

**Internship Proposition**  
**(one page max)**

**Master 2 GP Immunology & ImmunIntervention (I<sup>3</sup>)**  
**2026-2027**



**Lab: CR2TI**

**Team: 2A**

**Name and position of the supervisor: Carole Guillonneau, PhD, Director of Research**

**Email of the supervisor: [carole.guillonneau@univ-nantes.fr](mailto:carole.guillonneau@univ-nantes.fr)**

**Candidate (if internship filled):**

**Title of the internship: Impact of AIRE deficiency on CD4<sup>+</sup> and CD8<sup>+</sup> regulatory T cell development and function**

**Summary of the internship proposal:**

The establishment of immune tolerance relies on complementary mechanisms of central and peripheral tolerance that prevent the emergence of autoreactive lymphocytes. The transcription factor AIRE (Autoimmune Regulator) plays a pivotal role in central tolerance by promoting the expression of tissue-restricted antigens in the thymus, thereby enabling the deletion of autoreactive T cells. Mutations in AIRE cause Autoimmune Polyendocrine Syndrome Type 1 (APECED), a rare but severe autoimmune disease characterized by multi-organ immune-mediated damage. While the contribution of AIRE to negative selection is well established, its impact on the development and function of regulatory T cells (Tregs), which represent a critical second layer of immune tolerance, remains incompletely understood.

Our laboratory has a long-standing interest in immune tolerance and regulatory T cells, with a particular focus on CD8<sup>+</sup> Tregs, whose therapeutic potential is currently being evaluated in an ongoing Phase I clinical trial in kidney transplantation. In parallel, our group generated and characterized an Aire-deficient rat model reproducing key features of APECED (Ossart et al., JI 2018; Besnard et al., JCI 2022), providing a unique platform to investigate mechanisms of autoimmune disease and tolerance restoration.

The recent generation of Foxp3-GFP Aire-deficient rats now offers an unprecedented opportunity to study regulatory T cells *in vivo*. The objective of this Master 2 internship is to perform the first comprehensive characterization of CD4<sup>+</sup> and CD8<sup>+</sup> Tregs in this model. The student will compare Treg populations from Aire-deficient and control rats in the thymus, blood, spleen and lymph nodes using multiparameter spectral flow cytometry. Particular attention will be given to markers associated with Treg activation, fitness and survival, including the CD25/IL-2 signaling axis.

Functional analyses will include Treg isolation by cell sorting and assessment of suppressive activity in *ex vivo* assays. Depending on progress, the project may be extended to the analysis of Treg distribution in peripheral tissues and their responsiveness to IL-2 stimulation.

Form to be sent by email to : [gpi3@univ-nantes.fr](mailto:gpi3@univ-nantes.fr)

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This project will provide fundamental insights into how defects in central tolerance affect the biology of CD4<sup>+</sup> and CD8<sup>+</sup> regulatory T cells and may identify mechanisms contributing to immune dysregulation in APECED and related autoimmune diseases.

Option(s) linked to the project:

- Clinical Research Profile (Recherche Clinique)
- Data Analyst Profile (Recherche et Analyse de Données Omiques)
- Experimental Biology Profile (Recherche Expérimentale)