



TEMPLATE RICHIESTA ATTIVAZIONE TOPIC AGGIUNTIVI SU FONDI PNRR

D.M. 9 aprile 2022 n. 351

Project title/Titolo del Progetto	Precision medicine in cardiovascular diseases: identification of cellular and molecular determinants of Heart Failure with Preserved Ejection Fraction
Principal Investigator	Gianluigi Condorelli
Main field of interest/Ambito principale di ricerca	Cardiovascular diseases – Precision Medicine
Abstract	Thanks to the increasing applications of single-cell analyses, cellular variety of the cardiovascular system at a single-cell level has just started to be appreciated by means of nucleic acid sequencing or tissue mass spectrometry. These technologies applied to cardiovascular diseases are contributing to a better understanding of the molecular mechanisms underlying them. For instance, we have applied single-cell sequencing for defining the spectrum of immune cells contributing to heart failure disease (Martini et al., Circulation 2019). Further preliminary data generated in our laboratory have highlighted the variety of cellular sub-phenotypes other than immune cells in the myocardial tissue and how they are modified during disease. By combining ATAC-seq and RNA-seq, we have also identified the main genes regulated by epigenetic mechanisms in the cardiac endothelial compartment. We plan to apply similar technologies for identifying the cellular diversity and the epigenetic-induced modifications of gene expression in models of HFpEF, a form of heart failure more frequent in women which is projected to be the prevalent one in the near future. This form of HF is also more dependent upon systemic diseases compared to HFrEF, typically related to myocardial infarction and decreased inotropic capacity. Thus, insulin resistance, obesity and hypertension are very frequently associated with this disease (Schiattarella et al., NCR 2022). How these risk factors influence the cellular composition of the heart in the context of HFpEF will be the subject of this doctoral proposal.
Type of Co-funding	<ul style="list-style-type: none"> ○ D.M. 351/2022 - Borse di dottorato per la transizione digitale
Lab name and address	Molecular cardiology; Building C
Brief description of the coherence of the Project in relation to the PNRR objectives ³	One of the aims of the PNRR is precision medicine. Our proposal fits 100% with this aim since the plan is to define at a cellular level a specific type of disease, generating knowledge which will help generate new diagnostic and therapeutic tools for HFpEF
N. of months abroad (min. 6, max. 18) [compulsory]	6-12
Name of the research institution/company abroad	Stanford University, Palo Alto (CA), USA; or King's College, London, UK; or UT Southwestern Medical Center, Dallas (TX), USA or Charité, University of Berlin, (DE).
N. of months of internship (min. 6, max. 18)	12-18



[compulsory only for D.M. 352/2022]	
Name of the company ³	
Scientific references	<p>Martini E, Kunderfranco P, Peano C, Carullo P, Cremonesi M, Schorn T, Carriero R, Termanini A, Colombo FS, Jachetti E, Panico C, Faggian G, Fumero A, Torracca L, Molgora M, Cibella J, Pagiatakis C, Brummelman J, Alvisi G, Mazza EMC, Colombo MP, Lugli E, Condorelli G,* Kallikourdis M*. Single cell sequencing of mouse heart immune infiltrate in pressure overload-driven heart failure reveals extent of immune activation. Circulation 2019 Dec 17;140(25):2089-2107. doi: 10.1161/CIRCULATIONAHA.119.041694.</p> <p>Schiattarella GG., Alcaide P, Condorelli G, Gillette TG, Heymans S, Jones EAV, Kallikourdis M, Lichtman A, Marelli-Berg F, Shah SJ, Thorp EB , Hill JA. Immunometabolic mechanisms of heart failure with preserved ejection fraction. Nature Cardiovascular Research, 2022; 1 (3): 211 DOI: 10.1038/s44161-022-00032-w</p>
Type of contract	<p>PhD scholarship of € 18.000 gross per year awarded by Humanitas University. This sum is exempt from IRPEF income tax according to the provisions of art. 4 of Law no. 476 of 13th August 1984, and is subject to social security contributions according to the provisions of art. 2, section 26 and subsequent sections, of Law no. 335 of 8th August 1995 and subsequent modifications.</p>