PhD in Materials Science and Technology

Research Title: BeBoP - Functionalization of implantable biomaterials with biomolecules of plant origin: from surface engineering to biological response

Funded by	Politecnico di Torino (Joint Research Projects with Top Universities)

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Context of the research activity	The research will be developed within a joint project with Universidade de São Paulo, Brazil (USP). The research is focused on development of smart biomaterial surfaces coupling biomolecules of plant origin, with proven biological activities, together with traditional biomaterials for bone implants. A lot of surface treatments have already been developed for implants focusing on fast bone integration. However, fast bone integration can be associated with significant inflammation. The focus of future researches must move to physiological healing, through modulation of local host response and infection prevention. The control of host response and infection is still an unmet need with frequent complications: too high risk of inadequate long-term outcome of dental implants, significant heterotopic ossification, fibrosis and infections of the spinal and orthopedic ones. Surface functionalization will follow a bio-inspired approach by using natural biomolecules of plant origin derived from extracts or scraps of vegetal industrial processing. Polyphenols derived from grape pomace, tea leaves and coffee beans have a proven antioxidant, anti-inflammatory, antibacterial and bone stimulating activity; even if their bioavailability is usually poor by oral dosing, a local action of these biomolecules coupled to the implant surfaces can be much more effective. The expected result is development of innovative

	biomaterials, starting from well-established materials used for bone implants (titanium and titanium alloys), through surface pre-treatments (in order to get the necessary surface reactivity) and functionalization with natural biomolecules. POLITO is owner of a granted European patent on this topic. In situ reduction of silver nanoparticles will be tested in order to increase antibacterial activity. The chemical/physical properties and stability of the surfaces, in vitro response to single cell/bacteria cultures and co-cultures (osteoblasts/osteoclasts, healthy/cancer cells, macrophages/monocytes, fibroblasts/osteoblasts) will be tested, as well as post-processing issues.
Objectives	Overall objective: development of innovative bioactive surfaces of interest for bone contact applications (spinal, orthopedic and dental implants) for physiological healing and recovery, avoiding the risks of implant infection. Methodology: a bio-inspired approach based on grafting natural biomolecules (polyphenols) extracted from natural sources (grape pomace, tea leaves or coffee beans). Grafting will be performed without the employment of synthetic spacers for a better biocompatibility. The substrates will be pre-treated in order to get a proper surface charge, topography and chemical reactivity for an effective grafting of the biomolecules, according to the well-established expertise of the involved partners. Grafted biomolecules will be also exploited for in situ reduction of metallic silver nanoparticles in order to increase their antibacterial properties. The final experimental objective will be to assess the ability of the functionalized materials to modulate the biological response by means of advanced in vitro tests. Incubation with co-cultures of monocytes and peritoneal macrophages, assessment of the pro-inflammatory response by quantification of markers of inflammation, resolution of inflammation and evaluation of osteoblasts/osteoclasts, healthy/cancer cells, fibroblasts/osteoblasts competitive activity will be performed. USP has a well-assessed expertise on this approach. Concerning the risk of infection, polyphenols have proven antibacterial properties, moreover their antioxidant/reduction activity can be exploited for the in situ reduction of metallic silver nanoparticles in order to increase the surface antibacterial action. Bacterial adhesion and biofilm formation will be investigated on bare and functionalized materials. The synergies will be investigated through co-cultures of bacteria and cells of different types. The research has also some objectives finalized to implementation, industrialization of the process, mainly

	concerning post-processing. Stability of the grafted biomolecules after packaging, sterilization and storage will be investigated in order to obtain innovative biomaterials able to carry natural principles in an active state through the whole production process up to the implantation site and suitable for an industrial manufacturing process. Stability of the grafted biomolecules in simulated “working conditions” (physiological solution at 37°C) will be investigated in order to guarantee the bioavailability of the natural biomolecules after implantation for the time requested for tissue healing.

Skills and competencies for the development of the activity	Skills covering material science and engineering, as well as biomedical engineering are requested. The student is requested to attend 18 months of the PhD course at USP (Brazil).