Artificial blood vessels

Studies on endothelial cell and blood interactions with bacterial cellulose

Akademisk avhandling

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av

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Avhandlingen baseras på följande delarbeten:

I. Modification of Nanocellulose with a Xyloglucan-RGD Conjugate Enhances Adhesion and Proliferation of Endothelial Cells: Implications for Tissue Engineering.
Bodin A, Bäckdahl H, Fink H, Brumer H, Risberg B, Gatenholm P
Biomacromolecules. 2007 Dec;8(12):3697-704.

II. Bacterial cellulose modified with xyloglucan bearing the adhesion peptide RGD promotes endothelial cell adhesion and metabolism - a promising modification for vascular grafts
Fink H, Ahrenstedt L, Bodin A, Brumer H, Gatenholm P, Krettek A, Risberg B
Submitted to Journal of Tissue Engineering and Regenerative Medicine

III. Real time measurements of coagulation on bacterial cellulose and conventional vascular graft materials
Fink H, Faxälv L, Drotz K, Risberg B, Lindahl T, Sellborn A
Acta Biomaterialia. Sept 2009 [Epub ahead of print]

IV. An in vitro study of blood compatibility of bacterial cellulose
Fink H, Hong J, Drotz K, Risberg B, Sanchez J, Sellborn A
In manuscript

V. In vitro evaluation of endothelial cells on fibrin-coated Bacterial cellulose exposed to shear stress
Fink H, Skog A, Drotz K, Redl H, Risberg B, Gatenholm P
In manuscript

UNIVERSITY OF GOTHENBURG

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Abstract

Cardiovascular diseases are still the number one cause of death or invalidity in the western world today. Atherosclerotic plaques and restenosis can result in severe occlusions of peripheral and coronary arteries. Treatment depends on the severity of the disease and includes drug therapy and bypass surgery. Generally, autologous vessels are used as replacement grafts and are the first choices as vascular graft materials. However, if the patient does not have vessels with sufficient quality, as a result of previous operations or other diseases, artificial grafts may be used to replace vessels. Today's materials are limited to substitute large vessels (>5 mm) because of frequent thrombosis and occlusion of small diameter grafts. About 10% of patients with coronary artery disease are therefore left untreated. Considering the high number of patients in the need of replacement grafts, the demand for an alternative small-caliber graft is enormous and has driven scientist to search for new materials. Bacterial cellulose (BC) has unique qualities and is an interesting material for vascular grafts.

In this thesis, bacterial cellulose has been investigated as a potential new vascular graft material by evaluating cell and blood interactions with BC. The specific aims were to evaluate if surface modifications could promote human endothelial cells and to investigate the thrombogenic properties of BC compared to conventional graft materials.

Modification of BC with a novel technique, were xyloglucan is used as a carrier molecule for the adhesion-promoting peptide RGD, resulted in increased cell adhesion, metabolism and cell spreading. Luminal coating of BC-tubes with fibrin glue resulted in increased cell adhesion during static experiments and good cell retention during physiological shear stress.

The evaluation of thrombogenicity in human blood plasma revealed that BC induces a slower coagulation compared with clinically available materials such as Gore-Tex® and Dacron®. In addition, BC induced the least contact activation evaluated by XIIa generation.
A Chandler loop system with freshly drawn blood showed that BC consumed low amounts of platelets and generated low thrombin values compared with Dacron® and Gore-Tex®.

This Thesis shows that BC is a promising, novel vascular graft material based on low thrombogenicity and promising endothelial cell adhesion.

Keywords: bacterial cellulose, endothelial cells, vascular grafts, cell adhesion, thrombogenicity, RGD, xyloglucan, bioreactor, imaging of coagulation, contact activation

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