

1

Introduction

2

Executive
summary

3

Research
areas
and groups

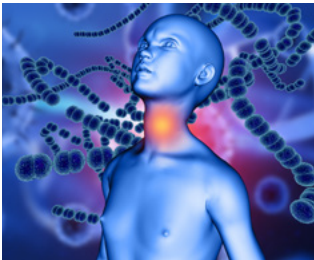
4

Associated
clinicians



3.3.9 MicroRNA Regulation of Immune Tolerance, Autoimmunity and Cancer

Publications: 1 | Q1: 1



COMPOSITION

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STRATEGIC OBJECTIVES

- 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, autoimmune diseases, and antitumor immunity. In addition, we are actively developing innovative genomic engineering strategies for therapeutic purposes.
- MicroRNAs have recently emerged as important factors in the post-transcriptional control of protein concentrations in metazoan organisms. In recent years, we have studied the functions of miRNAs in the mammalian immune system. We identified the first miRNA that regulates B cell tolerance and established its causal role in the development of lethal autoimmunity (González-Martin et al., Nature Immunology, 2016 Apr; 17: 433–40). We also discovered critical roles for other microRNAs in different mechanisms of immune tolerance and autoimmune diseases (González-Martin 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). Furthermore, we developed the first B-cell receptor reprogramming strategy using the latest genome editing technologies (Elife, 2019 Jan 17; 8). Previous work on tumor immunology established an important role for the chemokine receptor CCR5 in T-cell antitumor responses (Gonzalez-Martin et al, Cancer Research, 2011 Aug 15; 71: 5455–66). Overall, our studies have established that microRNAs are critical regulators of immune tolerance and autoimmunity, and have revealed novel mechanisms that control antitumor immunity.
- Current research in the laboratory continues to identify and study the functions of microRNAs (miRNAs) and their target genes in immune tolerance, autoimmunity, and tumor immunology by combining genetic, genomic, biochemical, and functional screening approaches to understand the molecular functions and mechanisms of miRNA control at the molecular, cellular, and system levels. The identified mechanisms could 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 effectiveness of cancer immunotherapy.
- B-cell genome engineering for the development of cell-based vaccines.

RESEARCH ACTIVITY

Master Theses

- **Tapia Narváez JC.** The role of microRNAs in the regulation of immune tolerance and autoimmunity[dissertation]. Madrid: UAM: 2025(26/06/2025). Director: González Martín A.

Final Degree Theses

- **Calderón Sacristán R.** Caracterización funcional de miRNAs y sus genes diana en inmunidad antitumoral[dissertation]. Madrid: UAM: 2025(26/06/2025). Director: González Martín A.

Publications

- **Mastrangelo A, Robles-Vera I, Mañanes D, Galán M, Femenia-Muñia M, Redondo-Urzainqui A, Barrero-Rodríguez R, Papaioannou E, Amores-Iniesta J, Devesa A, Lobo-González M, Carreras A, Beck KR, Ivarsson S, Gummesson A, Georgiopoulos G, Rodrigo-Tapias M, Martínez-Cano S, Fernández-López I, Nuñez V, Ferrarini A, Inohara N, Stamatelopoulos K, Benguría A, Cibrián D, Sánchez-Madrid F, Alonso-Herranz V, Dopazo A, Barbas C, Vázquez J, López JA, González-Martin A, Nuñez G, Stellos K, Bergström G, Bäckhed F, Fuster V, Ibañez B, Sancho D.** Imidazole propionate is a driver and therapeutic target in atherosclerosis. Nature. 2025; 645(8079): 254–61. Article. IF: 56.1; D1

Research projects

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

Patents and trademarks

- **Gonzalez-Martin A, González-Molina MdP, inventors; UAM, assignee.** MicroRNAs for use in the stimulation of T-cell anti- tumor response. PCT/EP2024/064900; EP24728247. 2024 May 30
- **Voss J, Huang D, Gonzalez-Martin A, Andrabi R, Burton D, inventors; The Scripps Research Institute, assignees.** B Cell receptor modification in B cells. WO2019028417A1-PCT/US/45255. 2018 August 3.