Postdoctoral position:

Laboratory: Cardio-thoracic research center of Bordeaux. INSERM U1045 headed by Pr. Marthan

Team: Bronchial Remodelling headed by Pr. Berger

Contacts: Pr Berger: patrick.berger@u-bordeaux.fr and Dr.Trian: thomas.trian@u-bordeaux.fr

Grant: 1-year post-doctoral position renewable 2 times for a potential total of 3 years

Salary: from 2087€ to 2305€ net of charges depending on the candidate experience

Starting date: September 2017

Research project:

Asthma is a chronic and frequent respiratory disease that affects about 8% of the population. Severe asthmatic patients are still a real public health issue because they are largely insensitive to therapeutics, responsible for more than 90% of the cost of the disease, and almost 1000 deaths a year. In these patients, bronchial remodeling including, in particular, an increase of the bronchial smooth muscle (BSM) mass is present. This BSM remodeling appears crucial since it is associated with both lung function decline and high number of asthma exacerbations.

The team is a world leader evaluating the mechanisms of the BSM remodeling in severe asthma. We have previously demonstrated the role of mitochondrial biogenesis in this remodeling and particularly the initial calcium homeostasis alteration within the BSM cell from severe asthmatics (Trian *et al*. J Exp Med 2007). Recently, we have also demonstrated a dysfunction of the p53 protein involved in this mitochondrial dysregulation (Trian *et al*. JACI 2016). Along the same way, we performed a study in non-severe asthmatic patients showing that both the size of the BSM and the excess of mitochondria were prognostic factors in the fate of the disease (Girodet *et al*. AJRCCM 2015). Finally, we evaluated the effect of gallopamil in severe asthmatic patients in a clinical trial showing a decrease in the BSM size and in the number of exacerbations (Girodet *et al*. AJRCCM 2015). However, although these studies validate the therapeutic potential of targeting asthmatic mitochondria, additional knowledge must be obtained.

This project aims to explore more widely this mitochondrial dysfunction within the BSM based on both bronchial samples of asthmatic / non-asthmatic patients and innovative animal models in order to highlight new therapeutic targets.

Our team received a grant from the national medical research foundation (FRM) to complete this project with a 3-years post-doctoral grant.

Postdoctoral profile:

The applicant should have some expertize in primary cell culture, molecular biology and cellular biology. Calcium knowledge, virology and animal experience will be a plus.

5 main publications of the team since the last 2 years:

1. House dust mites induce proliferation of severe asthmatic smooth muscle cells via an epithelium-dependent pathway.

TRIAN T, ALLARD B, DUPIN I, Carvalho G, OUSOVA O, MAURAT E, Bataille J, THUMEREL M, Begueret H, GIRODET PO, MARTHAN R, BERGER P.

Am J Respir Crit Care Med 2015, 2015, 191 (5): 538-546. Recommandé par la "Faculty of 1000".

2. A Double-Blind, Placebo-Controlled Trial of Gallopamil for Severe Asthma.

GIRODET PO, DOURNES G, THUMEREL M, Begueret H, Dos Santos P, Ozier A, DUPIN I, TRIAN T, MONTAUDON M, LAURENT F, MARTHAN R, BERGER P.

Am J Respir Crit Care Med 2015, 191 (8): 876-883.

3. Blood fibrocytes are recruited during acute exacerbations of chronic obstructive pulmonary disease through a CXCR4 dependent pathway.

DUPIN I, ALLARD B, Ozier A, MAURAT E, OUSOVA O, Delbrel E, TRIAN T, Bui HN, Dromer C, Guisset O, Blanchard E, Hilbert G, Vargas F, THUMEREL M, MARTHAN R, GIRODET PO, BERGER P.

J Allergy Clin Immunol 2016, 137(4): 1036-1042.

4. Bronchial smooth muscle remodeling in non-severe asthma.

GIRODET PO, ALLARD B, THUMEREL M, Begueret H, DUPIN I, OUSOVA O, MAURAT E, Ozier A, TRIAN T, MARTHAN R, BERGER P.

Am J Respir Crit Care Med 2016, 193(6): 627-633. Recommandé par la "Faculty of 1000".

5. CT evaluation of small pulmonary vessels area in patients with COPD with severe pulmonary hypertension.

COSTE F, DOURNES G, Dromer C, Blanchard E, Freund-Michel V, GIRODET PO, MONTAUDON M, Baldacci F, Picard F, MARTHAN R, BERGER P*, LAURENT F*. *co-dernier auteur

Thorax 2016, 71(9): 830-837.

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