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Human corneal limbal epithelial cell response to varying silk film geometric topography in vitro

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ABSTRACT

Silk fibroin films are a promising class of biomaterials that have a number of advantages for use in ophthalmic applications due to their transparent nature, mechanical properties and minimal inflammatory response upon implantation. Freestanding silk films with parallel line and concentric ring topographies were generated for in vitro characterization of human corneal limbal epithelial (HCLE) cell response upon differing geometric patterned surfaces. Results indicated that silk film topography significantly affected initial HCLE culture substrate attachment, cellular alignment, cell-to-cell contact formation, actin cytoskeleton alignment and focal adhesion (FA) localization. Most notably, parallel line patterned surfaces displayed a 36–54% increase on average in initial cell attachment, which corresponded to a more than 2-fold increase in FA localization when compared to other silk film surfaces and controls. In addition, distinct localization of FA formation was observed along the edges for all patterned silk film topographies. In conclusion, silk film feature topography appears to help direct corneal epithelial cell response and cytoskeleton development, especially with regard to FA distribution, in vitro.

1. Introduction

Silk proteins have evolved as the arthropod's material for producing external structures over the last 380 million years [1], and produce the world's strongest natural fibers once extruded from the insect's body [2]. Silk fibers are commonly associated with textile manufacturing and use as a medical suture; however, recently a silk biopolymer solution derived from these fibers has been used to produce a wide range of material forms, such as films, sponges, hydrogels and solid blocks [3]. In this regard, silk may be considered an engineering-grade biopolymer in which the formed material properties may be modulated primarily through the induction of protein secondary structure formation (i.e. alpha-helices and beta-sheets) and by controlling water content through a variety of processes [4–6]. One of the primary uses of regenerated silk materials is in the production of scaffolding material in the fields of tissue engineering and regenerative medicine due to their inherent biocompatibility [7,8]. Specifically, silk films offer a wide platform for biomaterial innovation due to their highly controlled material properties, ease of fabrication, biocompatible nature and potential for chemical modification [5,9–11]. One interesting material property of silk films is their ability to produce topographic features on the micro- and nanometer scales, which allows for the formation of surface patterned culture surfaces for cell growth [12–14]. Topographic contact guidance of cells by surface topography can have dramatic effects upon cellular development, extracellular matrix (ECM) alignment and formation, cellular adhesion, and cell proliferation and apoptosis [13–16]. In this way, silk film substrates offer an elegant system to produce customized patterned surfaces that can be designed to promote a desired cellular response with potential to elicit a clinically desirable effect [9].

Silk films are currently being developed for ophthalmic use, specifically in the cornea, due to their transparent nature and biomaterial properties [13,17,18]. Recent work has focused on developing silk films for use in ocular surface repair and corneal tissue engineering applications [17,18]. The role of the surface topography in influencing corneal epithelial response is a subject of interest due to the potential ramifications in expediting the wound-healing process post-injury. Engineered surfaces can be designed to enhance corneal epithelial adhesion, migration, proliferation, ECM production, and cellular alignment, which are all important aspects in the wound-healing response [19–22]. However, these studies have been performed upon material surfaces not suitable for in vivo implantation (i.e. silicon and plastic) and future in situ tissue integration and regeneration. Therefore, silk films offer the potential to optimize the material in vitro with the added potential benefit for in vivo translation.

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