Abstract No.: 63 **Category:** Research **Time:** 4 **CR:** No

Event : 32nd Annual EURAPS Meeting, NAPLES, Italy, 26-28 May 2022

Title : Smart hydrogels with Spheroids of Adipose stem cells for minimally invasive bone and cartilage regeneration

Introduction:
In-situ gelling biocompatible polymers laden with stem cells can be very useful for minimally invasive tissue regeneration. They can avoid uncontrolled cell spreading and poor integration with the surrounding tissue. Adipose stem cells (ASCs) represent a great promise for tissue regeneration. When they are cultured in specific conditions, they form three-dimensional spheroids (S-ASCs). They express mesenchymal stem cell markers and display enhanced ability to differentiate towards MSCs lineages.

Materials and Methods:
S-ASCs were obtained from liposuction of healthy patients. They were cultured in stem cell medium (SCM) or mesenchymal differentiation media (osteoblastic, ODM, and condroblastic, CDM). Physicochemical, morphological and mechanical properties of partially degalactosylated xyloglucan (dXG) hydrogels and k-Carrageenan/Polyvinyl-alcohol (k-C/PVA) systems were defined. S-ASCs compatibility with hydrogels was evaluated by viability test, mesenchymal differentiation abilities and gene analysis. The practical printability of the formulations was also tested using the ROKIT Invivo printer.

Results:
SASCs were uniformly distributed on the surface but also through the thickness of the hydrogel. The cell viability was preserved in SCM both in dXG and k-C/PVA systems. It increased of 3fold in ODM and 10fold in CDM in dXG1 and 5fold in k-C2/PVA4 system. The gene analysis demonstrated the maintenance of stemness and the ability to differentiate of SASCs in dXG. The feasibility of injection of SASCs-laden formulations was verified. The k-C2/PVA4 system was printed and proposed as an ideal bio-ink for 3D bioprinting processes.

Conclusions:
The incorporation of SASCs into injectable hydrogels was an effective methodology to grant SASCs viability and preserve their stemness. As well as, the forming hydrogel promote SASC differentiation in osteogenic or chondrogenic cells. Our study also explores the suitability of k-C/PVA systems for the 3D printing. These formulations are very promising for the repair of both cartilage and bone defects, that are still a challenge for modern medicine.

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