BIOENGINEERING AND MEDICAL-SURGICAL SCIENCES

Ateneo - Design of advanced experimental in vitro models applying smart biomaterials and instructive substrates (joint curriculum with KMU)

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Context of the research activity	Integrating biomedical science with novel engineering technologies and advanced materials is a key strategy for developing breakthrough approaches to solve yet unmet clinical needs and to respond to the societal need for more efficient treatments with low ethical and environmental impact. In this context, in vitro experimental models are widely recognized as a powerful tool for advancing understanding of various pathologies and for testing the efficiency of new therapies. 3D scaffolds optimized at the molecular scale to mimic nature can finely replicate in vitro the architecture, the physicochemical and mechanical properties, as well as the porous structure of the extracellular matrix (ECM) of the native tissue, at different degrees of aging, in healthy or pathological conditions. Taking inspiration from nature, it is also possible to design novel therapies using natural-based agents that can be properly loaded into advanced systems (micro/nanoparticles, hydrogels) for a controlled and sustained release. Experimental platforms (i.e. 3D in vitro models and Organ-on-Chip - OoC) combine the features of the experimental organ models with physiological or pathological stimuli and flow conditions to recapitulate the complex human physiology in vitro, with the ultimate goal of reducing and refining animal experiments. However, this breakthrough technology is not yet fully exploited, since the majority of the available in vitro models fail in reproducing the complexity of organs functionality with respect to their interplay with the different cell phenotypes found in vivo. Regarding in vitro tissue modelling, an advanced design of 3D matrices that could provide both physiological and mechanical support to cell homing, growth, and organization is a key aspect for stimulating and controlling the formation of a new functional tissue as well as to guide stem cells' differentiation.

Objectives	This PhD programme will aim to the design of advanced in vitro models recapitulating the architecture and composition of physiological organs including also the key elements and actors of physiological processes. With the final aim of creating reliable models, human induced pluripotent stem cells (iPSCs) and adipose-derived stem cells (ASCs) will be used to derive mature tissue-specific cells. Smart polymers will be ad hoc designed to recreate both physiological composition and properties of the native ECM, and instructive substrates will be engineered to steer cell differentiation and to guide cell organization in a biomimetic framework. The above-proposed multi-parameters approach will be applied to several tissues and organs. In this PhD programme, lymph nodes have been selected for their key role in proper functioning of the immune system, acting as filters for foreign particles including cancer cells. Indeed, the complex anatomical structure and physiological functions of the lymphatic system present challenges in designing and developing effective lymphatic-targeted nanocarriers for drug delivery, limiting clinical translation of novel drugs. Therefore, the development of in vitro models of lymphatic tissues can help in unravelling the role of lymph nodes in pathology progression and in developing more effective drugs for cancer treatment. The Ph.D. student will be responsible for the synthesis and processing of the biomaterials into 3D constructs via additive manufacturing techniques, electrospinning and micro/nano- particles for localized and prolonged drug release. Then, the effect of these materials and constructs on cell differentiation will be tested using iPSCs and ASCs. More in detail, the Ph.D. student will develop and validate bioengineered lymph node models and will test lymph node role on cancer progression and newly designed therapeutics. These research goals will be achieved through a bottom-up approach encompassing the following steps: (i) Design and characterization of new polymeric materials of natural, synthetic or bioartificial origin, with the aim to create a library of different compositions with a wide range of physicochemical properties (e.g. mechanical properties, degradation kinetics), with the potential to meet the properties of different tissues of the human body; (ii) Synthesis of novel polymers incorporating functional groups and possessing mechanical properties that mimic both chemical composition and mechanical response of the extracellular environment (iii) Microfabrication of the optimized polymeric biomaterials via advanced fabrication technologies (e.g. melt- and solution- electrospinning, bioprinting, fused deposition modeling) into 3D scaffolds that in vitro mimic and fully recapitulate the functionalities of targeted human tissues; (iv) Surface or bulk functionalization of the designed constructs with proteins or peptide sequences to enhance their capability to mimic the native environment from a biochemical point of view; (v) Development of protocols for differentiation of immune cells using iPSCs and ASCs; other possible sources of immune cells will be considered, as well. (vi) Validation of the designed bioengineered tissue models from a biochemical, structural, (nano)mechanical, and functional point of view; including in situ verification of physiological features with advanced spectroscopic and imaging techniques (vii) Design of polymeric micro/nano particles encapsulating natural-derived drugs for targeted and sustained release of their payload.

	We are looking for talented and motivated candidates, preferably with a Master Degree in Biomedical Engineering and with previous experience in the fields of biomaterials, nanotechnology, cell culturing and tissue

Skills and competencies for the development of the activity	engineering. In detail, the optimal candidate should have the following skills: - direct experience on in vitro cell experiments with biomaterials; - knowledge of biomaterials design and functionalization; - knowledge of rapid prototyping technologies. The candidate should also possess a good knowledge of the English Language in both written and oral forms. The PhD program includes a joint curriculum with Kansai Medical University, which involves a mandatory period of at least 12 months at the partner university. The position requires the activation of a cotutelle agreement with Kansai Medical University. The attainment of the PhD degree will be subject to meeting the minimum requirements for admission to the final examination at both institutions.