



## Magali IRLA, PhD

Group leader:

Immune tolerance and T-cell differentiation

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## Background

I obtained a PhD in Immunology under the supervision of Dr. Nguyen (TAGC, Marseille). I studied a gene expressed by thymic epithelial cells (TECs) and developed an approach of gene delivery into the thymus.

I performed my post-doctoral studies in the laboratory of Pr. Reith at the University of Geneva in Switzerland. I made seminal discoveries on the development of medullary TECs that control central tolerance. I also studied the interplay between pDC and Foxp3<sup>+</sup> Treg during CNS autoimmunity.

I was then awarded junior group leader at the University of Geneva where I studied the topology of the thymic medulla.

I obtained a CR1 Inserm position and joined the group of Dr. Ferrier, then of Pr. Naquet, where I continued leading my own projects on thymus biology. In 2016, I obtained the habilitation thesis (HDR).

I settled my own research group at the CIML in 2021.

## Awards

- 2019-2022 PEDR - Inserm
- 2019 Laureate of the French National Academy of Medicine
- 2015-2019 Marie Curie Career Integration Grant
- 2014 Installation Award - City of Marseille
- 2012 Young Investigator Award - International Cytokine Society (ICS)
- 2011 Young Investigator Award - French Society for Immunology (SFI)
- 2010 Biogen-Dompé Award - Swiss Multiple Sclerosis Society
- 2006-2007 EMBO long-term fellowship
- 2004 Laureate of Innovact Awards for European Innovation

## Membership

Member of the French Society of Immunology (SFI)

Member of the International Cytokine Society (ICS)

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## Main achievements

- During my post-doc, I found that pDCs, via their ability to promote the selective expansion of myelin-antigen-specific Tregs, confer a natural protection against the development of Experimental Autoimmune Encephalomyelitis (EAE), a mouse model of multiple sclerosis.
- I also showed that the cellularity of Aire<sup>+</sup> mTECs, responsible for central tolerance, is controlled by self-reactive CD4<sup>+</sup> thymocytes. As junior group leader, I further established, by developing an automated method, called FOR3D (Full organ reconstruction in 3D), that self-reactive CD4<sup>+</sup> thymocytes regulate the complex organization of the thymic medulla.
- I found that lymphotoxin  $\alpha$  (LT $\alpha$ ) expressed by self-reactive CD4<sup>+</sup> thymocytes controls the entry of peripheral DCs into the thymus by regulating CCR2 ligands in mTECs. This LT $\alpha$ -regulated fine-tuning mechanism substantially controls the efficiency of clonal deletion.
- I identified RANKL as a therapeutic cytokine to boost thymic regeneration and *de novo* T-cell production. Given the potential clinical benefit of RANKL to ameliorate T-cell recovery in patients with thymic injury, I deposited an international patent (WO/2018/154122).

## Selected publications

- Carron MJ\*, [Irla M\\*](#), Sergé A, Soudja SM, Marie JC. Transforming Growth Factor-beta signaling in  $\alpha\beta$  thymocytes promotes negative selection. **Nat Commun.** 2019 Dec 19;10(1):5690. \*Equal contribution.
- Lopes N, Charaix J, Cédile O, Sergé A, [Irla M\\*](#). Lymphotoxin  $\alpha$  fine-tunes T cell clonal deletion by regulating thymic entry of antigen-presenting cells. **Nat Commun.** 2018 Mar 28;9(1):1262. \*Corresponding author.
- Lopes N, Vachon H, Marie J, [Irla M\\*](#). Administration of RANKL boosts thymic regeneration upon bone marrow transplantation. **EMBO Mol Med.** 2017 Jun;9(6):835-851. \*Corresponding author.
- Emre Y, [Irla M](#), Dunand-Sauthier I, Ballet R, Meguenani M, Jemelin S, Vesin C, Reith W, Imhof B. Thymic epithelial cell expansion through matricellular protein CYR61 boosts progenitor homing and T-cell output. **Nat Commun.** 2013;4:2842.
- [Irla M](#), Kupfer N, Benkhoucha M, Lalive P, Suter T, Fontana A, Reith W, Hugues S. MHC class II restricted antigen presentation by plasmacytoid dendritic cells inhibits T-cell mediated autoimmunity. **J Exp Med.** 2010 Aug 30;207(9):1891-905.
- [Irla M](#), Hugues S, Gill J, Nitta T, Hikosaka Y, Williams IR, Hubert FX, Scott HS, Takahama Y, Holländer GA, Reith W. Autoantigen-specific interactions with CD4<sup>+</sup> thymocytes control mature medullary thymic epithelial cell cellularity. **Immunity.** 2008;29(3):451-63.