

IC-3i International PhD Program
PhD thesis project
 2017 Call for application



Study of Lung Regeneration after Radiotherapy

General information

Call	2017
Reference	2016-12-LONDONO-VALLEJO
Keyword(s)	Single-cell RNA-seq, Stem cell, Telomere, Senescence, Tissue regeneration

Director(s) and team

Thesis director(s)	José-Arturo Londono-Vallejo
Research team	Telomeres and Cancer
Research department	UMR 3244 - Dynamics of Genetic Information

Description of the PhD thesis project

Radiotherapy is one of the main therapeutic option in cancer treatment. The major drawback of this technique is the toxicity induced by irradiation to the surrounding healthy tissue that, once damaged, may lead to severe complications (e.g. pulmonary fibrosis). Tissue regeneration in response to radiotherapy remains poorly studied, particularly in the case of lung regeneration after thoracic irradiation.

To understand how lung regenerates after radiotherapy and how irradiation may alter the regenerative capacity paving the way to fibrosis, we propose in this project to i) identify by single-cell RNAseq the stem/progenitor cells that proliferate after irradiation to support lung regeneration ii) investigate the implication of dysfunctional telomere and/or persistent DNA damages in this stem/progenitor compartment iii) evaluate, using the p16-3MR transgenic mice which allow tracking, sorting and killing of senescent cells in vivo, the role of senescent cells present in the lung in the months following irradiation.

This project will give the PhD fellow a solid foundation in bioinformatics analysis as well as molecular biology. She/he will benefit from collaborations with radio-oncologists from Curie Hospital and international mentors in the field of senescence.

International, interdisciplinary & intersectoral aspects of the project

International:

The host laboratory benefits from established international collaborations, more specifically with Dr Marco Demaria (ERIBA, Netherlands) and with Prof. Judith Campisi (Buck Institute, USA). The PhD fellow will visit Dr Demaria's lab to acquire the know-how to study the p16-3MR mice. Prof. Campisi will mentor the PhD student and give advices on the senescence research strategy.

Interdisciplinary:

The research project encompasses bioinformatics and biology with clinical perspectives.

Intersectoral:

The laboratory will have exchanges with companies developing single-cell technologies, in particular those providing devices and material to Institut Curie.

Recent publications

1. Verlingue L, Dugourd A, Stoll G, Barillot E, Calzone L, **Londoño-Vallejo A.**

A comprehensive approach to the molecular determinants of lifespan using a Boolean model of geroconversion.

Aging Cell. 2016 Sep 9. doi: 10.1111/ace.12504

2. Schertzer M, Jouravleva K, Perderiset M, Dingli F, Loew D, Le Guen T, Bardoni B, de Villartay JP, Revy P, **Londoño-Vallejo A.**

Human regulator of telomere elongation helicase 1 (RTEL1) is required for the nuclear and cytoplasmic trafficking of pre-U2 RNA.

Nucleic Acids Res. 2015 Feb 18;43(3):1834-47. doi: 10.1093/nar/gku1402.

3. Castro-Vega LJ, Jouravleva K, Ortiz-Montero P, Liu WY, Galeano JL, Romero M, Popova T, Bacchetti S, Vernot JP, **Londoño-Vallejo A.**

The senescent microenvironment promotes the emergence of heterogeneous cancer stem-like cells.

Carcinogenesis. 2015 Oct;36(10):1180-92. doi: 10.1093/carcin/bgv101.

4. Episkopou H, Draskovic I, Van Beneden A, Tilman G, Mattiussi M, Gobin M, Arnoult N, **Londoño-Vallejo A**, Decottignies A.

Alternative Lengthening of Telomeres is characterized by reduced compaction of telomeric chromatin.

Nucleic Acids Res. 2014 Apr;42(7):4391-405. doi: 10.1093/nar/gku114.

5. Le Guen T, Jullien L, Touzot F, Schertzer M, Gaillard L, Perderiset M, Carpentier W, Nitschke P, Picard C, Couillault G, Soulier J, Fischer A, Callebaut I, Jabado N, **Londono-Vallejo A**, de Villartay JP, Revy P.

Human RTEL1 deficiency causes Hoyeraal-Hreidarsson syndrome with short telomeres and genome instability.

Hum Mol Genet. 2013 Aug 15;22(16):3239-49. doi: 10.1093/hmg/ddt178.

Expected profile of the candidate

We are looking for a highly motivated candidate with bioinformatics skills as well as some molecular and/or cell biology training. Previous knowledge and/or experience on stem cell biology or tissue regeneration will be a plus.

Dedication, initiative, as well as ability to interact in a highly interdisciplinary environment will be much appreciated.