Biomaterials 32 (2011) 5320–5329

Contents lists available at ScienceDirect

Biomaterials

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

A 3D aligned microfibrous myocardial tissue construct cultured under transient perfusion

Halime Kenar [a,b,1], Gamze T. Kose [b,c], Mehmet Toner [d], David L. Kaplan [e], Vasif Hasirci [a,b,*]

[a] BIOMAT, Dept. of Biological Sciences, Biotechnology Research Unit, Middle East Technical University, Ankara 06531, Turkey
[b] BIOMATEN Center of Excellence in Biomaterials and Tissue Engineering, METU, Biotechnology Research Unit, Ankara 06531, Turkey
[c] Department of Genetics and Bioengineering, Yeditepe University, İstanbul 34755, Turkey
[d] Surgical Services and Center for Engineering in Medicine, Massachusetts General Hospital, Harvard Medical School and Shriners Hospital for Children, Boston, MA 02114, USA
[e] Department of Biomedical Engineering, Bioengineering & Biotechnology Center, Tufts University, 4 Colby Street, Medford, MA 02155, USA

ARTICLE INFO

Article history:
Received 28 February 2011
Accepted 6 April 2011
Available online 12 May 2011

Keywords:
Cardiac tissue engineering
Stem cell
Cell morphology
Polyhydroxybutyric acid
Polylactic acid
DMA (dynamic mechanical analysis)

ABSTRACT

The goal of this study was to design and develop a myocardial patch to use in the repair of myocardial infarctions or to slow down tissue damage and improve long-term heart function. The basic 3D construct design involved two biodegradable macroporous tubes, to allow transport of growth media to the cells within the construct, and cell seeded, aligned fiber mats wrapped around them. The microfibrous mat housed mesenchymal stem cells (MSCs) from human umbilical cord matrix (Wharton's Jelly) aligned in parallel to each other in a similar way to cell organization in native myocardium. Aligned micron-sized fiber mats were obtained by electrospinning a polyester blend (PHBV (5% HV), P(L-D,L)LA (70:30) and poly(glycerol sebacate) (PGS)). The micron-sized electrospun parallel fibers were effective in Wharton's Jelly (WJ) MSCs alignment and the cells were able to retract the mat. The 3D construct was cultured in a microbioreactor by perfusing the growth media transiently through the macroporous tubing for two weeks and examined by fluorescence microscopy for cell distribution and preservation of alignment. The fluorescence images of thin sections of 3D constructs from static and perfused cultures confirmed enhanced cell viability, uniform cell distribution and alignment due to nutrient provision from inside the 3D structure.

1. Introduction

With progress in scaffold development technology, the field of tissue engineering is advancing toward the generation of tissue substitutes, which better mimic the complexity of the natural tissues. The availability of materials and processing techniques suitable for the construction of tissue substitutes with unique mechanical properties and complex structures is opening the door for functional tissue replacements. It is now more evident that the microenvironment where the cells reside is very influential in controlling cellular behavior, which in turn is reflected in engineered functionality. The mesenchymal stem cells (MSCs), which are increasingly utilized in tissue engineering applications due to their pluripotency, are highly sensitive to the chemical, mechanical and structural properties of the scaffolds they are grown on [1–3].

With the realization of this fact, many investigators have been modifying polymer bulk properties through blending of existing polymers or synthesis of new polymers. Also increasing efforts are being spent on introducing structural complexity to the scaffolds as MSCs behave differently in two and three-dimensional (3D) environments [4,5]. In the past decade, electrospinning has gained popularity over simpler solvent casting and particulate leaching techniques in the creation of a more natural 3D microenvironment for the cells. Electrospinning enables the fabrication of highly porous scaffolds with extensively interconnected pores which allow cell-to-cell contact, migration in all directions, transportation of nutrients and metabolites, and encourage blood vessel formation; all of these combined help cell survival and proliferation. The fibrous scaffolds obtained through electrospinning have a size scale and architecture similar to those of the native extracellular matrix and are very useful especially in introducing anisotropy, particularly important in mimicking aligned fibrous tissues like myocardium, skeletal muscle, tendon, ligament and meniscus [6,7].

Both the architecture of native myocardium and its cardiomyocyte arrangement which enable a forceful syncytial contraction point out the necessity to align cardiomyocytes in the

* Corresponding author. Tel.: +90 312 2105180; fax: +90 312 2101542.
E-mail address: vhasirci@metu.edu.tr (V. Hasirci).
[1] Present address: Kocaeli University, Center for Stem Cell and Gene Therapies Research and Practice, 41380 Izmit/Kocaeli, Turkey.

0142-9612/$ – see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.biomaterials.2011.04.025