

EuReCa International PhD Program
PhD thesis project
2022 Call for application

**Studying the role of lung resident myeloid cells
in the response to radiation**

General information

Call	2022
Reference	2022-09-LONDONO_FOUILLADE
Keyword(s)	Lung fibrosis; Myeloid cells; Single cell analyses; Spatial transcriptomics; Cell-cell interaction

Director(s) and team

Thesis director(s)	Arturo Londoño-Vallejo & Charles Fouillade
Research team	DNA repair, radiations and innovative cancer therapies
Research department	UMR 3347/U1021 - Signaling, Radiobiology and Cancer

Description of the PhD thesis project

The team has been working on radiation-induced pulmonary fibrosis for several years and has introduced state-of-the-art technologies such as single cell (sc) RNAseq and single molecule (sm) FISH to the study of the cellular and molecular mechanisms that lead to failure in the regeneration response of the irradiated lung. We use a well characterized mouse mode, have sequenced almost half a million lung cells and collected data corresponding to several time points after irradiation under conditions that lead (or not, as a control) to irreversible lung fibrosis.

We have also access to human specimens of irradiated lungs, which should allow us to facilitate results extrapolations. Our data has revealed previously unrecognized events affecting capillary endothelial cells. We have also data pointing to fibrosis-specific response involving resident macrophage cells. Specifically, transcriptional signatures can be detected involving both inflammatory and anti-inflammatory pathways, as well as the implication of ligand production that potentially target other cell types.

In this project, we will use available genetically modified mice to determine the role of lung resident myeloid populations in response to radiation.

We propose to:

- i) characterise, by scRNAseq analysis, the molecular alterations induced by radiation in the different subsets of lung myeloid cells
- ii) map, by smFISH-based spatial transcriptomic approaches, interesting subsets of lung macrophages or dendritic cells that may play a role in the development of radiation-induced pulmonary fibrosis
- iii) select, from the scRNAseq data, putative interactions between resident myeloid cells and other lung cell types that will be validated by in vitro functional assays.

International, interdisciplinary & intersectoral aspects of the project



The research project encompasses bioinformatics and immunology with clinical perspectives. The applicant, with the help of bioinformatician of the team and collaboration with image analysis specialists will develop his/her computational skills to analyse single cell RNAseq data and spatial transcriptomic images. The student will benefit from international collaborations with experts on the roles of macrophages in radiation-induced toxicities. They will mentor the student all along the three years and short visits to acquire specialised techniques to analyse macrophages will be possible. In addition, the student will be exposed to industrial projects through funded collaborations of the team with industrial partners in the field of radiation oncology.

Recent publications

1. PD-L1high AT2 cells: a new player for alveoli regeneration. **Fouillade C, Londoño-Vallejo A**. Eur Respir J. 2021 Nov 4;58(5):2101417. doi: 10.1183/13993003.01417-2021. Print 2021 Oct. PMID: 34737193
2. Evidence that SARS-CoV-2 Induces Lung-Cell Senescence: Potential Impact on COVID-19 Lung Disease. Lipskaia L, Maisonnasse P, **Fouillade C**, Sencio V, Pascal Q, Flaman JM, Born E, **Londoño-Vallejo A**, Le Grand R, Bernard D, Trottein F, Adnot S. Am J Respir Cell Mol Biol. 2021 Oct 14. doi: 10.1165/rcmb.2021-0205LE. Online ahead of print. PMID: 34648725
3. Spatial transcriptomics for respiratory research and medicine. Curras-Alonso S, Soulier J, Walter T, Mueller F, **Londoño-Vallejo A, Fouillade C**. Eur Respir J. 2021 Jul 29;58(1):2004314. doi: 10.1183/13993003.04314-2020. Print 2021 Jul. PMID: 33833036
4. FLASH Irradiation Spares Lung Progenitor Cells and Limits the Incidence of Radio-induced Senescence. **Fouillade C**, Curras-Alonso S, Giuranno L, Quelennec E, Heinrich S, Bonnet-Boissinot S, Beddok A, Leboucher S, Karakurt HU, Bohec M, Baulande S, Vooijs M, Verrelle P, Dutreix M, **Londoño-Vallejo A**, Favaudon V. Clin Cancer Res. 2020 Mar 15;26(6):1497-1506. doi: 10.1158/1078-0432.CCR-19-1440. Epub 2019 Dec 3. PMID: 31796518

Expected profile of the candidate

The ideal, highly motivated, candidate will have bioinformatics skills as well as some molecular and/or cell biology training. The applicant will show dedication and initiative as well as ability to interact in a highly interdisciplinary environment. Previous knowledge and/or experience on immune cell biology or tissue regeneration will be a plus.

