



RESEARCH TOPIC MECM_8

Innovative Strategies for Modulating Immune Tolerance in Autoimmune Hepatitis: Antigen-Specific Tregs and Nanoparticle-Enhanced Liver Delivery

Curriculum

MECM Clinical

Research Area

Immuno

Laboratory name

Hepatobiliary Immunopathology Lab.

Research Supervisor

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Abstract

Autoimmune hepatitis (AIH) is a chronic autoimmune liver disease characterized by impaired regulatory T cells (Tregs) and a breakdown of immune tolerance, leading to progressive liver inflammation and damage. Current therapies rely on corticosteroids and immunosuppressants, which are associated with significant side effects and limited efficacy. The overarching objective of this project is to develop innovative, antigen-specific strategies to modulate immune tolerance and transform the treatment landscape for AIH. The selected resource will characterize the phenotype of T-cell responses at the single-cell level, with a focus on defining regulatory T-cell stability by assessing Treg-specific demethylated regions and performing single-cell chromatin accessibility assays. Leveraging the identification of antigenic protein subsets in AIH patients, we will generate antigen-specific induced Tregs (iTregs) and evaluate their capacity to suppress immune responses and restore immune tolerance in vitro. In addition, the resource will support the generation of a murine model of type 1 AIH to facilitate mechanistic studies and therapeutic validation. In collaboration with the Mario Negri Institute, we will test a nanoparticle-based system for the targeted induction of iTregs within the liver in murine models of liver disease. In summary, this research aims to achieve localized, antigen-specific immune modulation, thereby minimizing systemic immunosuppression and improving patient outcomes.

Main technical approaches

Flow Cytometry, T cell culture, regulatory T cell induction, single-cell sequencing.

Scientific references

1. Akamatsu 2019 - [10.1126/sciimmunol.aaw2707](https://doi.org/10.1126/sciimmunol.aaw2707)
2. [10.1016/j.autrev.2024.103591](https://doi.org/10.1016/j.autrev.2024.103591)



3. Lapierre 2013 - 10.1002/hep.26023

4. 10.1136/gutjnl-2020-322362

Type of contract

PhD scholarship of € 22.400 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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