BIOENGINEERING AND MEDICAL-SURGICAL SCIENCES

Advanced therapies by bioengineering tools

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 PhD student will develop new technologies for RNA-based therapies to counteract age-related and/or rare genetic diseases, making use of nanomedicine, biomaterial design and scalable additive manufacturing approaches, for improved therapeutic outcomes, such as release kinetics, efficacy and accessibility. The need for improved administration routes will be addressed by designing RNA-patches for skin/mucosa application or single implantation (through mini-invasive injection).
	Progressive aging of the world population increases the demand for new advanced approaches addressing the main health challenges of aged population, such as cancer and cardiovascular diseases. Furthermore, aged people are generally the most sensitive to infectious diseases, caused by bacteria and viruses. In this context, advanced RNA therapies have progressively attracted interest, particularly in the last years of Covid pandemic, due to their ability to rapidly provide new safe and effective protection (through mRNA-based vaccines) against newly arising virus variants. However, the interest in RNA-based therapies is also motivated by their potential wide range of applications, including the treatment of cancer and cardiovascular diseases. Through RNA therapies, cell behavior (i.e., gene expression) can be modulated to correct pathological mechanisms and re-establish a normal

Objectives	physiological functionality of cells/tissues, or immune response can be potentiated. However, the design of effective and safe RNA-delivery systems for successful clinical translation requires a multidisciplinary approach, with the contribution from bioengineering and medicine. In more detail, precise and personalized treatments are demanded, consisting of tailored drug-delivery systems, able to preserve RNA stability under storage and after in vivo administration, to allow their specific release to target cells (with the required kinetics) and to avoid off-target effects. Furthermore, efficacy of RNA-based delivery systems should be ideally combined with non-laborious, simple and scalable manufacturing methods for their production. Indeed this additional aspect may ensure easy accessibility of the future RNA-therapy to all patients. Additive-manufacturing production processes combine the possibility for custom-based design and scalability of the final drug delivery systems, thus representing a real innovation in the field, with the ambition to promote industrial development. Furthermore, due to the sensitivity of RNA molecules to degradation, mild processing conditions have to be optimized avoiding toxic solvents. Hence, the optimization of RNA-delivery systems demand for environmentally-friendly manufacturing processes. The development of RNA-based delivery systems for clinical translation should ensure: (i) process scalability; (ii) minimization of manufacturing steps; (iii) aseptic process; (iv) batch-to-batch consistency; (v) mild procedures; (vi) stability and (vii) preclinical validation following directives. Hence the PhD student will also be trained on these fundamental aspects. The research activity will cover 2 of the missions of the National Recovery and Resilience Plan (PNRR): 4. Education and research and 6. Healthcare. Nanomedicine, hydrogels and additive manufacturing approaches will be combined to achieve the following aims: (1) Design of RNA-loaded additive-manufactured patches, able to preserve RNA bioactivity, regulate their release kinetics, ensure a precision therapeutic effect, through a simple, non-laborious, non-expensive (i.e., easily accessible), reproducible and mini-invasive approach (Polito); (2) Study of regulatory requirements and sterilization methods (Polito); (3) Study of scale-up (Polito with possible collaboration with a foreign research center/company); (4) Proof-of-concept preclinical validation in models of the target human disease (Polito with possible collaboration with a foreign research center/company). The aim is to develop effective and accessible RNA-therapies to counteract age-related diseases, by accurate design of a new process ensuring limited final cost of the treatment for accessibility and improved efficacy. Other

	patients' need will be considered such as the need of improved administration routes, avoiding continuous and painful administrations by intravenous or intramuscular injections of nano-formulations, by designing RNA-patches for skin/mucosa application or single implantation (through mini-invasive injection).

Skills and competencies for the development of the activity	We are looking for talented and motivated candidates, preferably with skills/experience in: - Tissue engineering - Hydrogel based-additive manufacturing - Mechanical design - Nanomedicine - Image and data processing - In vitro validation Good communication skills and good knowledge of Written and Spoken English are required. The PhD student will work in a multidisciplinary team: team-working and willingness to learn new techniques/methods are required.