3.3.9 MicroRNA Regulation of Immune Tolerance, Autoimmunity and Cancer Group

COMPOSITION

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STRATEGIC OBJETIVES

- Our laboratory is interested in understanding the cellular and molecular mechanisms of immune tolerance, autoimmunity and cancer. Specifically, we focus on studying how microRNAs (miRNAs) and their target genes regulate immune tolerance, autoinmune diseases and antitumor immunity. In addition, we are actively developing innovative genome engineering strategies for therapeutic purposes.
- MicroRNAs have recently emerged as important factors in the post-transcriptional control of protein concentrations in metazoan organisms. For the past few years, we studied the functions of miRNAs in the mammalian immune system. We identified the first miRNA that regulates B cell tolerance and established its causative role in the development of lethal autoimmunity (González-Martín et al, Nature Immunology, 2016 Apr; 17: 433-40). We also discovered critical roles for other microRNAs in different immune tolerance mechanisms and autoimmune diseases (González-Martín and Lai et al, Nature Communications, 2016 Aug 2; 7:12207, Ichiyama et al, Immunity, 2016 Jun 21; 44:1284-98 and Liu et al, Journal of Experimental Medicine, Aug 22; 213:1901-19). In addition, we developed the first B cell receptor reprogramming strategy using the latest genome editing technologies (Elife, 2019 Jan 17; 8). Previously, work on tumor immunology established an important role for the chemokine receptor CCR5 in T cell antitumor responses (González-Martín et al, Cancer Research, 2011 Aug 15; 71:5455-66). Overall, our studies have established miRNAs as critical regulators of immune tolerance and autoimmunity, and revealed new mechanisms controlling antitumor immunity.
- Current research in the laboratory continues to identify and study the roles of miRNAs and their target genes in immune tolerance, autoimmunity and tumor immunology by combining genetic, genomic, biochemical, and functional screen approaches to understand the functions and molecular mechanisms of miRNA control at molecular, cellular, and system levels. The mechanisms identified might provide valuable biomarkers or therapeutic targets for the treatment of autoimmune diseases and for cancer immunotherapy.

RESEARCH LINES

- Identification of miRNAs and target genes that regulate B lymphocyte tolerance and study of their potential role in the development and progression of autoimmune diseases, with the aim of identifying new therapeutic targets for the treatment of these diseases.
- Identification of new therapeutic targets to improve the efficacy of cancer immunotherapy.
- B-lymphocyte genome engineering for the development of cellular vaccines.

RESEARCH ACTIVITY

Final Degree Theses

- **Villadangos Reyes L.** Regulation of B cell activation by microRNAs[dissertation]. *Madrid: UAM: 2023(29/05/2023). Director: González Martín A.*

Research projects

- **González Martín A.** Systematic analysis of tumor-specific B cell immunity (CNS2022-136069). AEI. 2023-2025. *Managment centre: UAM*
- **González Martín A.** Harnessing microRNAs for improved lung cancer immunotherapies. Fundación Ramón Areces. 2023-2026. *Managment centre: UAM*
- **González Martín A.** MicroRNA regulatory networks in B cell tolerance and autoimmunity (PID2021-128244OB-I00). AEI. 2022-2025. *Managment centre: UAM*
- **González Martín A.** Harnessing microRNAs for improved lung cancer immunotherapies. Fundación FERO. 2023-2026. *Managment centre: UAM*
- **González Martín A.** B cell engineering in murine and human primary B cells (OPP11839562019). Bill and Melinda Gates Foundation. 2019-2024. *Managment centre: UAM*

Patents and trademarks

- **Voss J, Huang D, González-Martín A, Andrabi R, Burton D, inventors; The Srcipps Research Institute, assignees.** B Cell receptor modification in B cells. PCT/US/45255. 2018 August 3