Tissue Engineering
- Motta -

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Contents

Part I

Introduction

Chapter 1

General course information

1.1 Textbooks

- Scaffold for Tissue Engineering: Biological Design, Materials, and Fabrication
- Introduction to Tissue material interactions (PDF)
- Selected chapters from : Principles of Regenerative Medicine (prof. Atala) (PDF)
- Selected chapters from: Adult wound healing (Yannis), and Extreme Tissue Engineering
- Selected scientific papers

1.2 Assessment

- *TODO Still trying to define exactly*

1.3 Topics

- Concept of therapeutic device, transplant or implant?
- From tissue substitution to tissue regeneration: Introduction to tissue engineering
- Biocompatibility: concept evolution, mechanism, new approaches
- Structure, function, of ECM, role in cell activity, Cell/ECM interactions
- Wound healing: repair, regeneration, scar tissue formation
- Foreign body reaction: immuno, inflammatory, blood coagulation, complement system ECM as a model for scaffold design: engineering biomimetic scaffolds
- Polymers, biopolymers, hydrogels, fabrication methods
- Material/biological system interactions
- Strategies to control scaffold vascularization

- Strategies in TE: from top down to bottom up approach
- Organ printing and cell encapsulation
- TE applied to 3D in vitro models and lab-on-chip: drug screen, cancer studies, personalized medicine.
- In vitro-in vivo evaluations: bioreactors
- Lectures in lab: practical demonstration on scaffold fabrication

Tissue engineering is a biomedical engineering discipline that uses a combination of cells, engineering, materials, methods and suitable biochemical and physicochemical factors to restore, maintain, improve or replace different types of biological tissues.

Tissue/organ transplant is a heavily limited solution for tissue/organ failure; some of the main limitations being:

- Donor-recipient compatibility: it is almost impossible to find a fully compatible donor (all major histocompatibility complexes matching with the recipient) and the use of non-fully compatible organs/tissues requires the recipient to undergo immunosuppresive therapy (generally chronically) to avoid rejection of the transplant.
- Rejection risk: rejection can occur regardless of compatibility and immunosuppressive therapy, therefore this risk can never be avoided completely.
- Organ/tissue scarcity: even not considering compatibility, the amount of organs/tissues that can be donated is very scarce, since most of them come from car accident victims or relatives.

For this reasons implanting artificial devices has grown more popular since:

- They are ready to use
- They immediately restore the function of the organ/tissue
- They can be personalyzed
- They do not cause rejection

Still, implants present many limitation:

- They require invasive surgery
- They can cause foreign body reaction
- They cannot replace completely the functions of the organ/tissue (limited performance)
- They have limited duration

Examples of implant devices:

- Hip joint prosthesis: made of metallic alloys (mostly based on titanium) and ceramic (for the joint socket). It immediately restores the function of the joint but it requires very invasive procedures (long segment inside the femur) and overtime it sticks to the bone, making it really hard to substitute it. This last point is of little relevance if we consider older people, but it is a big problem for younger ones.

- Vascular stent: a stent is a cylindrical tool that is used in angioplastic procedures, meaning it prevents the stenosis (blockage) of (usually coronary) arteries. A flexible probe mounted with a stent, a balloon and some way to visualize the probe from outside the body (via ecography for example) is inserted in the femural artery; then the probe is navigated to the damaged region and the balloon inflates positioning the stent. This allows to restore blood flow to the miocardium without open heart surgery, even in an emergency setting such as in case of heart attack. The main problem is that the artery keeps contracting and expanding, therefore the stent can damage the vessel causing necrosis, proliferation of fibrotic tissue, inflammation; one way to reduce the problem is to use polymers rather than metallic alloys, since they are more flexible, but they are also less durable. Moreover stents are in contact with the blood and thus provide an abnormal surface that can start platelette aggregation and coagulation, creating blood clots; the use of slow release anticoagulant drugs stents helps with that aspect.

- Artificial heart: heart shaped device with valves. This device does not work as a pump since it cannot contract like miocardial fibres, therefore it require some form of auxiliary external pump. Just like with stents you can have abnormal coagulation on the surface of the device or due to turbolences in the blood flow.

- Bone scaffolds are three-dimensional biomaterial structures used for bone defect reconstruction. An ideal scaffold should have features such as 2 improving cell adhesion, proliferation, osteogenic differentiation, vascularization, host integration, and, where necessary, load bearing • These design parameters should lead to specific scaffold properties, which include biocompatibility, porosity, micro and nano-scale structure, degradation rate, mechanical strength, and growth factor delivery, all of which dictate the biomaterial to be used or developed.

• Personalised medicinal devices - Devices do not replace all the functions of a lost organ or tissue and often fail in long term - New approach: • Routine assembly of living tissues and organs and reliably integrated to body to restore, replace or enhance tissue/organ functions • Using a material like Biomaterials that can influence cell function and response - Hence, Biomaterial is interacting with the living tissue and generating response Tissue Engineering Paradigma: - What type of cell to be used as cells can be heterogenous when taken from a particular location • Usually stem cells , sometimes primary cells - Biopsy - Seeding cells on a scaffold • Appropriate scaffold with suitable growth factors and cytokines - Cell stimulation in a bioreactor - Implantation of tissue engineered construct in the patient • Re-implant engineered tissue in the damaged site - Disadvantages: • Labour-intensive 3 • Time consuming • Not-ready to use - Improvements/Alternatives: • In-situ regeneration • Development of a Polymer that should be functional - Precision biomaterial • Directly implant scaffold in the damaged site of the body • Advantages: - Low cost - Customisable - Ready-to use 4

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