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Research line: ***Surface biofunctionalization (SBF)***
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• The concept

To fulfill the clinical needs of the present and future medical devices, biomaterials have to be accepted by the body, replace the function of the diseased tissue and interact with biological environments in order to control specific interfacial events. Therefore, they require multiple surface biofunctionalities. Our surface biofunctionalisation approach involves synthesis of novel porous architectures designed as reservoirs for bioactive/drug release, tissue ingrowth and combination thereof. The targeted biomaterials are metallic such as titanium alloys (including Nitinol), tantalum, zirconium, niobium, magnesium, iron and their alloys. Further, surface pretreated stainless steel and cobalt chromium are also included. Ceramic and polymeric biomaterials are used as carriers for biological/drug bioactive agents. The applications include orthopedic, dental, cardiovascular, tissue regeneration and medical instruments.

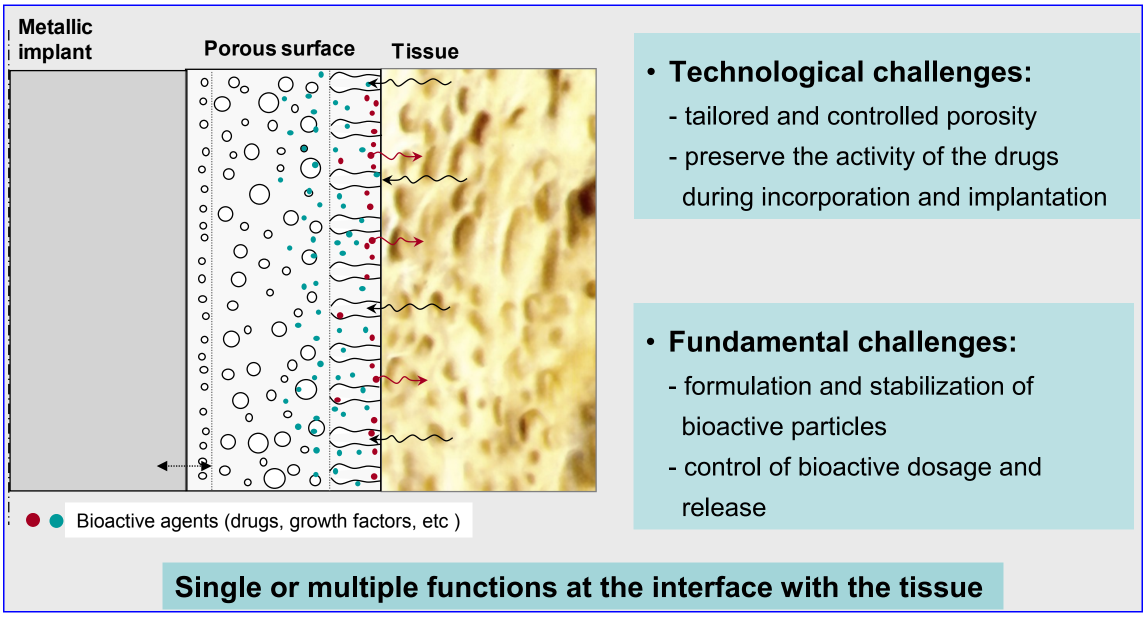

Figure 1. Concept of surface biofunctionalization for orthopedic medical devices - Medical Combination Device (drug/device, biologic/device, drug/biologic/device)

• Highlights of the research activities

1. Antibacterial and anti-inflammatory porous surfaces

The approach involves incorporation of nano/micro-sized antibacterial and anti-inflammatory agents into the porous metal oxide structures using a single step process based on plasma electrolytic oxidation. The fundamentals of bioactive incorporation and bactericidal mechanisms are in the focus of the research as well as the development of novel assays for the in vitro evaluation of bacteria killing efficiency. Antimicrobial and anti-inflammatory agents used are: inorganic nanoparticles (e.g. Ag), pharmaceutical drugs and antimicrobial peptides.

2. Porous surfaces for implant osseointegration

Osteoconductive surfaces are developed with the aim of enhancing implant osseointegration. The approach consists in incorporation into the porous surfaces of the osseoinductive/osseconductive bioactive agents, such as hydroxyapatite, bioglass, growth factors (e.g. BMP, VEGF). Relationships between process conditions and surface characteristics are established and exploited to create novel surface porous architectures.

3. Synthesis of bioactives micro/nano particles

This research involves:

(i) Synthesis of bioactive nanoparticles and

(ii) Encapsulation of specific drugs/bioactives in polymeric carriers using emulsification and spray drying technologies.

The micro/nano spheres are dispersed in aqueous environments and prepared for loading onto/into the porous surfaces of specific medical devices.

4. Drug eluting surfaces for drug/device combinations

The resultant spheres are immobilized on the surface of metallic biomaterials and the *in vitro* drug release profiles are examined. Various combinations between spheres and surface characteristics allow the design of tailored release kinetics for a specific medical application. In this way, surfaces that can stimulate tissue regeneration or control inflammatory response and healing events are developed. Typical examples are drug eluting stents for treatment of restenosis and preventing late thrombosis.

5. Mechanical biocompatibility of porous oxide surfaces

Notwithstanding biological integration, an implantable medical device requires a long service life. Therefore, the whole system biofunctional surface and substrate have to withstand body (structural and biological) conditions and should not cause premature failure. Metallic biomaterials especially titanium alloys are very sensitive to notches such as grooves, pores, coatings and the like. In this respect an important part of the research is devoted to test the fatigue behavior of each layer/substrate system in simulated physiological conditions. Furthermore, the real challenge of this research is to find solutions to improve the fatigue behavior of biofunctional surfaces on metallic implants.