

## Proposition de sujet de thèse

### **Leishmania cure and immune response associated**

#### **Renseignements relatifs à l'Equipe :**

Nom de l'Equipe d'Accueil : Mort cellulaire Programmée et Signalisation

Nom et prénom du responsable : ESTAQUIER Jérôme

Qualité du responsable : DR INSERM

Téléphone : 0142864136 Télécopie :

Courriel : jerome.estaquier@parisdescartes.fr

#### ***Contenu scientifique du programme de la thèse***

Our research focus on molecular mechanisms associated with programmed cell death in the context of microbe infections. The specificity of our research lies in upstream research aimed at elucidating the molecular mechanisms involved in the process of PCD associated with immune cells, and downstream research studying these mechanisms in vivo in non-human primates (NHP). In particular we have developed a model of Leishmania infection in NHPs, which is the first model developed in Europe. Using this model, we are assessing the dynamics of innate and adaptive immunity in relationship with the dissemination of Leishmania in lymphoid and non-lymphoid organs during both the acute and chronic phases of infection. Despite drug therapy, it has been shown in Humans that parasites persist leading to parasite relapse in particular in region of poverty or in immunosuppressed individuals such as Aids. In particular, we are interest to determine the role of microbiota in such context. Therefore, the main objective of this proposal is to determine the impact of drugs on parasite dissemination in deep tissues, immune response related to exhaustion and cell death, and evaluated novel strategy based on immunotherapy.

#### **Publications récentes de l'équipe :**

Laforge M, Silvestre R, Rodrigues V, Garibal J, Campillo-Gimenez L, Mouhamad S, Monceaux V, Cumont MC, Rabezanahary H, Pruvost A, Cordeiro-da-Silva A, Hurtrel B, Silvestri G, Senik A, Estaquier J. The anti-caspase inhibitor Q-VD-OPH prevents AIDS disease progression in SIV-infected rhesus macaques. *J Clin Invest.* 2018 Apr 2;128(4):1627-1640

Rodrigues V, Cordeiro-da-Silva A, Laforge M, Silvestre R, Estaquier J. Regulation of immunity during visceral Leishmania infection. *Parasit Vectors.* 2016 Mar 1;9:118.

Moreira D, Rodrigues V, Abengozar M, Rivas L, Rial E, Laforge M, Li X, Foretz M, Viollet B, Estaquier J, Cordeiro da Silva A, Silvestre R. Leishmania infantum modulates host macrophage mitochondrial metabolism by hijacking the SIRT1-AMPK axis. *PLoS Pathog.* 2015 Mar 4;11(3):e1004684.

Rodrigues V, Laforge M, Campillo-Gimenez L, Soundaramourty C, Correia-de-Oliveira A, Dinis-Oliveira RJ, Ouaiissi A, Cordeiro-da-Silva A, Silvestre R, Estaquier J. Abortive T follicular helper development is associated with a defective humoral response in Leishmania infantum-infected macaques. *PLoS Pathog.* 2014 Apr 24;10(4):e1004096.

Rodrigues V, Cordeiro-da-Silva A, Laforge M, Ouaiissi A, Akharid K, Silvestre R, Estaquier J. Impairment of T cell function in parasitic infections. *PLoS Negl Trop Dis.* 2014 Feb 13;8(2):e2567.