index, density and matrix degradation. Further, scaffold suitability was assessed through diverse in vitro tests, including measurement of cell viability, glucose consumption and time dependant insulin secretion [2]. Enhanced cellular viability and proliferation using rat primary islets and RIN-5F rat β cell line suggested successful encapsulation and compatibility. RIN-5F cells increased 2.5 folds in 4 weeks of culture whereas primary islets maintained their native morphology within silk-macro-encapsulates. Islets showed better cell adherence and insulin production with glucose stimulation index of 1.5–2 after 14 days of culture. Live cell imaging confirmed formation of 3D pancreatic spheroid like structures within scaffolds in vitro. Further, improved glucose consumption index of nine (09) after 4 weeks of culture suggested metabolically active cells. In vivo studies revealed fewer inflammatory responses and surrounding implantation was completed in 4 weeks of culture [3]. In conclusion, this novel 3D silk platform demonstrated successful encapsulation of insulin producing islet cells with enhanced cellular viability and function. Further development may have potential towards clinically viable bio-artificial pancreas.

Silk Protein Fibroin and Fibroin Based Nanoparticles Influence Implant Topography, Anti-Bacterial Activity and Osteogenesis

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Bare metal (Ti or its alloy with Cr, Ni and Ta) orthopedic implants are accepted as standard for bone/dental tissue replacement treatment throughout the world. However, sub-optimal osseo-integration and microbial infections are considered as the major challenges in the field. Modifications of the implant surfaces are employed as an opportunity to control tissue-metal interactions and to reduce the bone fixation period. The present study reports the performance of non-mulberry silk protein fibroin for in vitro osteogenesis. Primarily, silk fibroin molecules are immobilized on Ti surface and modified surfaces are characterized by SEM, AFM, XPS, EDX, and FTIR. Non-mulberry fibroin facilitates initial cell adhesion followed by improved cell spreading and better mineralization in comparison to the fibroin of mulberry origin, which can be explained by the presence of inherent RGD motifs on the non-mulberry fibroin. Additionally non-mulberry fibroin shows reduced immunological responses (TNF and IL-10) and enhanced osteoblast adhesion. Secondly, the problem of microbial infection is answered by nanoparticle mediated delivery of antibiotics. Fibroin of non-mulberry silk is used to fabricate biodegradable and cytocompatible nanoparticle (100 nm) to deliver antibiotic drug (gentamicin). Deposit of fibroin nanoparticles enhances the nano-topography and hydrophilicity of the implant surface significantly as observed by SEM, AFM and contact angle measurement. The antibacterial activities of nanoparticle deposited surfaces are investigated against Streptococcus aureus. Presence of gentamicin shows no detectable effect on osteoblast proliferation and function. Osteogenic properties of the nanoparticle deposited surfaces are found to be superior in comparison to bare Ti surface.

Immune Tolerance of Silk Proteins

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Silk of silkworms is chiefly composed of two protein components; fibroin and sericin. Co-existence of fibroin-sericin evokes immune response; therefore, these proteins are extracted separately for biomedical applications. However, critical systematic investigation of immune tolerance of co-existed fibroin-sericin is yet elusive. The present study is conducted to investigate how the concentration of sericin in blends affects the immune tolerance of fibroin in Sprague-Dawley (SD) rats over a period of 4 weeks. In addition, the investigation also includes inter-specifics comparison of immune responses between fibroins of two different origins; mulberry (Bombyx mori) and nonmulberry (Antheraea mylitta) in order to elaborate nonmulberry silks as parallel biomaterials to mulberry silk. Natural silk cocoon composition is elucidated by choosing the bio-mimicking blending ratios of silk proteins; fibroin and sericin. The blends form porous interconnected 3D microstructure without any phase separations between the hydrophilic-hydrophobic components and exhibit good in vivo compatibility with human dermal fibroblasts. Subsequent subcutaneous implantation indicates no significant inflammatory responses associated with the physico-chemical characteristics of the mulberry and nonmulberry fibroins. However, the blends reveal moderate inflammatory responses with the formation of multi-layer fibrous capsule. Compared to non-mulberry scaffolds, the mulberry scaffolds (pure and blends) show relatively more homogenous cellular infiltration throughout the implants, which results in rapid degradation and absorbance within 4 weeks. Together, the data indicates well immune comparability of pure mulberry and nonmulberry silk fibroins, while the presence of sericin imparts minimal inflammatory responses to implants.

Exploring Silk Based Biomaterials Functionalized with Antimicrobial Peptides to Prevent Surgical Site Infections

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Surgical site infections (SSI) often occur after invasive surgery, which is a serious health problem, making it important to develop new biomaterials to prevent infections. Spider silk is a natural biomaterial with excellent biocompatibility, low immunogenicity and controllable biodegradability. Through recombinant DNA technology, spider silk-based materials can be bioengineered and functionalized with antimicrobial (AM) peptides 1. The aim of this study is to develop new materials by combining spider silk chimeric proteins with AM properties and silk fibroin extracted from Bombyx mori cocoons to prevent microbial infection. Here, spider silk domains derived from the dragline sequence of the spider Nephila clavipes (6 mer and 15 mer) were fused with the AM peptides Hepcidin and Human Neutrophil peptide 1 (HNP1). The spider silk domain maintains its self-assembly features allowing the formation of beta-sheets to lock in structures without any chemical cross-linking. The AM properties of the developed chimeric proteins showed that 6 mer + HNP1 protein had a broad microbialic activity against pathogens. The 6 mer + HNP-1 protein was then assembled with different percentages of silk fibroin into multifunctional films. In vitro cell studies with a human fibroblasts cell line (MRC5) showed nontoxic and cytocompatible behavior of the films. The positive cellular response, together with structural properties, suggests that this new fusion protein plus silk fibroin may be good candidates as multifunctional materials to prevent SSI.

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Reference:


Directing Neuronal Projection using Micropatterned Silk Hydrogels

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