4.3 Department for Functional Materials in Medicine and Dentistry

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Mission and structure

The Department for Functional Materials in Medicine and Dentistry is focused on materials development and positioned at the dental clinic. Mission of the department is the development of innovative biocompatible and bioactive materials for applications in biomedical basic research and applications in humans with focus on regenerative materials and therapies. Accordingly, an interdisciplinary team of biologists, chemists, pharmacists, and physicists in cooperation with clinicians is engaged in realizing the mission statement "higher quality of life through innovative materials". Research activities are tailored for the special needs of the respective clinical challenge and divided into the 5 competence fields biointerface engineering, bioactive inorganic scaffolds, Nanobiotechnology, artificial extracellular matrix and (mico-) biological testing. These activities are financially supported by the Interdisciplinary Center for Clinical Research, the Deutsche Forschungsgemeinschaft (DFG), the Bundesministerium für Bildung und Forschung (BMBF), and the European Union (FP7).

Main Research Interests

Biointerface Engineering

Metallic implant materials for load-bearing applications interact with the biosystem primarily via their physico-chemical properties. The ideal implant surface should provide excellent biocompatibility and at the same time have antimicrobial potential to reduce the risk of postoperative infection and to support rapid osteointegration of the implant. In the work group for biointerface engineering two key methods of functional surface coating are being investigated: By means of electrochemically assisted and electrophoretic deposition refractory metal surfaces are being provided with ceramic coatings on the basis of calcium and magnesium phosphates, which are additionally doped with biologically active respectively bactericidal metal ions. Furthermore, magnetron sputtering – a physical vapor deposition technique – is being applied for the fabrication of multiphasic coating systems of refractory metals and their oxides and nitrides. Further functionalization of these coatings takes place by doping with metal ions (e.g. silver, see Figure 1), by electrochemical nanostructuring as well as by oxygen diffusion hardening for the improvement of surface properties.

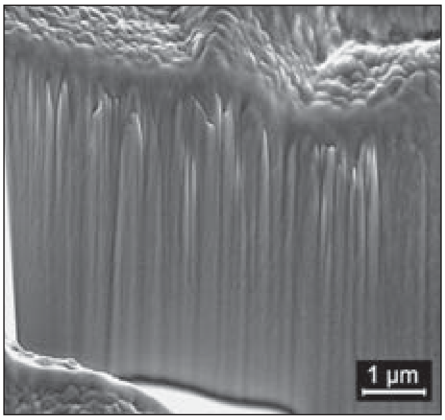

Fig. 1: FIB cut across a silver-doped titanium coating.

Bioactive Inorganic Scaffolds

The development of ceramic scaffold materials for bone regeneration at FMZ occurs from reactive cement powders based on calcium and magnesium phosphates that set after addition of an aqueous phase and form a stable implant without further sintering. The bone cements are processed in novel application forms, characterized regarding their chemical, physical, and biological properties, and optimized for the desired form of therapy. Depending on the application area, the presentation of biodegradable bone replacement materials in the form of pastes, simple molds or granulates is advantageous. The transfer of the cement systems to 3D powder printing allows the fabrication of patient-specific implants. All application forms result in microporous cement structures, which significantly contributes to the biocompatibility of the material. In addition, the processing at room temperature provides the possibility to incorporate organic modifications like antibiotics or proteins into the material. The local release of the agents from the cement matrix into the bone allows controlled release of pharmacologically active doses without systemic side effects. Besides the application of protein-based growth factors also the equipment of the ceramics with bioactive ions like Sr^{2+} or Cu^{2+} is being investigated. A further field of research is the fabrication of spherical granulates from bioresorbable cement pastes by means of an emulsion technique, resulting in particles with significantly reduced inflammatory potential.

Nanobiotechnology

Nanoparticles are big enough to take up and transport drugs but also small enough to be taken up by cells and to use active biological transport mechanisms. This opens a wide potential for targeted transport especially of sensitive drugs over barriers in the body to the area and tissue of interest.

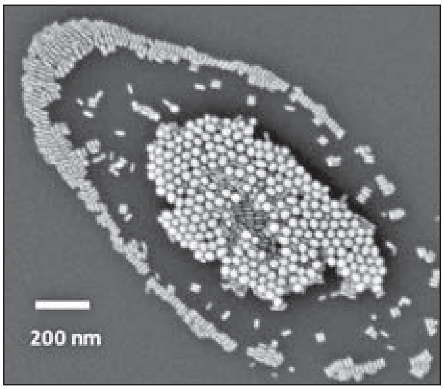

Fig. 2: Scanning electron micrograph of spherical and rod-shaped gold nanoparticles

Research at the department focuses on nanoparticles for different purposes. Systematic studies regarding the influence of nanoparticle shape, size and surface chemistry on the interaction with cells are one area of interest (Figure 2). Our results demonstrate that rather simple changes in surface chemistry of nanoparticles can significantly affect the behavior of human immune cells. This may be used to influence inflammation and healing processes for example after implantation. A particular research focus is put on colloidal hydrogels, so-called nanogels. They combine characteristics of hydrogels like biocompatibility, high-water content as well as tunable chemical and mechanical properties with the features of nanoparticles such as high-surface area and overall sizes in the range of cellular compartments. These properties make them intriguing candidates for entrapment of hydrophilic bioactive molecules to provide a hydrophilic environment and protect them from degradation. Oxidative cross-linking of thiofunctional polymers for example yields nanogels that are stable in extracellular spaces in the body and in the blood, while the reductive cytosolic conditions after cellular uptake lead to rapid degradation of the particles and release of the payload. Application of these special nanoparticles for targeted drug delivery is at the moment one core activity.

Artificial Extracellular Matrix

Within their natural surrounding cells are supported by an extracellular matrix (ECM) that enables their survival and determines their adhesion, growth, proliferation, migration, differentiation and function. Main components of all ECMs are hydrogels and insoluble protein fibers that serve as binding sites and mechanical scaffold for the cells as well as source of reversibly bound soluble factors, which control their growth and differentiation. Besides the 3D matrix of a specific tissue, thin layers of basal membranes control structural properties of our body and provide a basis for an unidirectional growth, as for example in skin.

Core activities at FMZ are the synthesis, formulation and evaluation of biodegradable materials to create structures that mimic the natural ECM as close as possible. For this approach modified biopolymers as well as biocompatible functional polymers are used to prepare coatings, hydrogels and nanofibrous constructs. To generate a structural hierarchy, methods such as electrospinning of solutions and melts and rapid-prototyping techniques are currently applied. In this field of activity, a novel and internationally unique method was further developed to prepare fibrous scaffolds with a controlled fiber deposition to control cell growth on a micrometer scale. Further modifications of the fibers with new polymeric additives towards biomimetic *in vitro* cell cultures and clinical applications are at the moment an intensive research focus (Figure 3).

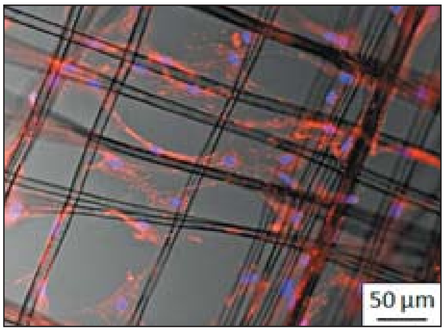

Fig. 3: Cell growth on melt electrospun fibers.

(Micro-)Biology

Focus of the biological laboratory is the interaction of cells with biomaterials and functional materials developed in the department. For this purpose preferentially human cell types, primary cells as well as cell lines, and prokaryotic cells of different strains are used. The microbiology section deals with testing of newly developed antimicrobial surface modifications like Ti(Ag)N coatings on metal substrates. Cell biology focuses on cell-surface interactions in 2D and 3D culture systems including matrices like gels and fibres. Additional key aspects are the interaction of cells with nanomaterials as well as co culture systems.

Furthermore, an accredited and ZLG approved testing laboratory is associated to this competence field. Here cytocompatibility testing according to DIN EN ISO 10993-5 is performed for materials developed in the department as well as by order of external customers.

Teaching

The teaching activity contains lessons about functional materials for clinical applications and their interaction mechanisms with the biological system, courses about quality management systems and risk analysis of medical devices, medical application of X-rays, as well as practical measuring techniques for material analysis and polymer chemistry. The lectures are designed for dental students, graduate students of Biomedicine and, together with the faculty of Physics and Astronomy for students of "Nanostrukturtechnik". Special attention is laid on the transfacultative and interdisciplinary bachelor- and master programme "Funktionswerkstoffe".

SELECTED PUBLICATIONS

Singh S, Topuz F, Hahn K, Albrecht K, Groll J. (2013) Embedding of Active Proteins and Living Cells in Redox-Sensitive Hydrogels and Nanogels through Enzymatic Cross-Linking. Angewandte Chemie International Edition 52:3000–3003.

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