institut cochin
CENTRE DE RECHERCHE

Post-Doc position

Title of the project:
Immunology of Diabetes

DeAR Lab R. Mallone & S. You

RESEARCH PROJECT

The Postdoc will work on a project entitled “Resetting self-tolerance in autoimmune diabetes by pro-resolving mediators derived from apoptotic cell efferocytosis”. Type 1 diabetes (T1D) is a chronic autoimmune disease resulting from the selective destruction of insulin-secreting pancreatic β-cells by autoreactive T lymphocytes. We hypothesize that administration of pro-resolving mediators, issued from apoptotic cell phagocytosis by macrophages (called efferocytosis), may constitute a promising strategy for controlling the dysregulated immune responses characteristic of T1D. Our research program will use both the non-obese diabetic (NOD) mouse model and samples from T1D patients. Our first objective is to assess the capacity of NOD macrophages to produce pro-resolving mediators after apoptotic cell efferocytosis. A strong focus will be brought on immunomodulatory cytokines and lipid subclasses (lipidomic approach). The second objective is to evaluate the therapeutic effect of the pro-resolving mediators in autoimmune diabetes (NOD mouse model). Third, production of human pro-resolutive factors from T1D and healthy subjects will be compared to identify biomarkers of T1D.

• **Activities**: The Postdoc will design and set up the *in vitro* and *in vivo* experiments required for the progression of the project: treatment and follow-up of mice, production of samples for lipidomic analysis, flow cytometry, functional T cell assays.

• **Knowledge**: A strong expertise in immunology research is required and previous experience in multiparametric flow cytometry, cell culture and animal (mouse) experiments is preferred. Fluent English, written and spoken.

• **Professional skills**: The candidate must be highly motivated and use creative thinking in the resolution of scientific questions. He/she will be able to adapt to rapidly evolving technologies and will have a broad interest for biomedical research. He/she will need to give proof of independent thinking and writing skills and capacity to undertake responsibility as project leader. It is essential that the candidate can work autonomously and as part of a team.

• **Education**: MD/PhD or PhD in biological sciences.

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STRUCTURE D'ACCUEIL/LOCATION

The **DeAR Lab** is part of the **Team « Immunology of Diabetes »** of the Cochin Institute located in central Paris. **The Cochin Institute** is one of the largest biomedical French Research Center that provides a multidisciplinary scientific environment and state-of-the-art core facilities. It is affiliated with the French National Institute for Health and Medical Research (INSERM), the Paris Descartes University, the CNRS and the Assistance Publique/Hôpitaux de Paris.

The **DeAR Lab** is associated with the Clinical Department of Diabetology of the Cochin Hospital. It belongs to different international consortia such as the European IMI2 Innodia (www.innodia.eu) and the Network for Pancreatic Organ Donors (nPOD; www.jdrfnpod.org). Our research interest focuses on the understanding of the immune pathogenesis of type 1 diabetes (T1D), the discovery of new biomarkers and therapeutic tools, using both human and mouse experimental systems.

We offer a stimulating and productive lab environment of young researchers with strong team spirit. This is an excellent career opportunity, as the candidate will have a senior role within the Laboratory and interact with several international collaborators.

For further information about our Laboratory: www.dearlab.org

For further information about our institute: www.institutcochin.fr

CONTRAT/FINANCIAL SUPPORT

Type: Temporary position **Funding:** ANR

Beginning: January 2018

Duration of contract: 12-month contract renewable for up to 30 months.

POUR POSTULER/HOW TO APPLY?

Applicants should send their CV, list of publications, a summary of previous research experience and the names of two references to Sylvaine You and Roberto Mallone:

sylvaine.you@inserm.fr, Roberto.mallone@inserm.fr

Recent publications:

1) Besançon A, Goncalves T, Valette F, Salling-Dahllöf M, Mandrup-Poulsen T, Chatenoud L and You S. Oral histone deacetylase inhibitor synergizes with T-cell targeted immunotherapy to preserve beta cell metabolic function and induce stable remission of new-onset autoimmune diabetes in NOD mice. *Diabetologia***.** 2017.

2) Besançon A, Baas MC, Goncalves T, Valette F, Waldmann H, Chatenoud L and You S**.** The induction and maintenance of transplant tolerance engages both regulatory and anergic $CD4^+$ T cells. *Frontiers Immunol***.** 2017.

3) Pérol L, J.M. Lindner, P. Caudana, N. Nunez, A. Baeyens, A. Valle, C. Sedlik, D. Loirat, O. Boyer, A. Créange, J.L. Cohen, U.C. Rogner, J. Yamanouchi, M. Marchant, X.C. Leber, M. Scharenberg, P. Santamaria, M.-C. Gagnerault, R. Mallone, M. Battaglia, A. Hartemann, E. Traggiai, E. Piaggio. Loss of immune tolerance to IL-2 in type 1 diabetes. *Nat Commun*, 2016.

4) Baas MC, Besançon A, Goncalves T, Valette F, Yagita H, Sawitzki B, Volk HD, Waeckel-Enée E, Rocha B, Chatenoud L and You S. TGFβ-dependent expression of PD-1 and PD-L1 controls $CD8^+$ T cell anergy in transplant tolerance. *Elife*. 2016.

5) Culina S, Gupta N, Boisgard R, Afonso G, Gagnerault MC, Dimitrov J, Østerbye T, Justesen S, Luce S, Attias M, Kyewski B, Buus S, Wong FS, Lacroix-Desmazes S, Mallone R. Materno-Fetal Transfer of Preproinsulin Through the Neonatal Fc Receptor Prevents Autoimmune Diabetes. Diabetes. 2015.

6) Gupta N, Culina S, Meslier Y, Dimitrov J, Arnoult C, Delignat S, Gangadharan B, Lecerf M, Justesen S, Gouilleux-Gruart V, Salomon BL, Scott DW, Kaveri SV, Mallone R, Lacroix-Desmazes S. Regulation of immune responses to protein therapeutics by transplacental induction of T cell tolerance. *Sci Transl Med*. 2015.

7) Baas MC, Kuhn C, Valette F, Mangez C, Segovia-Duarte M, Hill M, Besançon A, Chatenoud L, Cuturi MC and You S. Combining autologous dendritic cell therapy with CD3 antibodies promotes regulatory T cells and permanent islet allograft acceptance. *J Immunol*. 2014.

8) Scotto M, Afonso G, Østerbye T, Larger E, Luce S, Raverdy C, Novelli G, Bruno G, Gonfroy-Leymarie C, Launay O, Lemonnier FA, Buus S, Carel JC, Boitard C, Mallone R. HLA-B7-restricted islet epitopes are differentially recognized in type 1 diabetic children and adults and form weak peptide-HLA complexes. Diabetes. 2012.