POLITECNICO DI MILANO

PhD in BIOINGEGNERIA / BIOENGINEERING - 39th cycle

PNRR 118 PNRR Research Field: DISEASE-SPECIFIC VESSEL-ON-CHIP FOR A PERSONALIZED ASSESSMENT OF THROMBUS FORMATION AND DRUG TESTING

Monthly net income of PhDscholarship (max 36 months)
€ 1400.0 In case of a change of the welfare rates during the three-year period, the amount could be modified.

Context of the research activity	
Motivation and objectives of the research in this field	Endothelium-blood interaction is key in the regulation of hemostasis and thrombosis. This project focuses on the complex interplay between blood and inflamed endothelium and its role in atherosclerosis. The aim of the work is to create a microfluidic chip lined with primary endothelial cells (ECs) and perfused by whole blood for the personalized assessment of thrombus formation and the evaluation of antithrombotic drugs. The microfluidic platform will allow: (i) to mimic both physiological (straight channels) and pathological vascular conditions (stenotic channels with different degrees of constriction) allowing to study the effect of disturbed hemodynamic on blood cells-endothelium interaction; (ii) to study the effect of endothelium dysfunction (obtained by treating EC with tumor necrosis factor) in vascular thromboinflammation; (iii) to test the efficacy of anticoagulant treatments in a patient specific vascular model; (iv) to study various forms of thrombosis, depending on the type of ECs lined in the chip. The advantages of the device are the possibility to create realistic vessel geometries mimicking human anatomy and physiology and the use of primary ECs combined with whole blood which provide a patient specific model allowing for personalized assessments.
Methods and techniques that will be developed and used to carry out the research	Task 1: A CAD software will be used to sketch the chip design, the negative of which will be created on a silicon wafer via photolithographic technique at PoliFAB facility.

	wafer via photolithographic technique at PoliFAB facility. Soft lithography will be used to obtain microfluidic chips primarily made of polydimethylsiloxane (PDMS) at MiMic lab. The needle technique will be performed to obtain hollow perfusable cylindrical microchannels embedded in a gel matrix. Straight channels and stenotic geometries will be designed and produced. Stenotic geometry will allow us to mimic the presence of an atherosclerotic plaque and to investigate its effect. This channel will be lined with endothelial cells (EC). The chip will also potentially allow co-culture of EC and other cell types (e.g., pericytes, smooth muscle cells), to better reconstruct the physiological microenvironment in vitro. Task 2: Human umbilical vein endothelial cells (HUVEC) will be seeded in the microfluidic chip. Once a confluent and tight endothelial cell monolayer will be achieved, blood will be perfused in the endothelialised channel lumen, at various flow rates, to mimic different physiological and pathological shear stress levels. Both healthy and inflamed endothelial phenotypes will be studied. Biological and functional assays will be employed (e.g., microscopy, RNA quantification). Task 3: Once the model will be validated with HUVEC, endothelial colony forming cells (ECFC) will be seeded and cultured in the microchannels, to obtain an individual-specific model. ECFC isolation and culture protocols will be learnt at Imperial College London. Blood withdrawn from the same donor of ECFC will be perfused in the channel. ECFC isolated from peripheral blood of patients affected by endothelial or coagulation dysfunction will retain the patient's phenotype, allowing for patient-specific studies to unravel disease mechanisms.
Educational objectives	The main educational objectives of the project are: - Learn the process of lab-on-chip design and microfabrication - Become an expert on ECFC isolation and culture - Learn to perform microfluidic experiments and drug testing with organ-on-chip technologies
Job opportunities	After finishing the PhD, the candidate could find job opportunities in biological research laboratories as expert

	of lab- and organ-chip technologies, at the academic level, thanks to the knowledge acquired in the mimicking of complex living systems, at pharma industry and CROs for the knowledge in advanced preclinical models and drug toxicity text without the use of animals.
Composition of the research group	1 Full Professors 1 Associated Professors 2 Assistant Professors 1 PhD Students
Name of the research directors	PROF SILVIA BOZZI

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Additional support - Financial aid per PhD student per year (gross amount)	
Housing - Foreign Students	--
Housing - Out-of-town residents (more than 80Km out of Milano)	--

Scholarship Increase for a period abroad	
Amount monthly	700.0 €
By number of months	6

National Operational Program for Research and Innovation	
Company where the candidate will attend the stage (name and brief description)	
By number of months at the company	0
Institution or company where the candidate will spend the period abroad (name and brief description)	Imperial College, Faculty of Medicine, National Heart & Lung Institute, Vascular Science Section
By number of months abroad	6

Additional information: educational activity, teaching assistantship, computer availability, desk availability, any other information
The PhD student will be involved in educational activities along with teaching assistantship. A shared desk and computer will be given to the student for the time needed to carry out the research.