RESEARCH TOPIC MEM4

Immunological mechanisms underlying cardiovascular disease
Curriculum MEM

Laboratory name
Adaptive Immunity Laboratory, Humanitas University

Pre-clinical Supervisor
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Abstract
Adaptive immunity evolved enabling defense from pathogens and, in mammals, the necessary tolerance of paternally-derived fetal antigens during pregnancy. Adaptive immunity is thus mal-adapted for the conditions found after the reproductively active age of the female, when cardiovascular diseases are prevalent.
We recently found that T cells are required for the progression of Heart Failure (HF). By inhibiting T cells via a safe Rheumatoid Arthritis drug, we were able to treat HF, in a manner since hailed as paradigm-shifting and used for treatment of patients with tumor therapy-induced cardiotoxicity (Kallikourdis Nat Comms 2017; Martini Circulation 2019; Martini Circulation Res 2020; Martini Front Immunol 2020).

We are currently extending this work, by analyzing the immune profile of patients with a wide range of cardiovascular ailments, in the effort to map the link between adaptive immunity and cardiovascular disease progression. This includes Heart Failure patients, Coronary Artery Disease patients, tumor patients with cardiac side-effects arising from tumor therapy, and also women post-partum; the latter is an important cohort as post-partum the fetal tolerance-inducing immune changes are reverted, and this may create a window for cardiac symptom incidence.

In parallel, we are developing innovative ways to manipulate the link between adaptive immunity and cardiac disease for therapeutic purposes, in a series of novel immunotherapies for cardiac disease.

We seek a PhD student to work on the role of T cell responses in the cardiovascular diseases mentioned above.

Main technical approaches
The applicant should have some experience with multi-parameter FACS and ELISA. The project will also use Next Generation Sequencing, proteomics, Immunohistochemistry, and models of disease.

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) Salem et al, 2019 Abatacept for Severe Immune Checkpoint Inhibitor–Associated Myocarditis N Engl J Med 2019 DOI: 10.1056/NEJMc1901677

Type of contract

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.

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