**PhD in Scienza e Tecnologia dei Materiali**

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

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**Context of the research activity**

The research will be developed within a joint project with CHUBU UNIVERSITY (NAGOYA – JAPAN). 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 or tea leaves, as well as vitamin E and some vegetal oils, 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.
### Objectives

The expected result is development of innovative biomaterials, starting from well-established materials used for bone implants (titanium and titanium alloys). Surface pre-treatments are necessary in order to get enhanced surface reactivity, proper roughness (cells and bacteria are very sensitive to topographical stimulus) and bioactivity (ability to stimulate in vitro apatite precipitation). The, the treatment of functionalization with natural biomolecules will be applied. Both POLITO and CHUBU are owners of granted patents on these topics. In situ reduction of silver nanoparticles or surface enrichment with silver and others metal ions, will be tested in order to increase antibacterial activity and get osseo-induction ability. The chemical/physical properties and stability of the surfaces, in vitro response to single cell/bacteria cultures and co-cultures will be tested, as well as post-processing issues (packaging, sterilization, shelf life).

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 extracted from natural sources (polyphenols derived from grape pomace or tea leaves, as well as vitamin E and some vegetal oils). 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.

Incubation with co-cultures of monocytes and macrophages, assessment of the pro-inflammatory response by quantification of markers of inflammation and evaluation of osteoblasts/osteoclasts, healthy/cancer cells, fibroblasts/osteoblasts competitive activity will be performed. 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 CHUBU UNIVERSITY (Japan) – supervisor prof. Seiji Yamaguchi.