Engineered microenvironment with biomimetic biochemical and physical signalling cues enhancing direct cardiac reprogramming

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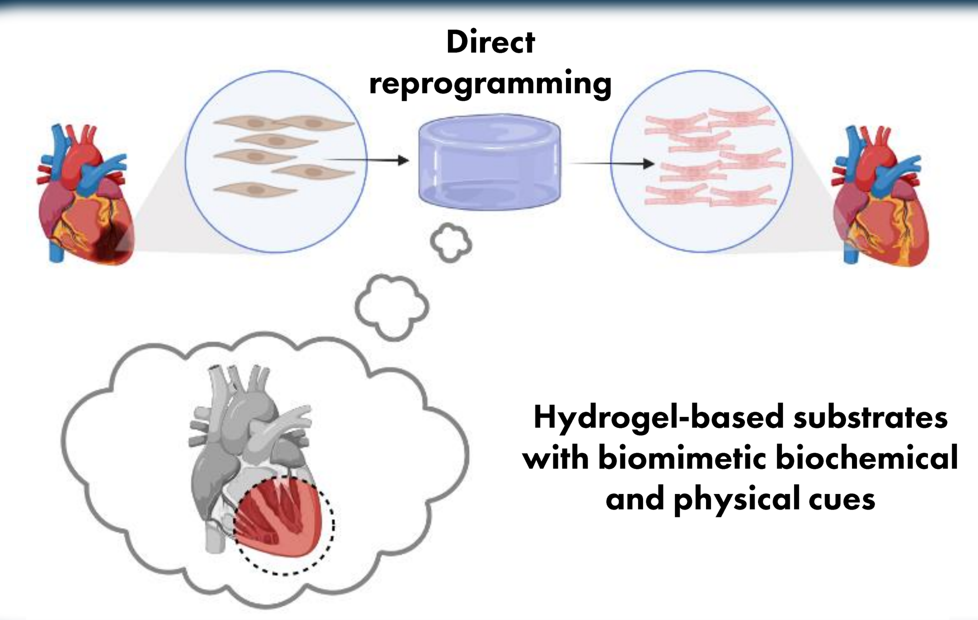
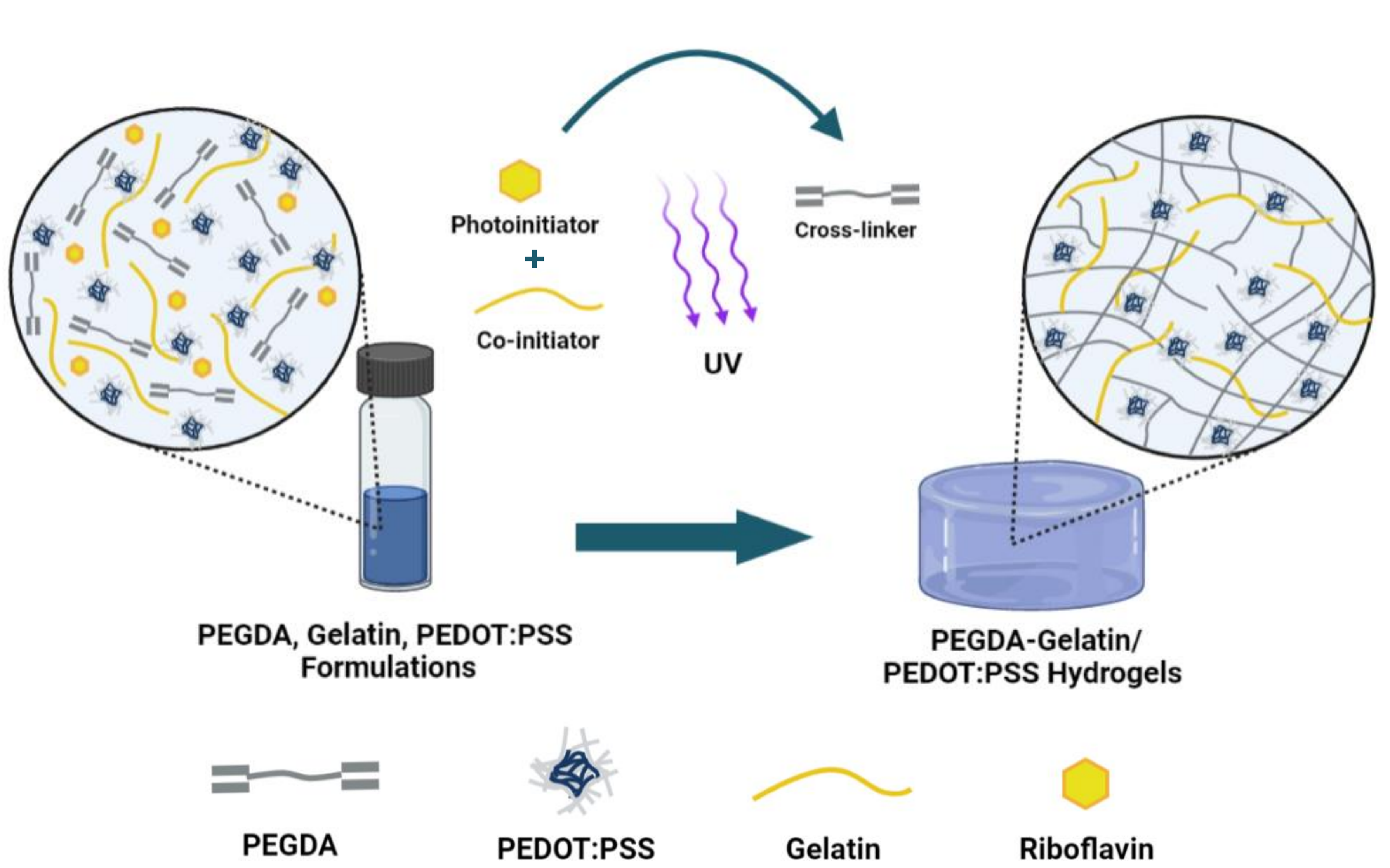
INTRODUCTION & AIM OF THE WORK



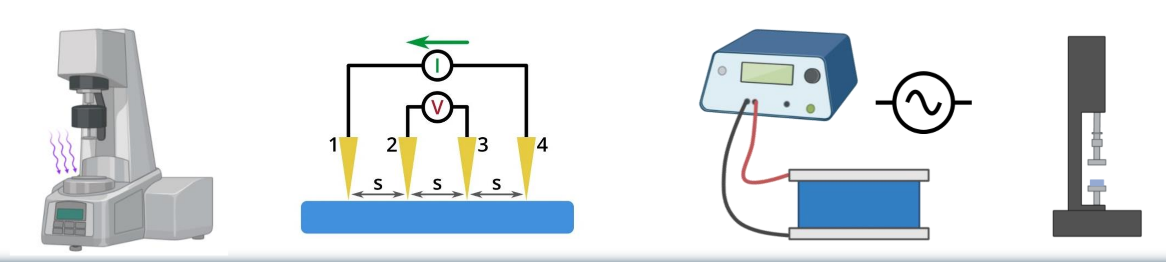
Direct reprogramming of fibroblasts (CFs) into cardiomyocytes (CMs) has emerged as a new promising strategy for cardiac regeneration. **Biomimetic 3D culture microenvironments** might provide cardiac tissue-like physical and biochemical cues able to enhance direct reprogramming outcomes. Recent studies have shown that **electrically-conductive substrates** can re-synchronize heart contraction, after myocardial infarction, as well as increase the efficiency of direct CF reprogramming into CMs. The aim of the work is to **design biomimetic hydrogel-based substrates** and their physicochemical characterization and exploitation **for enhancing direct cell reprogramming of CFs into CMs**. Different cross-linking strategies, are under investigation as also hydrogel functionalization with different electrically conductive molecules.

MATERIALS AND METHODS

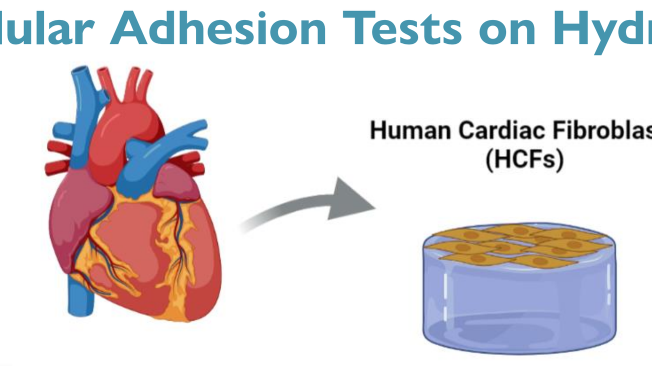
Hydrogels Formulation



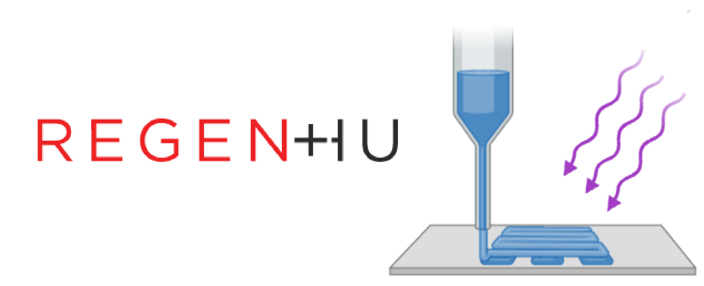
Hydrogels Characterization



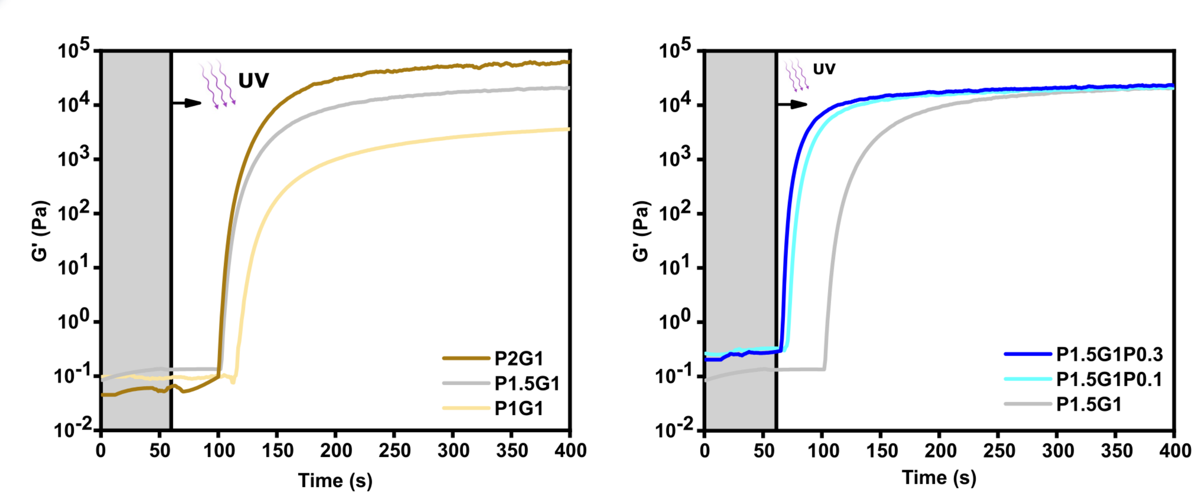
Cellular Adhesion Tests on Hydrogels



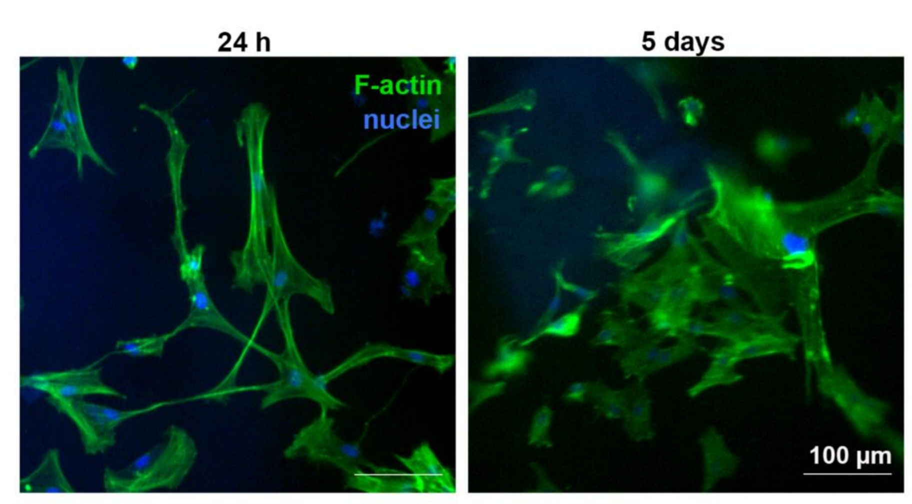
Micro-extrusion 3D-printing of Hydrogels



RESULTS AND DISCUSSION

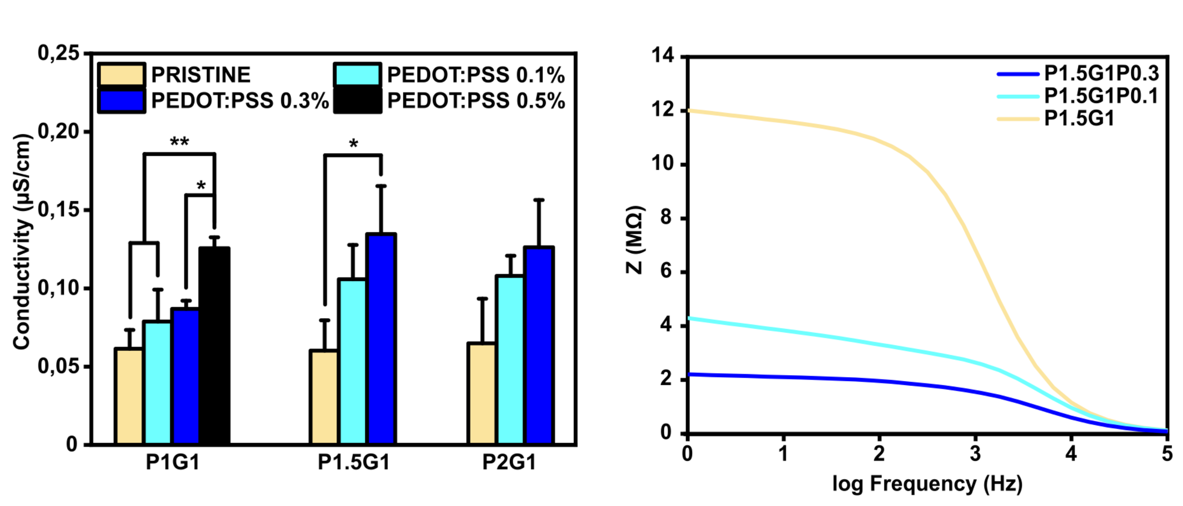


Viscoelastic properties of hydrogels increased by increasing PEGDA:gelatin ratio. The addition of PEDOT:PSS remarkedly increased photo-crosslinking kinetics.

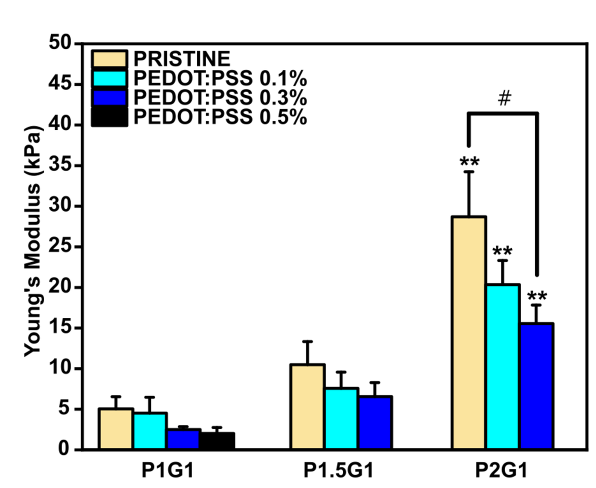


Cell attachment was promoted by gelatin incorporation withing hydrogel networks. The highest adhesion and spreading were observed on P1.5G1 hydrogels.

P1.5G1 hydrogels were 3D-printed into grid-shaped geometries of 3 layers, exploiting layer-by-layer UV cross-linking.



Surface conductivity increased as a function of PEDOT:PSS content. Moreover, hydrogels containing PEDOT:PSS possessed lower impedance (Z) than pristine hydrogels.



Elastic modulus of hydrogels increased by increasing PEGDA:gelatin ratio. Notably, the obtained values of stiffness matched the range of healthy cardiac tissue (≈10–30 kPa).

RESEARCH IMPACT

Traditional treatments for cardiovascular diseases remain limited due to the poor regenerative capacity of the myocardium. Cardiac tissue engineering solutions, are promising strategies to overcome these issues. With this purpose, electroconductive hydrogels have emerged as a new class of smart biomaterials, however, the design of such new class of biomaterials is still challenging. Here, for the first time, novel biocompatible electroconductive hydrogels were carefully optimized and by simply changing the production parameters, all their properties could be easily tuned without involving any other laborious experimental process.

TRAINING ACTIVITY

Hard Skills

Course	Description	Hours
From science to business: how to get technology out of laboratories and into practical applications.	Acquired basic knowledge on technological transfer from basic research level to industry.	20
Advanced therapies (nanomedicine, gene and cell therapy) in surgery.	Acquired advanced knowledge on clinical application of nanotechnology.	20

PUBLICATIONS

D. Testore, A. Zoso, G. Kortaberria, M. Sangermano, V. Chiono. Electroconductive Photo-Curable PEGDA-Gelatin/PEDOT:PSS Hydrogels for Prospective Cardiac Tissue Engineering Application. Front. Bioeng. Biotechnol., 2022

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