institut cochin
CENTRE DE RECHERCHE

Post-Doc position

Title of the project:
Immunology of Diabetes

DeAR Lab R. Mallone & S. You

PROJET/RESEARCH PROJECT

The Postdoc will work on a project entitled “Identifying T-cell responses against viral epitopes and their potential cross-reactivity with islet autoantigens”. T lymphocytes are key effectors in the autoimmune destruction of insulin-producing pancreatic beta cells. Environmental factors play a dominant role over genetic predisposition, yet these factors remain elusive. We will be examining the potential role of viral infections and mechanisms thereof, with a particular focus on the cytotoxic effects directly exerted on beta cells and/or on triggering of autoimmune T cells through viral amino acid sequences sharing homology with beta-cell epitopes. The ultimate goal is to establish whether a causal relationship between viral infections and beta-cell autoimmunity may exist, and to gain information to guide the development of preventative vaccines.

• **Activities**: The Postdoc will design and set up experiments as required for the progression of the project. Candidate epitopes are identified using mass spectrometry-based peptidomics techniques. He/she will validate these candidates for their (cross)recognition by T cells from T1D and healthy subjects, using different T-cell assays based on flow cytometry, HLA tetramers, T-cell cloning and in vitro functional assays. He/she will use this information to formulate novel hypotheses and to test them using both T-cell and beta-cell culture systems.

• **Knowledge**: A strong expertise in multiparametric flow cytometry, cell sorting, cell culture and previous experience in immunology research is preferred. Fluent English, written and spoken. Applications not fulfilling these criteria will not be considered.

• **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.

HR EXCELLENCE IN RESEARCH
Inserm
cnrs
UNIVERSITÉ PARIS DESCARTES

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: Juvenile Diabetes Research Foundation

Beginning: January 2018

Duration of contract: 12-month contract renewable for up to 5 years.

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 Roberto Mallone and Sylvaine You:

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