Functionalization of biointerfaces - Design and monitoring of ECM analogous biointerfaces for biomedical and biophysical applications

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Within a scientific network supported by the Thuringian government, new approaches for functionalized biointerfaces will be developed to combine structural elements of technical three-dimensional environments with bioactive material properties.
The cultivation of cell populations within three-dimensional environments similar to natural tissue conditions represents one of the most important aspects to preserve cell specific responses during in-vitro applications in cell culture testing, biofunctional research or tissue engineering. The structure of the extra cellular matrix (ECM) in natural tissues is of major importance for cell growth and cell differentiation. The engineering of suitable three-dimensional biosurfaces which mimic ECM analogous interfaces lacks freely eligible parameters like surface microdimensions, 3D structure pattern and material properties.
The spectrum of necessary topics in development and application-oriented testing of ECM analogous biointerfaces will be covered by four research projects of partners with complementary research activities and expertises (A-D):

A Development of ECM analogous 3D biointerfaces for biological and medical applications by laser micro- and nanostructuring using two-photon polymerisation (2PP)

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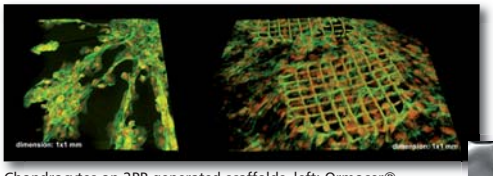
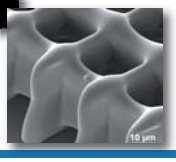
The research is focussed on the 2PP-structuring of biocompatible polymers to generate 3D scaffolds with properties of hydrogels:
- Optimization of excitation and scan parameters to polymerize (meth)acrylated biopolymers (e.g. dextrane, collagens, hyaluronic acid) and to build up biocompatible and mechanically stable scaffolds for cell cultivations
- Development of virtual 3D models as templates for 2PP-structuring
- Testing of biocompatibility and structural compatibility of 3D-biointerfaces for cartilage tissue engineering and BioMEMS
- Investigations of effects of cell specific differentiation processes by 2PP-structured scaffolds using mechanical loaded chondrocyte populations



Chondrocytes on 2PP-generated scaffolds. left: Ormocer® right: l-lactide copolymer (green: actin, red: nucleus, CLSM)



Regular structure of polymerized l-lactide copolymer generated by 2PP (rod thickness < 2 μm.)

B Synthesis and evaluation of photochemically polymerisable biomaterials for manufacturing of ECM analogous matrices by laser structuring

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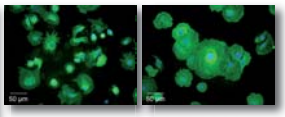
Hydrogels of cross-linked methacrylated hyaluronic acid (left) and dextran (right)



Cell spreading visualised by antivinculin immnofluorescence on unloaded (left) and RGD-ligand loaded hydrogel layers (right)

The main field of research is the synthesis of biopolymers especially (meth)acrylated compounds enabling two photon polymerisation with formation of hydrogels possessing suitable properties in view of mechanic stability, degradation and biocompatibility.
- Analytical investigations of the functionalised biopolymers
- Selection and testing of suitable photoinitiators
- Immobilisation of bioactive ligands to the hydrogel surface to increase cell adhesion
- Development of methods for purification of nanostructured hydrogels
- Investigation of cytocompatibility of the formed hydrogels

C Biological functionalization of titanium surfaces to promote the bone growth at implant interfaces

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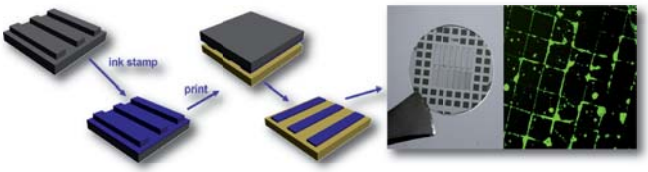
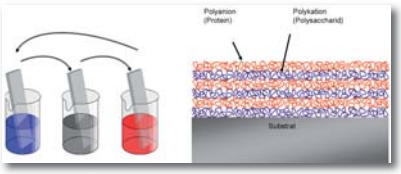
Functionalization of implant materials surfaces through the lateral chemical structuring and multilayered coatings consisting of biopolymers and proteins promotes bone ingrowth. The combination of lateral structuring and the deposition of multilayers lead to the formation of a three-dimensional ECM analogous biointerface.

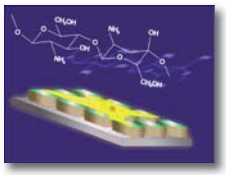
The aim:
- Selection and testing of biopolymers (polysaccharides, gelatine, proteins)
- Fabrication of ECM analogous biointerfaces from these biopolymers in view of the target requirements (biocompatibility, biodegradability, stability against sterilization, etc.)



Microcontactprinting technology



Layer by layer technology



Structured multilayer coating

D Standardized technical micro environments for the characterization of 3D ECM analogous biointerfaces

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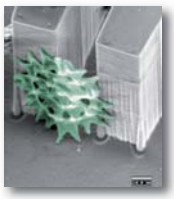
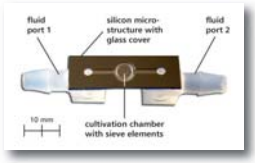
Microsystems are a powerful and versatile tool for the evaluation of small scaffold structures under constant environmental conditions. Therefore, different components with surface functionilizations on a modular platform will be characterized and optimized for medical application.

The aim:
- Standard, robust and cost effective modular microsystems
- Development of microsystem based cultivation and handling systems
- Development and implementation of 3-dimensionally structured inorganic or organic ECM-analogous (ECM extra cellular matrix) biointerfaces

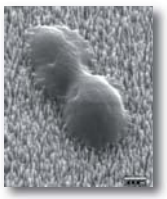
These systems will complement the equipment of cell and tissue engineering laboratories in future.



Alga in microsystem (REM)



Microfluidic chip (Si, glass, polymer)



Cells adhered on Black Silicon

INTERNET

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