PhD Position - 3 years - Starting Fall 2021

Title: Role of self-nucleic acids as danger signals activating the STING signaling pathway in pulmonary disorders

Abstract:

Idiopathic pulmonary fibrosis (IPF), the most severe interstitial lung disease, is a devastating pathology caused by repeated alveolar epithelium injury and characterized by dysregulated alveolar repair leading to lung scarring. IPF has unknown causes even if it often develops in smokers or former smokers. According to the World Health Organization, **chronic obstructive pulmonary disease** (COPD) is the third leading cause of death worldwide. Repeated exposure to cigarette smoke is the main cause of chronic pulmonary inflammation and emphysema, a major complication of COPD characterized by alveolar walls destruction. COPD and IPF are irreversible and current treatments display limited efficacy. The immunological events leading to these pathologies are not well understood.

Our CNRS team led by Dr Isabelle Couillin aims to decipher the physiopathological mechanisms of these diseases. We study danger signals (endogenous molecules released following tissue damage), sensors and signaling pathways involved during lung sterile inflammatory processes. We previously identified uric acid and ATP as danger signals activating the NLRP3 inflammasome, leading to the maturation and secretion of interleukin (IL-) 1β, an essential cytokine in fibrotic processes.

This thesis project focuses on the role of **self-nucleic acids** as activators of innate signaling pathways such as cGAS-STING and its connections with type I and III interferons production. Our recent publications using mouse models showed that while STING enhances cigarette smoke-induced acute inflammation, it displays protective effect against pulmonary fibrosis. The PhD student will perform in vivo and in vitro experiments to investigate the mechanisms of STING-dependent responses. He/she will address the cell types involved as well as the contribution of type III interferon. Translational aspects related to STING pathway in human IPF/COPD will be covered through the analyses of patient samples.

Funding: The 3-year doctorate will be funded by a "University of Orleans" grant obtained by the PhD supervisor.

Starting date: Fall 2021 at CNRS INEM laboratory, Orleans, France
https://www.univ-orleans.fr/fr/inem

Supervision: The PhD will be performed under the supervision of Dr Nicolas Riteau and co-supervision of Isabelle Couillin.

Candidate Profile: The applicant should have a strong background in immunology and/or cell biology. Prior experiences with in vivo mouse studies and flow cytometry/imaging and/or

molecular biology will be favored. However, motivation and willingness to learn will be a critical determinant. Excellent written and communication skills in English is a requirement.

How to apply: Interested and motivated students should send a CV, a cover letter, master scores/ranking and reference letters to: Nicolas.riteau@cnrs-orleans.fr +33238255443. Note that all applications must be uploaded on ADUM.fr

References:

Protective Role of the Nucleic Acid Sensor STING in Pulmonary Fibrosis. Savigny F, Schricke C, Lacerda-Queiroz N, Meda M, Nascimento M, Huot-Marchand S, Da Gama Monteiro F, Ryffel B, Gombault A, Le Bert M, Couillin I and Riteau N. Front Immunol. 2021 PMID: 33488589

B-Cell Activating Factor Secreted by Neutrophils Is a Critical Player in Lung Inflammation to Cigarette Smoke Exposure. Nascimento M, Huot-Marchand S, Gombault A, Panek C, Bourinet M, Fanny M, Savigny F, Schneider P, Le Bert M, Ryffel B, Riteau N, Quesniaux VFJ, Couillin I. Front Immunol. 2020 PMID: 32849550

Self-DNA release and STING-dependent sensing drives inflammation to cigarette smoke in mice. Nascimento M, Gombault A, Lacerda-Queiroz N, Panek C, Savigny F, Sbeity M, Bourinet M, Le Bert M, Riteau N, Ryffel B, Quesniaux VFJ, Couillin I. Sci Rep. 2019 PMID: 31619733