Biomedicine & Pharmacotherapy 138 (2021) 111425

Contents lists available at ScienceDirect

Biomedicine & Pharmacotherapy

journal homepage: www.elsevier.com/locate/biopha

Review

# Stem cell-based approaches in cardiac tissue engineering: controlling the microenvironment for autologous cells

Robin Augustine [a,b,*], Pan Dan [c,d], Anwarul Hasan [a,b,*], Israa Magdi Khalaf [e], Parvathy Prasad [f], Kajal Ghosal [g], Carmine Gentile [h,i,j], Lana McClements [k], Pablo Maureira [c]

[a] Department of Mechanical and Industrial Engineering, College of Engineering, Qatar University, 2713, Doha, Qatar
[b] Biomedical Research Center (BRC), Qatar University, PO Box 2713, Doha, Qatar
[c] Department of Cardiovascular and Transplantation Surgery, Regional Central Hospital of Nancy, Lorraine University, Nancy 54500, France
[d] Department of Thoracic and Cardiovascular Surgery, Zhongnan Hospital of Wuhan University, Wuhan 430071, China
[e] Qatar Biobank, Qatar Foundation, PO Box 5825, Doha, Qatar
[f] International and Inter University Center for Nanoscience and Nanotechnology, Mahatma Gandhi University, Kottayam, Kerala 686560, India
[g] Dr. B. C. Roy College of Pharmacy and AHS, Durgapur 713206, India
[h] School of Biomedical Engineering, Faculty of Engineering and IT, University of Technology Sydney, NSW 2007, Australia
[i] School of Medicine, Faculty of Medicine and Health, University of Sydney, NSW 2000, Australia
[j] Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA 02215, USA
[k] School of Life Sciences, Faculty of Science, University of Technology Sydney, NSW 2007, Australia

ARTICLE INFO

*Keywords:*
Cardiovascular disease
Stem cells
Microenvironment
Cardiac tissue engineering
Cardiac patch
Injectable hydrogels
Mesenchymal stem cells
IPSCs
Bioprinting

ABSTRACT

Cardiovascular disease is one of the leading causes of mortality worldwide. Cardiac tissue engineering strategies focusing on biomaterial scaffolds incorporating cells and growth factors are emerging as highly promising for cardiac repair and regeneration. The use of stem cells within cardiac microengineered tissue constructs present an inherent ability to differentiate into cell types of the human heart. Stem cells derived from various tissues including bone marrow, dental pulp, adipose tissue and umbilical cord can be used for this purpose. Approaches ranging from stem cell injections, stem cell spheroids, cell encapsulation in a suitable hydrogel, use of pre-fabricated scaffold and bioprinting technology are at the forefront in the field of cardiac tissue engineering. The stem cell microenvironment plays a key role in the maintenance of stemness and/or differentiation into cardiac specific lineages. This review provides a detailed overview of the recent advances in microengineering of autologous stem cell-based tissue engineering platforms for the repair of damaged cardiac tissue. A particular emphasis is given to the roles played by the extracellular matrix (ECM) in regulating the physiological response of stem cells within cardiac tissue engineering platforms.

## 1. Introduction

Cardiovascular disease (CVD) is the leading cause of mortality worldwide accounting for over 30% of deaths [1]. Despite currently available pharmacological approaches for the management of CVD, the quality of life and prolonged survival remain a challenge in the vast majority of patients. Cell-based therapies represent a potential promising approach to promote cardiac regeneration following myocardial infarction (MI), heart failure, heart valve damage, and in congenital heart diseases [2,3]. Over the past several decades, life-saving organ transplantations and the use of biomaterial-based implants have been employed extensively in people with organ damage or failure [4]. However, such interventions are associated with limitations including the lack of available or suitable organs and the need for continuous use of immunosuppressive drugs post organ transplantation, often associated with severe side effects [5]. Recent technological developments in tissue engineering including 3D bioprinting [6] and utilization of pluripotent and multipotent stem cells for organ or tissue regeneration, have shown promising potential [7]. One of the key factors in tissue engineering is the ability to have access to permissive biomaterials for optimal cell viability and function [8]. For instance, porous substrates and biodegradable materials are used to generate scaffolds and facilitate cell adhesion and proliferation [9,10]. Scaffolds based on biodegradable polymers (polylactic acid, polycaprolactone, collagen) or bioresorbable

* Corresponding authors at: Department of Mechanical and Industrial Engineering, College of Engineering, Qatar University, 2713, Doha, Qatar.
*E-mail addresses:* robin.augustine@qu.edu.qa (R. Augustine), ahasan@qu.edu.qa (A. Hasan).

https://doi.org/10.1016/j.biopha.2021.111425
Received 11 November 2020; Received in revised form 8 February 2021; Accepted 21 February 2021
Available online 23 March 2021