11º COLAOB
11º Latin American Congress of Artificial Organs and Biomaterials
11th Congress of Latin American Society of Artificial Organs, Biomaterials, and Tissue Engineering

3D BIOPRINTING OF FIBROBLAST SPHEROID CONSTRUCTS FOR THE PRODUCTION OF BIOMIMETIC HUMAN COLLAGEN

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SUMMARY

Recent advances in additive manufacturing have been allowing 3D printing of biocompatible materials, cells and structural components. One of the main materials to produce those scaffolds is type I collagen, which became a big propellant of pharmaceutical, medical, food and cosmetic industries. Fibrillar collagen is capable of forming well organized fibrils *in vitro* under ideal conditions through hydrophobic and electrostatic interactions, as well as hydrogen bonding[1]. Moreover, due to its nature analogous to extracellular matrix (ECM), fibrillar networks exhibit better cellular response, a very important feature in tissue engineering[2]. Considering new tendencies in bioengineering and animal-free methods, the aim of this work is to develop an innovative method to biofabricate human collagen. The starting point of the production is the cell culture of human fibroblast spheroids, using proliferation inductors and growth factors, in which some ECM is produced. Then, Quantis produces a bioink

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composed by type I collagen previously synthesized by spheroids, a synthetic polymer, growth factors, inductors and spheroids from human fibroblasts (patented process) and evaluates its characteristics regarding cell viability in the bioink, bioprinting parameters and regenerative potential of QMatrix solution. After bioprinting, spheroids diameter and its three-dimensional arrangement is analyzed by fluorescence microscopy for up to 6 days. The diameter is standardized in 100 µm by settling the number of cells per spheroid in 500, with that more than 80% of viability is achieved. For the bioprinting process, parameters were optimized and settled at 10 mm/s for the speed, extrusion multiplier of 0,13 and a 0,4 mm nozzle. Constructs are left to mature for 5 days and ECM is extracted from it through an innovative method that allows cells to be reused (cell cycling), making the process sustainable. QMatrix is a new generation of bioidentical human ECM bioidentical solution, maintaining protein's structural integrity, mimicking the natural environment for cells to grow. Preliminary studies on the regenerative potential showed that a low concentration (80ug/mL) of QMatrix was capable of stimulating cell proliferation and viability after 48 hours of treatment.

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