RESEARCH TOPIC MEM23

Deciphering the triangular axis of immune, cardiac and pregnancy-related disease via multi-omics analysis, as a path to improved personalized therapy

Curriculum MEM

Laboratory name
Adaptive Immunity Laboratory
Humanitas university

Pre-clinical Supervisor
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Abstract
Early work from our lab has shown that adaptive immunity is necessary for the tolerance of paternally-derived fetal antigens during pregnancy, without which mammals cannot reproduce (Aluvihare Nat Immunol 2004). In more recent work, we have shown that adaptive immunity is not adapted (in evolution) for conditions of cardiovascular stress, rendering T cells a key mediator of cardiovascular diseases (Kallikourdis Nat Comms 2017, Martini Circ 2019, Martini Circ Res 2020, Martini Front Immunol 2020, Cremonesi Circ 2023).
These mechanisms intersect during human pregnancy, in ways that drive a variety of cardiovascular physiopathological events. This project aims to decipher these mechanisms, using cutting-edge -omics techniques developed in the lab for the immunological analysis of cardiovascular disease: multi-parameter flow cytometry and Next Gen Sequencing, applied to human patients and disease models. As the lab is developing innovative immunotherapy techniques for the therapy of cardiovascular disease, the project is expected to generate insight to guide the development and application of personalized immunotherapy solutions for cardiovascular disease.

Main technical approaches
Experience with multi-parameter FACS, ELISA, immunohistochemistry and familiarity with bioinformatics analysis approaches (assisted by experts) are welcome skills, though training on all these will be provided.

Scientific references
1) Martini, Giugliano, Rescigno and Kallikourdis, 2020 Regulatory T Cells Beyond Autoimmunity: From Pregnancy to Cancer and Cardiovascular Disease Front Immunol. 11:509. doi: 10.3389/fimmu.2020.00509.

2) Aluvihare, Kallikourdis and Betz, 2004 Regulatory T Cells Mediate Maternal Tolerance to the Fetus. Nat Immunol 5, 266-271. doi: 10.1038/ni1037

3) Kallikourdis et al 2017 T cell costimulation blockade blunts pressure overload-induced heart failure. Nat. Commun. 8, 14680 doi: 10.1038/ncomms14680

4) Martini et al 2019 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

5) Cremonesi et al, 2023 Circulation (in press) Long COVID-19 cardiac complications are associated with autoimmunity to cardiac self-antigens sufficient to cause cardiac dysfunction.

Brief description of the coherence of the project in relation to the PNRR objectives

The project will provide immunophenotyping of cardiovascular ailments associated with gestation and the post-partum period, and thus it will help guide the application of novel cardio-immunotherapy solutions already being developed in the lab, in a patient- and/or disease-specific personalized manner.

N. of months abroad

6 months, at Kararigas Lab, Dept of Physiology, Faculty of Medicine, University of Iceland (Reykjavik)

Type of contract

PhD scholarship of € 18.000 gross per year awarded by Humanitas University on institutional funds and cofounded with PNRR funds under M.D.M. D.D. N. 118/2023.
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.

Borsa di dottorato pari a € 18.000 annui lordi erogata da Humanitas University su fondi istituzionali e fondi da D.M. 118/2023. Importo non soggetto a tassazione IRPEF a norma dell'art. 4 della L. 13 agosto 1984 n. 476 e soggetto, in materia previdenziale, alle norme di cui all'art. 2, commi 26 e segg., della L. 8 agosto 1995, n. 335 e successive modificazioni.