Title of the PhD project: Exploration of immune alterations in myositis
Disciplines: Immunology
Laboratory: EA4130 (Pr Miossec), Immunogénomique & Inflammation
Doctoral school: Interdisciplinary Doctoral program in health-sciences (EDISS) - ED 205

Description
Scientific background and rationale:
The focus of the group is to better understand the pathogenesis of chronic inflammatory/autoimmune diseases that affect joints and muscles. In particular, we are interested in the role of autoantibodies specifically associated with myositis in the immunopathogenesis of these autoimmune diseases. Various autoantibodies are detected in the sera of patients with myositis, and some of them are closely associated with clinical manifestations of the disease. One of them, the anti-MDA5 antibody, is specifically found in a subgroup of myositis characterized by various skin manifestations and complicated with rapidly progressive interstitial lung disease. We observed that patients positive for anti-MDA5 antibody and under corticotherapy display infections exclusively found in a context of profound immunosuppression. Interestingly, MDA5 is a cytosolic pathogen recognition receptor involved in the early host response to pathogens.

Aim:
The objective of the PhD project is to evaluate the functional innate and adaptive immune system of patients positive for anti-MDA5 antibodies with whole-blood stimulation systems and to investigate the role of MDA5 targeted antibodies in the status of immunosuppression observed in patients under corticotherapy.

Description of the project methodology:
To address these questions, we will use whole-blood assays for assessing innate and adaptive immune responses of patients with anti-MDA5 antibodies. These assays include a broad array of immune stimuli, including agonists specific for defined innate immunity sensors, various cytokines and activators of T cell immunity. The responses of cells to these stimuli will be subsequently evaluated by multiplex protein immunoassay. By this way, we will compare functional immune responses of patients with anti-MDA5 positive myositis, before and after treatment, and with functional responses obtained from patients with anti-MDA5 negative myositis, and healthy subjects. The PhD candidate will investigate the molecular and cellular mechanisms involved in the observed changes.

Expected results:
The PhD student will have the opportunity to work with an interdisciplinary and highly motivated team of scientists and clinicians. He/She will have opportunities in acquiring fundamental knowledge in Immunology as well as technological and conceptual skills. Publication of the research results in international journals of high impact factor is strongly expected.

Perspectives:
The goal of this project is to apply the knowledge generated through fundamental approaches to biomarker discovery and the design of novel therapeutic strategies in the field of autoimmune results.

Skills required:
A successful candidate will hold a Master’s degree in immunology, or cell biology. Candidates who already have research experience are also welcome to submit their applications. Experiences in cell tissues and human cell culture will be a plus.

Bibliography:
- Tournadre A Lenief V, Eljaafari A, Miossec P. Immature muscle precursors are a source of interferon-β in myositis: role of Toll-like receptor 3 activation and contribution to HLA class I up-regulation. Arthritis Rheumatism, 2012; 64: 533-41

Key-words: Myositis, autoimmune disease, autoantibody, Th17 cells, dendritic cells

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