



**Lab: CR2TI**

**Team: 4**

**Name and position of the supervisor: HAN-YEE-YU Jérôme, PhD student**

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**Candidate (if internship filled):**

**Title of the internship: Galectins as Biomarkers and Therapeutic Targets to Prevent Fibrosis After Kidney Transplantation**

**Summary of the internship proposal:**

**Scientific Context.** Galectins are proteins characterized by their capacity to bind Beta-galactoside pattern through their linking domain to carbohydrates. Interestingly, galectins-1, -3, and -9 are overexpressed by the kidney tubular epithelial, mononuclear cells and macrophages, notably in case of inflammation or tissue injury. These galectins are implicated in both inflammation resolution and organ fibrosis, notably because of their capacity to activate the TGF- $\beta$  cellular pathway through nuclear retention of transcription factors SMAD2 and SMAD3. Because of the particular setting of transplantation, combining organ injury, calcineurin inhibitor use and tolerance, galectins-1, -3 and -9 are overexpressed in recipients and might be responsible for graft fibrosis, a major cause of kidney transplant loss.

**Objectives:** This research internship intends to explore the link between galectins-1, -3 and -9 overexpression after kidney transplantation and the apparition of graft fibrosis. Initially, we will investigate if recipients with fibrosis detected on graft biopsy present high expression of galectins on circulating mononuclear cells using flow cytometry. Then, we will determine if this expression correlates with galectins expression on kidney transplant biopsy, especially with intense fibrosis. Finally, with the use of available inhibitors, we will test if galectin inhibition has an impact on epithelial-to-mesenchymal transition of kidney epithelial cells cultured with pro-fibrotic macrophages (using commonly used markers such as morphology, loss of E-cadherin, and production of collagen I).

**Methods:** Isolation and culture of human mononuclear cells from peripheral blood; Flow cytometry to assess phenotype; ELISA for galectins secretion; Confocal histopathological analysis. Clinical samples from healthy volunteers and kidney transplant recipients from the DIVAT biocollection will be used.

**Expected Outcomes.** To assess if galectins expression on circulating mononuclear cells is associated with kidney transplant fibrosis. To evaluate the impact of galectin inhibition on the relationship between macrophages and kidney epithelial cells. To provide argument for a future *in vivo* model testing galectins inhibitor in kidney transplant fibrosis.

Option(s) linked to the project:

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