INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
SHORT ABSTRACT OF THESIS

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SHORT ABSTRACT

Blood vessels are the main component of the circulatory system which essentially carry blood to the distal parts of our body. An obstructed blood flow leads to oxygen scarcity and hypoxia in the affected tissue. One of the most common examples is myocardial infarction (commonly known as 'heart attack'), which results from coronary artery occlusion due to various reasons. Current treatment modalities attempt to correct it by replacing the diseased portion with artificial plastic-based counterparts (e.g., Gore-Tex, ePTFE, etc.). While these grafts are an apt choice for larger vessels (>6mm diameter), they fail under low flow, high-pressure conditions in smaller vessels (<6mm diameter) due to compliance mismatch. Recent progress in the field suggests that bioengineered strategies stand strong in providing a pragmatic solution.

The current thesis delineates various potential strategies to progressively develop bioresorbable tissue-engineered vascular grafts that employ natural silk biomaterial (mulberry- Bombyx mori; non-mulberry- Antheraea assama and Philosamia ricini). Investigation of cell-material interaction revealed biocompatibility of vascular cells with silk biomaterials. Nanoengineered silk film substrates effectively induced the unidirectional alignment of vascular cells via contact guidance. Leveraging the former capability, a multilayered biomimetic vascular graft based on primary porcine vascular cells is developed, exhibiting an adequate burst strength comparable to native human blood vessels. While patient-specific primary vascular cells are immunocompetent, limited in vitro proliferation ability restricts their clinical implementation. To overcome former setbacks, a novel bi-layered vascular scaffold is further designed and seeded with human adipose stem cells (stromal vascular fraction). In vivo studies suggested the clinical feasibility of grafts that was validated in terms of ease of handling during interposition grafting in rat abdominal aorta, adequate mechanical properties (suture retention, dynamic compliance, etc.), patency, and constructive remodeling.

Further efforts were inclined towards developing cell-free grafts to improve upon the clinical feasibility of tissue-engineered vascular grafts bypassing the cell seeding. Leveraging the notion that stem cells facilitate graft remodeling via paracrine signaling, two rational approaches were adopted to confer bioactivity in acellular grafts. The bi-layered scaffold system is functionalized with human Wharton's jelly-derived matrix presumed to preserve stem cell-secreted factors and with monocyte chemoattractant protein-1 (MCP-1). Both approaches were effective and improved in vivo acute patency by immunomodulation.

In this thesis, various designs of vascular grafts are progressively developed and tested in pre-clinical animal models. The outcomes of this thesis open new avenues in the field of vascular regeneration.