BIOENGINEERING AND MEDICAL-SURGICAL SCIENCES

3D in vitro models for cytotoxicity testing

Funded By	Dipartimento DIMEAS FONDAZIONE CRT CASSA DI RISPARMIO DI TORINO [P.iva/CF:06655250014]
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Context of the research activity	The set-up of standardized and reliable preclinical characterization tools is becoming an urgent need to respond to the advancement of research in the biomedical, chemical, and pharmaceutical fields. This Ph.D. project aims at the design and validation of 3D bioengineered in vitro tissue and organ models as new approach methodologies to assess the cytotoxicity of chemical compounds (e.g., plasticizers, drugs) and implantable devices (e.g., prostheses) in a more relevant scenario.
	In vivo animal models currently represent the gold standard for medical device and chemical testing. However, they often fail in the proper replication of the real human physio-pathological scenario and their use is subjected to many ethical and economic concerns. Thus, there is an urgent need for Novel Approach Methodologies providing more reliable and robust methods to assess the cytotoxicity of chemical compounds (e.g., plasticizers, drugs) and implantable devices (e.g., prostheses) in a more relevant scenario. In this regard, the design of 3D bioengineered in vitro tissue/organ models represents a significant advancement, overcoming the limitations of already used models (e.g., poor repeatability and standardization), with additional advantages in terms of ethical and economic issues. In a recently emerging approach, the traditional tissue engineering/regenerative medicine principles are being explored to develop 3D tissue/organ models, which could work as useful tools to (i) screen among newly designed therapeutics, (ii) set-up

	patient-specific therapeutic protocols, (iii) elucidate fundamental aspects of cell functions, and (iv) assess the cytotoxicity of chemicals and medical devices. In this scenario, the proper design of the 3D matrix that provides 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 cell differentiation and cross-talk. By mimicking nature, the optimal 3D scaffold should finely replicate in vitro the physico-chemical and mechanical properties as well as the porous structure of the extracellular matrix of the native tissue, at different degrees of aging, in healthy or pathological conditions. Moreover, the degradation of the scaffold should match the rate of the specific tissue growth, without releasing toxic products. In order to design scaffolds with these properties, the selection of the raw materials and the scaffolding technology is a crucial issue to be addressed.
Objectives	This Ph.D. program has been conceived within this context and will be aimed at the design, characterization and validation of 3D bioengineered in vitro models of human tissues (i.e., cardiac and bone tissues) in different physio-pathological conditions and degrees of ageing to be applied as tools for the testing of chemicals and innovative therapeutic options. This Ph.D. research program will be conducted in the framework of the H2020 projects EVPRO (http://www.evpro-implant.eu/) and ALTERNATIVE (https://alternative-project.eu/), which aim to develop 3D bioengineered bone and cardiac tissue models to test newly-developed endoprostheses and chemicals. The European context in which this Ph.D. program will be conducted will provide the Ph.D. student with the opportunity to strongly collaborate with industrial and university/research partners with high experience in material design, biological testing, clinical translation of medical products, toxicity assessment, regulatory affairs. As a result, the research activities will be carried out in a highly market- and regulatory-driven framework, finally providing the Ph.D. student with critical sensitivity and high scientific scrupulousness. The developed bioengineered in vitro tools will represent reliable and predictive models allowing a reduction, refinement and replacement of the use of animals in research (3Rs principle). Thus, this Ph.D. program is completely in accordance with the newly adopted EU Directive on the protection of animals used for scientific purposes requiring that EU members increase their collaboration to follow the 3Rs principle. This Ph.D. program will be focused on the design and optimization of new polymeric biomaterials (of synthetic, natural or bioartificial origin) to be used as forming materials in the development of 3D scaffolds replicating the morphological and mechanical properties of the native tissue (bone and cardiac tissues) in different physio-pathological conditions and degrees of ageing. Scaffolds will be fabricated via advanced fabrication technologies (e.g., melt extrusion additive manufacturing, 3D bioprinting) and thoroughly characterized for their physico-chemical and biological properties. 3D bioengineered in vitro tissue models will be finally established by colonizing the 3D matrices with cells (e.g., an osteoblast/osteoclast co-culture, cardiomyocytes) and exploited to get new insights into tissue response to implanted devices and chemicals.

	The developed strategies are expected to significantly advance the biomedical field, contributing to the definition of a new material/technology platform, which, in principle, could answer to every specific need of researchers, patients, medical doctors, regulatory affairs, chemical and pharma companies. The acquired knowledge could be exploited also for the development of regenerative approaches in tissue engineering/regenerative medicine.

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 previous experience in biomaterial processing and characterization (natural/synthetic polymers), rapid prototyping (melt extrusion additive manufacturing, bioprinting), nanotechnology and tissue engineering. The candidate should possess a good knowledge of English Language and be available to work in our network of Labs in Alessandria and Turin, depending on the experimental needs.