



RESEARCH TOPIC MEM7
IMMUNOLOGICAL MECHANISMS OF TUMOR IMMUNOTHERAPY-INDUCED
CARDIOTOXICITY
Curriculum MEM Standard

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, 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 and oncological diseases are prevalent. This also applies to iatrogenic pathologies, such as tumor immunotherapy-induced cardiotoxicity, a novel but important problem. We found that T cells are required for the progression of Heart Failure (HF). By inhibiting T cells via a safe arthritis drug, we were able to treat HF, in a manner since hailed as paradigm-shifting and used for treating patients with tumor immunotherapy-induced cardiotoxicity. We seek a PhD student to help analyze T cell responses against the heart that can be triggered by cancer immunotherapy. The aims are i) decipher the mechanism/kinetics of this response, enabling cancer therapy management that reduces side-effects and ii) apply innovative immunotherapies already developed in our lab that may eliminate the side-effects. This may open up potential long-term clinical impact for tumors, heart disease, and multimorbidity.

Main technical approaches

The applicant should have experience in multi-parameter FACS and ELISA. The project will also use Next Generation Sequencing, -omics technologies, 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

Scholarship of € 21.000 gross per year awarded by Istituto Clinico Humanitas. This sum is subject to IRPEF income tax and exempt from social security contributions.

Borsa di studio pari a € 21.000 annui lordi erogata da Istituto Clinico Humanitas. Importo soggetto a tassazione IRPEF ed esente da contribuzione previdenziale.