Title

A novel 3D co-culture platform to evaluate ASC-derived secretome efficacy in counteracting osteoarthritis progression

Abstract

Osteoarthritis is a degenerative, chronic inflammatory disease that affects joints, at the ostechondral interface level, involving nociceptive sensitization. It is one of the most common causes of disabilities worldwide. Familiarity, mechanical insults and obesity are focal risk factors, other than sex and age. Among novel therapies against this pathology, conditioned medium derived from Adipose Derived Stem Cells (ASCs) is full of potentiality, not completely disclosed yet. Specifically, ASC regenerative potential has been attributed to their efficacy in orchestrating other cells' fate, through a plethora of extracellular signals. Therefore, the choice to investigate only the secretome is due to their ascertained paracrine action and to the peculiarities of the byproduct itself, which eliminates limitations proper of cell engraftment therapies. Herewith we obtain a more standardizable and clinically compliant product. A further step was made with the priming of donor cells, as a methodology to obtain a pathology-tailored ASC secretome. Indeed, the exposure of donor cells to the same cues that they would have faced *in vivo,* leads to a more enriched and functional product. In this context, we aim to implement a novel osteochondral interface harnessing the ductility of hydrogels as customizable materials able to mimic *in vitro* the physical properties of the involved tissues. It consists in a technological platform made of a bi-layered cell-laden hydrogel with compartments to specifically administer insults and drugs: an upper cartilaginous and a lower bony compartments made respectively with primary chondrocytes and osteoblasts, from OA patients. This model would be used to test ASC-derived secretome as a novel orthobiologic, able to restore cartilage morphology, joint homeostasis and investigating its effect on both compartments.

Keywords

Osteoarthritis, cell-free biologics, cell priming, 3D co-cultures, biocompatible hydrogel,