Internship Proposition
(one page max)

Master 2 GP Immunology & ImmunoIntervention (I^3)
2025-2026

Lab: CR2TI (INSERM UMR 1064)

Team: équipe 2a

Name and position of the supervisor: Dr Matthieu Giraud

Email of the supervisor: matthieu.giraud@inserm.fr
Candidate (if internship filled):

Title of the internship:

Control of self-antigen expression for T cell selection in the thymus

Summary of the internship proposal:

Epithelial cells of the thymus medulla (mTECs) possess the unique ability to express the self, *i.e.*, a wide array of self-proteins, also known as tissue-specific antigens (TSAs). This expression within the thymus enables the maturation of T lymphocytes and the elimination of self-reactive clones, thereby preventing the development of autoimmune diseases. A single protein, Aire (Autoimmune Regulator), has been shown to induce the expression of a subset of TSAs in mTECs. However, the factors responsible for the expression of a remaining very large fraction of TSAs remain unknown. Recent work from the laboratory, using epigenetic approaches, has identified a new set of transcription factors that could play a major role in the ability of mTECs to express these TSAs.

The M2 student will investigate the involvement and effects of these transcription factors in driving TSA expression using two complementary strategies. First, a CRISPR activation (CRISPRa) system will be implemented in a mTEC cell line expressing KRAB-dCas9 by lentiviral delivery of sgRNA constructs targeting the transcription factors of interest. High-throughput RNA sequencing (RNA-seq) will be performed on RNA extracted from infected and control mTECs to quantify TSA induction and assess the impact of these factors on mTEC maturation.

Second, an ex vivo model using primary rat mTECs already engineered to stably express dCas9 will be used. This system allows for both CRISPRa and CRISPR interference (CRISPRi) approaches and offers a more physiological context than immortalized cell lines. It provides a unique opportunity to evaluate transcriptional regulation of TSA expression in primary cells that retain key features of thymic epithelial identity.

This project addresses one of the most fundamental questions in immunology—how self-antigen expression is induced in the thymus to establish immune tolerance. It offers an ideal framework for a motivated Master's student (M2) interested in immunology, combining molecular engineering, transcriptomics, and primary cell biology to dissect a central mechanism of immune self-recognition.

Option(s) linked to the project:
☐ Clinical Research Profile (Recherche Clinique)
☐ Data Analyst Profile (Recherche et Analyse de Données Omiques)
X Experimental Biology Profile (Recherche Expérimentale)

Form to be sent by email to : gpi3@univ-nantes.fr