PI	*Gianluigi Condorelli*
PROJECT TITLE	Identification of epigenetic drugs for heart failure therapy through a single-cell sequencing approach
ABSTRACT	A key feature of heart failure (HF) is cardiac remodeling: a profound modification of myocardium, eventually resulting in dysfunction. The myocardium is composed of many cell types, including cardiomyocytes, endothelial and immune cells and fibroblasts. Recent advances in nucleic acid sequencing, such as single-cell sequencing, visual transcriptomics and molecular imaging, such as cellular mass spectrometry, has led to an appreciation of the complexity of cell types in tissues. Also epigenetics, which regulates gene expression, can be studied at the single-cell level. These allow us to study cell-cell interaction and the effects on myocardial remodeling and HF. Thus, our aim is to define the cellular characteristics of the myocardium in different types of HF, including primary cardiomyopathies, studying epigenetics and transcriptomics at a single-cell level and unravel the mechanisms of cell-cell interactions. Ultimately, we aim to identify drugs that improve cardiac function in HF.
FUNDING REFERENCE (AMOUNT, STARTING DATE AND DURATION)	*Ministero della Salute*: "Strategie di prevenzione primaria cardiovascolare nella popolazione italiana CV prevital" (2021-22) - €650.000 *Ministero della Salute:* Immune phenotyping in human heart failure: clinical correlates for potential therapeutic guidance. Italian Ministry of Health (€ 370.000) 2021-23
MAIN TECHNICAL APPROACHES TO CARRY OUT THE PRESENT PROJECT	Specific technologies include single-cell sequencing, spatial transcriptomics, ChIP sequencing tissue mass spectrometry, together with bioinformatics analyses.
SCIENTIFIC REFERENCES RELATED TO THE PRESENT PROJECT	Papait, R., Cattaneo, P., Kunderfranco, P., Greco, C., Carullo, P., Guffanti, A., Viganò, V., Latronico, MVG, Hasenfuss, G., Chen, J., **Condorelli, G**. (2013): Genome-wide analysis of histone marks identifying an epigenetic signature and promoters and enhancers underlying cardiac hypertrophy, **Proc. Natl. Acad. Sci. USA**, 110(50):20164-9 Greco CM, Kunderfranco, P., Rubino, M., Larcher, V., Carullo, P., Anselmo, A., Kurz, K., Carell, T., Angius, A., Latronico, MiVG, Papait, R., and **Condorelli G** (2016) DNA Hydroxymethylation controls cardiomyocyte gene expression in development and hypertrophy **Nature Comm**, 7:12418. doi: 10.1038/ncomms12418 Salvarani N, Crasto S, Miragoli M, Paulis M, Kunderfranco P, Forni A, Dal Ferro M, Sinagra G, Vezzoni P, Faggian G, Condorelli G*, Di Pasquale E: Lamin A/C mutations induce cardiac onduction defects through an epigenetically-mediated reduction of sodium currents: a study in a iPSC-derived model of cardiac laminopathy, **Nature Comm**, 2019 May 22;10(1):2267. doi: 10.1038/s41467-019-09929-w. Papait,S, Serio, S., Pagiatakis, C., Rusconi, F., Carullo, P., Mazzola, M., Salvarani, N., Miragoli, M., **Condorelli, G** (2017): Histone methyltransferase G9a is required for cardiomyocyte homeostasis and hypertrophy, **Circulation**, 2017 Aug 4. pii: CIRCULATIONAHA.117.028561, 136(13):1233-1246 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.