Biomaterials 31 (2010) 5945–5952

Contents lists available at ScienceDirect

Biomaterials

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

Biomimetic hybrid scaffolds for engineering human tooth-ligament interfaces

Chan Ho Park [a,b], Hector F. Rios [b], Qiming Jin [b], Megan E. Bland [a,b], Colleen L. Flanagan [a], Scott J. Hollister [a,c], William V. Giannobile [a,b,d,*]

[a] Department of Biomedical Engineering, University of Michigan, Ann Arbor, MI 48109-1078, USA
[b] Department of Periodontics and Oral Medicine, University of Michigan, Ann Arbor, MI 48109-1078, USA
[c] Department of Surgery, University of Michigan, Ann Arbor, MI 48109-0329, USA
[d] Michigan Center for Oral Health Research, University of Michigan, Ann Arbor, MI 48106, USA

ARTICLE INFO

Article history:
Received 29 March 2010
Accepted 12 April 2010
Available online 14 May 2010

Keywords:
Tissue engineering
Rapid prototyping
Periodontal disease
Interfacial tissue formation
Regenerative medicine
Composite scaffolds

ABSTRACT

A major clinical challenge in the reconstruction of large oral and craniofacial defects is the neogenesis of osseous and ligamentous interfacial structures. Currently, oral regenerative medicine strategies are unpredictable for repair of tooth-supporting tissues destroyed as a consequence of trauma, chronic infection or surgical resection. Here, we demonstrate multi-scale computational design and fabrication of composite hybrid polymeric scaffolds for targeted cell transplantation of genetically modified human cells for the formation of human tooth dentin-ligament-bone complexes *in vivo*. The newly-formed tissues demonstrate the interfacial generation of parallel- and obliquely-oriented fibers that grow and traverse within the polycaprolactone (PCL)-poly(glycolic acid) (PGA) designed constructs forming tooth cementum-like tissue, ligament, and bone structures. This approach offers potential for the clinical implementation of customized periodontal scaffolds that may enable regeneration of multi-tissue interfaces required for oral, dental and craniofacial engineering applications.

© 2010 Elsevier Ltd. All rights reserved.

1. Introduction

Collectively, periodontal diseases afflict over 80% of adults worldwide and nearly 15% display severe disease concomitant with early tooth loss [1]. In periodontitis, the detrimental changes that the tooth-supporting tissues undergo are primarily the result of specific microbial challenges [2]. These challenges in a susceptible host disrupt the functional and structural integrity of the tooth supporting apparatus and may progress to affect a number of systemic conditions [3]. Therefore, the periodontium represents a critical barrier that if breached by invasive pathogens, triggering local and systemic inflammatory responses that characterize oral infection.

Structurally, regeneration of the lost periodontium involves the formation of new cementum, periodontal ligament (PDL) and alveolar bone. However, the proper interfacial connection of this multi-tissue complex is what determines its function and stability in health. Its strength and mechanical integrity is the result of adequate PDL-fiber orientation and its incorporation to the newly formed bone and cementum. This interconnection allows the periodontal system to dissipate and translate the mechanical stimuli that are generated from the tooth to the surrounding structures [4]. Biologically, this arrangement facilitates crucial cell-matrix interactions, which within a mechanically dynamic environment, determines normal dental-alveolar adaptive responses [5]. Current available regenerative therapeutic approaches show promising results [6–8]. However, complete regeneration and adequate fiber organization in large defects remains a challenging and unpredictable clinical dilemma [9].

In regenerative medicine, many different factors have been reported to promote multiple tissue integration and cell/tissue directionality [10–16]. Novel approaches, such as the use of multi-phasic scaffold designs as well as stem cell therapies represent a significant step forward in tissue engineering [13,14,17,18]. Today, the ability to establish a 3-dimensional polarity and patterning within a predetermined inherent scaffold geometry to guide and establish cell/tissue directionality is a feasible concept [15,19–21]. Cell-based research has started to focus on designing and developing various physical and geometric approaches using biomaterials [22,23]. However, the orchestration of multiple tissue formation, spatial fibrous tissue organization, and endpoint functional restoration using a single *in vivo* scaffold system remains a significant challenge. To address these limitations, a computational topology design and a solid free-form fabrication technique

* Corresponding author at: Department of Periodontics and Oral Medicine, University of Michigan, 1011 N. University Ave., Ann Arbor MI 48109-1078, USA. Tel.: +1 734 998 1468; fax: +1 734 998 7228.
E-mail address: wgiannob@umich.edu (W.V. Giannobile).

0142-9612/$ – see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.biomaterials.2010.04.027

was used to create a hybrid periodontal-inspired model system containing PDL-specific and bone-specific polymer compartments [24,25].

2. Materials and methods

2.1. Hybrid scaffold design and fabrication

Periodontal ligament and bone architectures for the hybrid scaffold were designed and modeled with Unigraphics NX 5.0 (Siemens PLM software, Plano, TX USA). The designed structures were exported to the 3-D wax-printing system (ModelMaker II, Solidscape, Inc., Merrimack, NH USA) and manufactured using different wax molds (Fig. 1). After dissolving the Protobuild (Solidscape, Inc.) of PDL mold by 70% ethanol, two different biopolymers poly(glycolic acid) (PGA; MW > 100 kDa, Polysciences Inc. Warrington, PA USA) and poly-ε-caprolactone (PCL; MW 43-50KDa, Polysciences Inc.). 25w/v% PGA was dissolved in 1,1,1,3,3,3-Hexafluoro-2-propanol (HFIP, Sigma-Aldrich®, St. Louis, MO USA) solvent and the solution was cast for PDL interface architecture. 25 w/v% PCL solution in acetone (Sigma–Aldrich®) was cast in the bone architecture mold. These 2 different manufactured and fabricated architectures were assembled with PCL thin film membrane and BioAct® VSO (Petroferm Inc. Gurnee, IL USA) was used to remove Protosupport (Solidscape Inc.) for 2 days. The rest of Protosupport and BioAct VSO were dissolved in 100% ethanol overnight and hybrid scaffolds were stored in 70% ethanol.

2.2. Human tooth dentin slice preparation

Healthy human teeth were extracted from patients as previously described by the University of Michigan-Institutional Review Board (UM-IRB)-approved protocol. Approximately $3.0 \times 4.0 \times 0.8$ mm^3 dimensioned dentin blocks, which were fit to PDL interface of the hybrid scaffold, were sliced and surface-treated by 37% ortho-phosphoric acid to expose dentinal tubule topology and promote fibrous tissue attachment.

2.3. Cell cultures and gene delivery

Primary human gingival fibroblast (hGF) cells were provided as a kind gift from professor Martha Somerman (University of Washington, Seattle, WA USA). Passages

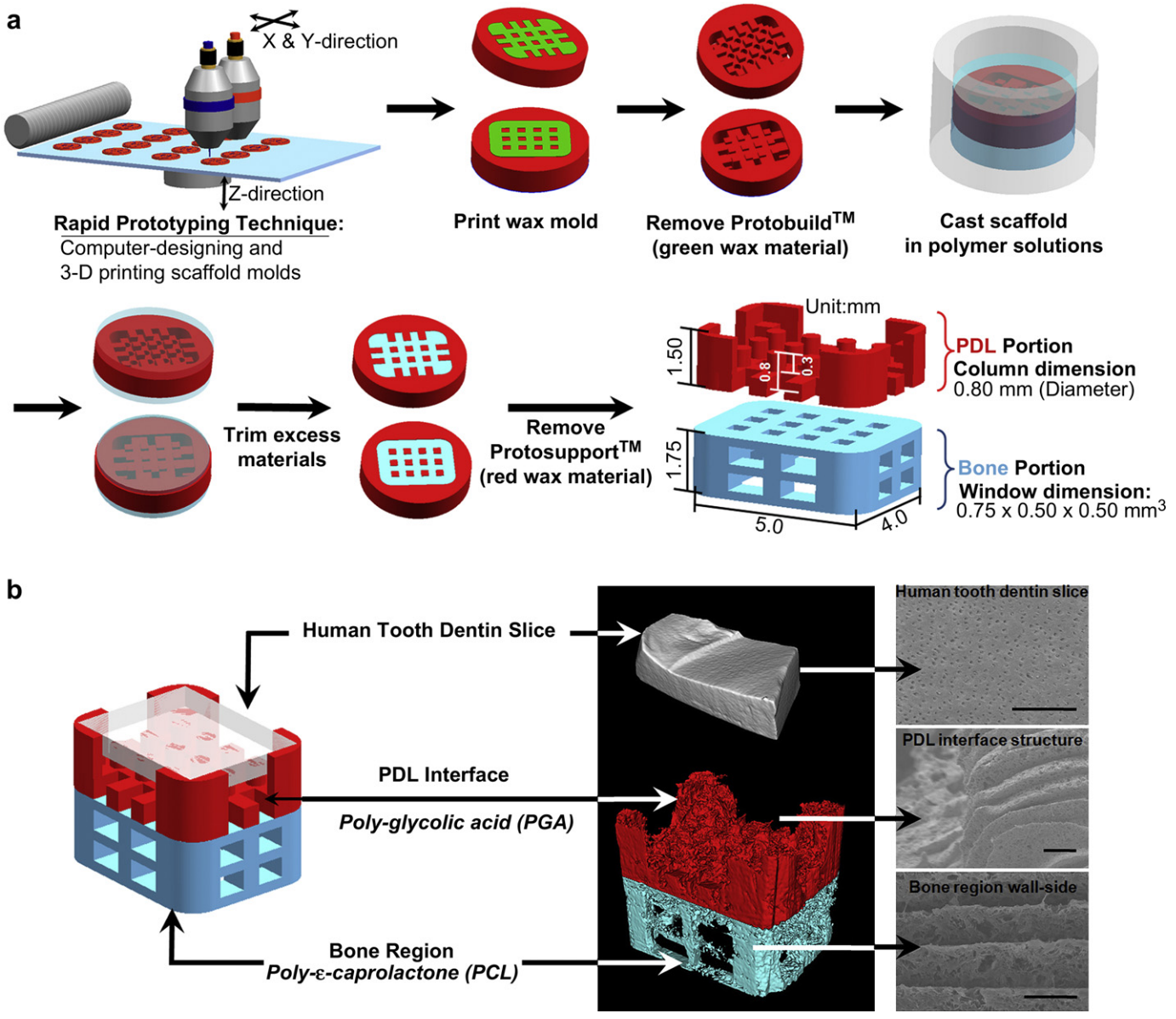

Fig. 1. a) Schematic illustration of the 3-D wax printing system and dimension of hybrid scaffold shows polymeric architecture manufacturing. For the PDL interface, column-like structures were 0.8 mm diameter and 0.3 mm exposed heights and casted using PGA-HFIP solution. For the bone region of the hybrid scaffold, PCL-acetone solution was used for casting. PCL-acetone, pasted on the PCL-casted mold and PDL interface architectures were placed on it. b) After the acid-treatment of human tooth dentin slices, the complex with a polymer-casted hybrid scaffold and a dentin slice was assembled using fibrin gel with or without cells. The left is the 3-D designed hybrid scaffold and the right panel is the micro-CT scanned and 3-D reconstructed hybrid scaffold and a dentin slice. The scale bar: 50 μm.

Download English Version:

https://daneshyari.com/en/article/9391

Download Persian Version:

https://daneshyari.com/article/9391

Daneshyari.com