BIOENGINEERING AND MEDICAL-SURGICAL SCIENCES

DIMEAS - Design of experimental in vitro models recreating the alveolar tissue

Funded By	Dipartimento DIMEAS
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Context of the research activity	Integrating biology with novel engineering technologies and advanced materials is a key strategy for developing breakthrough approaches to solve unmet clinical needs and to respond to the societal need for more efficient treatments with low ethical and environmental impact. In this contest, in vitro experimental models are starting to be recognized as a powerful tool to study pathologies affecting the alveolar tissue and to testthe efficiency of new therapies.
	In vitro 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. So far, this breakthrough technology is not fully exploited, since most models fail to model the complexity of organs by mimicking the interplay between the different cell phenotypes found in vivo. For in vitro tissue modelling, the proper design of 3D matrixes that provide the structural and mechanical support to cell homing, growth and organization is a key aspect to stimulate and control the formation of a new functional tissue as well as to guide the differentiation of stem cells. By mimicking nature, the optimal 3D scaffolds should finely replicate in vitro the physico-chemical 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. This PhD programme will aim to the design of advanced in vitro models recapitulating the architecture and composition of physiological alveoli including also the key elements and actors of physiological processes, such as the vasculature and the immune system. Advanced models are a powerful tool to improve our knowledge on pathologies, furthermore they are an alternative to in vivo models for testing and design effective therapies to treat uncurable diseases as well as to predict the effect of potentially harmful agents. The Ph.D. student will be responsible for the processing of the biomaterials into 3D constructs via

Objectives	additive manufacturing techniques (such as melt-electrowriting, 3D bioprinting) and conventional techniques (such as electrospinning and replica molding). More in detail, the Ph.D. student will develop bioengineered alveolar models and validate them as a new platform to perform toxicology tests of several compounds and to study the development of alveolus-related pathologies. These final goals will be achieved through a bottom-up approach encompassing the following steps: (i) the 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 physico-chemical properties (e.g. mechanical properties, degradation kinetics), with the potential to meet the properties of different tissues of the human body; (ii) the 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 recapitulate targeted human tissues at different stages of ageing and/or pathology progression; (iii) the 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; (iv) the definition of cellular protocols to create an effective co-culture including several cell phenotypes to recreate the physiological composition of human tissues; (v) the validation of the designed bioengineered tissue models from a structural, mechanical and functional point of view; (vi) the development of pathological models to study the pathology onset and progression and (vii) the use of developed alveolar models to predict the toxicity of compounds (such as pollutants and mineral fibres).

Skills and competencies for the development of the activity	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, nanomedicine and tissue engineering. In detail, the optimal candidate should have the following skills: - direct experience on in vitro cell experiments with biomaterials; - knowledge of methods for nanoparticle preparation and polymer hydrogels - knowledge of rapid prototyping technologies.