CV-35, Valencia, Spain*

[6]*BIONAND, Andalusian Center for Nanomedicine and Biotechnology, Málaga, 29590, Spain*

ABSTRACT: A new concept of a regenerative and resorbable prosthesis for tendon and ligament has been developed. The prosthesis consists of a poly-lactide acid (PLA) braid, microparticles in its interior serving as cell carriers, and a surface non-adherent coating. The aim of this study is to select the most suitable support, microparticles of poly-L-lactide (PLLA) or chitosan (CHT), for carrying the cells inside the hollow PLA braid. Microparticles of these polymers were manufactured and blended with microparticles of hyaluronic acid (HA). All of them were physically and biologically characterized. Cell viability, morphology and proliferation of human mesenchymal stem cells (hMSCs) on the different supports were evaluated and compared, revealing that PLLA microparticles were the most appropriate to be used as injectable cell-carrier. Finally, hMSCs differentiation into tenocytes was carried out on PLLA microparticles using bone morphogenetic protein-12 (BMP-12) and a mixture of transforming growth factor-β1 (TGF-β1) and insulin-like growth factor1 (IGF-1). Cell morphology was analyzed by electronic and confocal microscopy and cell differentiation was evaluated immunocytochemically for the presence of type I collagen and tenomodulin. Besides, the tenomodulin and decorin gene expression were measured by real-time quantitative polymerase chain reaction (RT-qPCR). Our results showed that the medium supplemented with BMP-12 promoted higher expression of tenomodulin and decorin, both of them differentiation markers of tenocytes. This approach might be relevant to future tissue engineering applications in reconstruction of tendon and ligament defects.

Authors acknowledge support of the Spanish Instituto de Salud Carlos III through CIBERbbn and the Spanish Network on Cell Therapy (Red TerCel) initiatives.