Bioengineering of stem cells for cardiac disease modeling

Student name and student number: Andrés Hulsz (23016346)

Background:

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a genetic disease where cardiomyocytes transform into fibrofatty tissue, leading to arrhythmias and sudden cardiac death.

Aims:

Create a 3D model to recapitulate ARVC pathology using stem cells, such as human-induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CMs) and human-induced mesenchymal stromal cells (hiMSCs), to recreate representative heart layers.

Methodologies:

A customizable hydrogel, Gelatin methacrylate (GelMA), was synthesized and characterized by determining its stiffness at different concentrations using a Testometric mechanical tester. The optimal concentration was used to bioprint with a BIOX CELLINK bioprinter, and conditions were optimized to achieve the best print fidelity. Different media conditions and triggers were examined to determine how they affect human-induced mesenchymal stromal cells (hiMSCs) to reproduce a fibrofatty transformation.

Results:

A concentration of 10% GelMA was determined to have a stiffness of 29 kPa, which resembles the stiffness of native cardiac tissue. Bioprinting conditions were optimized to a temperature of 20°C, a 50 kPa pressure to extrude the bioink at a speed of 2 mm/s, and a 22-gauge nozzle. These conditions did not compromise cell viability and obtained a printing resolution of 239 µm. The optimal condition for a fibrofatty transformation was an adipogenic media + TGFβ1.

Conclusions:

The GelMA concentration that best resembled the stiffness of cardiac tissue was 10%, which was used to optimize the bioprinting conditions. An adipogenic media with TGFβ1 could induce a fibrofatty transformation on hiMSCs. Future work includes assembling the

representative heart layers to recreate ARVC pathology and estimating predictions of the disease model using Myocyter AI software.

Keywords: ARVC, hiPSC-CMs, bioprinting, GelMA.