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A silk-based scaffold platform with tunable architecture for engineering critically-sized tissue constructs

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ABSTRACT

In the field of tissue engineering and regenerative medicine there is significant unmet need for critically-sized, fully degradable biomaterial scaffold systems with tunable properties for optimizing tissue formation *in vitro* and tissue regeneration *in vivo*. To address this need, we have developed a silk-based scaffold platform that has tunable material properties, including localized and bioactive functionalization, degradation rate, and mechanical properties and that provides arrays of linear hollow channels for delivery of oxygen and nutrients throughout the scaffold bulk. The scaffolds can be assembled with dimensions that range from millimeters to centimeters, addressing the need for a critically-sized platform for tissue formation. We demonstrate that the hollow channel arrays support localized and confluent endothelialization. This new platform offers a unique and versatile tool for engineering 'tailored' scaffolds for a range of tissue engineering and regenerative medicine needs.

1. Introduction

A prominent debilitating issue in the field of regenerative medicine and tissue engineering is the lack of comprehensive scaffold platforms for the development of fully vascularized tissue-engineered constructs that integrate successfully with host tissue. We describe a silk scaffolding platform, which addresses this need. The platform possesses versatile physical and mechanical properties and incorporates tunable hollow channels to enhance nutrient delivery to cells, enables scaffold pre-vascularization and supports cell compartmentalization.

The general approach for engineering tissue equivalents is to coordinately combine relevant cell types with biophysical/chemical cues on an appropriate scaffolding material. The scaffolding material plays a significant role in modulating cell behavior and tissue formation. To achieve desired cell and tissue function, scaffold properties, including stiffness, biodegradation rate, porosity, and surface chemistry must be optimized [1,2]. Silk fibroin is an exemplary scaffolding material because its material properties can be highly tuned while exhibiting excellent cell compatibility with no adverse immune responses *in vivo*. Silk has robust mechanical properties and slow degradation rates *in vivo* (weeks to years to completely resorb) both of which can be tuned via silk processing [3–7]. In contrast to many synthetic polymers which can release inflammatory degradation products, the degradation products of silk fibroin are amino acids [8]. Silk scaffolds can take on a variety of porosities and pores sizes (nanometer scale up to several hundred micrometers) depending on the scaffold assembly method [9–12]. The biological properties of silk scaffolds can be easily augmented through bulk loading, surface decoration or construction of composite materials [13]. Silk processing and scaffold assembly are performed in aqueous solutions thereby enabling the addition of bioactive components without loss of function. Furthermore, silk has been shown to stabilize bioactive agents, such as enzymes and therapeutics, thereby prolonging their activity under physiologic conditions [14–16]. In contrast to other biologically-derived polymers, silk is abundantly available as a raw material. Other biomaterials currently reported in the literature do not offer the same suite of advantages as silk or the same range of control over physical, mechanical and biological properties. Thus, silk-based scaffolding systems can serve as a comprehensive platform for the regeneration of a wide range of tissues.

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