Internship Proposition
(one page max)
Master 2 GP Immunology & ImmunoIntervention (I^3)
2024-2025

Lab: CR2TI

Team: 2 "Cell and gene engineering in tolerance, fertility and regenerative medicine"

Name and position of the supervisor: Séverine Bézie, Associate researcher

Email of the supervisor: severine.bezie@univ-nantes.fr

Candidate (if internship filled):

Title of the internship: Identification of peptides for selective expansion of CD8⁺Tregs.

Summary of the internship proposal:

Cell therapy using autologous and polyclonal CD8⁺Tregs has been shown to be effective in preclinical models of human skin graft allogeneic rejection and xenogeneic GvHD in humanized NSG mice and is about to be evaluated in a phase 1/2a safety clinical trial in kidney transplant patients (*1*). Identifying antigens specifically recognized by CD8⁺ Tregs would make it possible to track these cells in patients (using dextramers), to monitor the disease and therefore to adjust treatments; to selectively expand CD8⁺Tregs *ex vivo* and improve cell therapy efficacy while reducing side effects; and selectively expand CD8⁺Tregs *in vivo* in patients as a peptide-based treatment (*2–4*). We previously identified two MHC-derived allopeptides cross-recognized by CD8⁺Tregs in tolerant grafted rats, allowing tracking the alloreactive CD8⁺Tregs and inducing allograft specific tolerance (*5*, *6*).

The overall objective of the stage is to identify peptides that could be used for tolerogenic vaccination in transplant patients. This requires skills in flow cytometry and cell culture, as well as immunology knowledge of T cell development, thymic selection and Tregs.

Aim 1 is to design a library of peptides on frequently mismatched MHC sequences in transplantation that can be presented by predominant MHC class I molecules using prediction software (no need for special computer skills).

Aim 2 is to identify peptides specifically recognized by CD8⁺Tregs. PBMCs will be cultured for 5 days in presence of each single peptide, and analyzed for the expression of activation markers on Tregs and Tconv by flow cytometry.

Aim 3 is to assess the capacity of peptides to clonally expand CD8⁺Tregs *ex vivo*. Tregs will be isolated by FACS and cultured for 3 weeks with CpG-matured autologous APCs, and will be compared for their proliferation yield and suppressive activity.

1. *S. Bézie et al., Front. Immunol. **8**, 2014 (2017).*
2. *S. Bézie et al., Blood Adv. **3**, 3522–3538 (2019).*
3. *É. Picarda, J. Ossart, S. Bézie, C. Guillonneau, Médecine Sci. MS. **31**, 22–24 (2015).*
4. *E. Picarda, I. Anegon, C. Guillonneau, Immunotherapy. **3**, 35–37 (2011).*
5. *E. Picarda et al., J. Clin. Invest. **124**, 2497–2512 (2014).*
6. *E. Picarda et al., Cell Rep. **29**, 4245-4255.e6 (2019).*

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)

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