Postdoctoral Position in Computational Biology and Digestive Disease Immunology

Location: CRTI INSERM1064, Nantes, France
Date posted: JULY 2021
Application deadline: NOVEMBER 2021

The Martin's lab is seeking a talented **computational scientist** for a postdoctoral fellowship to study **the cellular and molecular heterogeneity and functions of mononuclear phagocytes in human digestive diseases** using high dimensional **single-cell technologies.**

General context

The objective of the Martin's lab is to harness the power offered by **new single-cell technologies** to deconvolute the **role and regulation of mononuclear phagocytes** in pathogenic responses driving tissue lesions in patients affected by digestive diseases. Our ultimate goal is to enhance the **rational for future drug and biomarker** discovery. In particular the clinical benefit of targeted immunotherapy in **IBD and gastric cancer** has remained limited to a subset of patients and the use of standard of care imaging and/or histological diagnostic assays has failed to confidently stratify potential responders from non-responders. Accordingly, none of the targeted immunotherapy approved to treat patients are provided with decision algorithms to maximize therapeutic responses. Besides, the poor understanding of disease pathophysiology significantly limits the identification of relevant targets. There is therefore an urgent need to gain a **better understanding of the cellular programs in normal and lesional human digestive tissues**.

Project

The applicant will be involved in leading the **computational analysis** in two funded projects aiming at characterizing **MNP molecular programs and cellular interactions** in tissues from patients with **ileum Crohn's disease**, or with **gastric precancerous and cancerous lesions**. Using state-of-the art machine-learning and exploratory data analysis tools, the study will dissect **single-cell RNA sequencing, single-cell ATACseq** and **spatial transcriptomics** datasets. It will combine profiling microenvironments in healthy and diseased tissues with analysis of **Electronic Medical Records**. Both projects involve close interactions with Gastrointestinal clinicians, pathologists and gut immunologist in Nantes (bi-monthly meetings in the context of the Nantes IBD-NeXT cluster for instance (https://next-isite.fr/ibd-next/).

In Crohn's disease our main objective is to characterize how pathogenic MNP populations drive resistance to current targeted therapies and contribute to stenotic complications through their interactions with stromal cells. This project is in direct follow-up of our previous study, which described the **MNP-organized GIMATS** response in patients resisting anti-TNF antibodies (Martin JC, Cell, 2019).

In gastric cancer, our main objective is to understand **how the MNP molecular landscape is progressively shaped to promote tumor growth** along the **stepwise progression of precancerous lesions to tumor**. This is a new project funded by ARC, which benefits from a unique cohort of patients built at CHU de Nantes.

Martin's lab people involved in these projects:

- **Gaelle Beriou,** PhD - permanent research engineer
- **Lucas Bruselle:** research technician
- **Thomas Laurent:** PhD student
- **Nicolas Chapelle:** MD (digestive oncologist) - PhD student
- **Pr Tamara Matysiak-Budnik:** MD-PhD (digestive oncologist) – Attending Physician

International scientific collaborators on these projects:

- MNP biology: Pr Miriam Merad (Icahn School of Medicine at Mount Sinai, New York, NY)
- Computational biology: Dr Ephraim Kenigsberg (Icahn School of Medicine at Mount Sinai, New York, NY)

Required Qualifications:

- The applicant must have a PhD or MD/PhD (or equivalent) with a track record demonstrating expertise in data-analysis, in particular scRNAseq and scATACseq
- Experience in mucosal immunology is a plus
- The ideal candidate will demonstrate scientific imagination, intellectual creativity, rigor, and a history of working well in teams.
- Excellent proficiency in scientific writing and communication is required

Postdoc Appointment Term:

- Two years
- Start Date: November 1, 2021 (negotiable)
- Applications will be accepted until the position is filled
- Anticipated start date is Fall 2021 but is flexible

Required Application Materials:

- Curriculum vitae
- A cover letter describing experience and research interests to be pursued during training
- One lead-author published or unpublished manuscript
- Names of two references

Contact:

Applications need to be addressed at Dr Jerome Martin: jerome.martin@univ-nantes.fr

Recent publications

Martin JC, Chang C, Boschetti G, Ungaro R, Giri M, Grout JA, Gettler K, Chuang LS, Nayar S, Greenstein AJ, Dubinsky M, Walker L, Leader A, Fine JS, Whitehurst CE, Mbow ML, Kugathasan S, Denson LA, Hyams JS, Friedman JR, Desai PT, Ko HM, Laface I, Akturk G, Schadt EE, Salmon H, Gnjatic S, Rahman AH, Merad M, Cho JH, Kenigsberg E. Single-Cell Analysis of Crohn's Disease Lesions Identifies a Pathogenic Cellular Module Associated with Resistance to Anti-TNF Therapy. **Cell. 2019** 5;178(6):1493-1508

Merad M & **Martin JC**, Pathological Inflammation in Patients With COVID-19: A Key Role for Monocytes and Macrophages, **Nat Rev Immunol 2020** 20(6):355-362

Martin JCJ, Bériou G, Heslan M, Chauvin C, Utriainen L, Aumeunier A, Scott CL, Mowat A, Cerovic V, Houston SA, Leboeuf M, Hubert FX, Hémont C, Merad M, Milling S, and Josien J. **Mucosal Immunol. 2014**. 7(1):101-113

Martin JC, Baeten DL and Josien R. Clin**. Immunol. 2014**. 154 (1):1-12

Martin JC, Beriou G and Josien R. **Methods Mol Biol. 2016** 1371:197-203

Martin JC, Beriou G, Heslan M, Bossard C, Jarry A, Abidi A, Hulin P, Ménoret S, Thinard R, Anegon I, Jacqueline C, Lardeux B, Halary F, Renauld JC, Bourreille A and Josien R. **Mucosal Immunol. 2016** 9(2):539-49

Martin JC*, Wolk K*, Bériou G, Abidi A, Witte-Händel E, Louvet C, Kokolakis G, Drujont L, Dumoutier L, Renauld JC, Sabat R**, Josien R**. **J Immunol. 2017** 198(9):3671-3678

Abidi A, Laurent A, Bériou G, Bouchet-Delbos L, Fourgeux C, Louvet C, Triki-Marrakchi R, Poschmann1* J, Josien R*, **Martin JC*.** Characterization of Rat ILCs Reveals ILC2 as the Dominant Intestinal Subset. **Front Immunol 2020** 11:255

Collaborations

Belarif L, Danger R, Kermarrec L, Nerrière-Daguin V, Pengam S, Durand T, Mary C, Kerdreux E, Gauttier V, Kucik A, Thepenier V, **Martin JC**, Chang C, Rahman A, Guen NS, Braudeau C, Abidi A, David G, Malard F, Takoudju C, Martinet B, Gérard N, Neveu I, Neunlist M, Coron E, MacDonald TT, Desreumaux P, Mai HL, Le Bas-Bernardet S, Mosnier JF, Merad M, Josien R, Brouard S, Soulillou JP, Blancho G, Bourreille A, Naveilhan P, Vanhove B, Poirier N. IL-7 receptor influences anti-TNF responsiveness and T cell gut-homing in inflammatory bowel disease, **J Clin Invest. 2019** 2;129(5):1910-1925

Lee JY, Hall JA, Kroehling L, Wu L, Najar T, Nguyen HH, Lin WY, Yeung ST, Moura Silva H, Li D, Hine A, Loke P, Hudesman D, **Martin JC**, Kenigsberg E, Merad M, Khanna KM, Littman DR. Serum Amyloid A Proteins Induce Pathogenic TH17 Cells and Promote Inflammatory Disease. **Cell. 2020** 180(1):79-91.

Uzzan M, Corcos O, **Martin JC**, Treton X, Bouhnik Y, Why is SARS-CoV-2 infection more severe in obese men? The gut lymphatics - lung axis hypothesis, **Medical Hypotheses 2020** 144:110023 (IF: 1.32)

Gruber C, Calis J, Buta S, Evrony G, **Martin JC**, Uhl S, Caron R, Jarchin L, Dunkin D, Phelps R, Webb B, Saland J, Merad M, Orange J, Mace E, Rosenberg B, Gelb B, Bogunovic D, Complex Autoinflammatory Syndrome Unveils Fundamental Principles of JAK1 Transcriptional and Biochemical Function, **Immunity 2020** 15;53(3):672-684

Bigenwald C, Le Bérichel J, Wilk W, Chakraborty R, Chen S, Tabachnikova A, Mancusi R, Abhyankar H, Casanova-Acebes M, Laface I, Akturk G, Jobson J, Karoulia Z, **Martin JC**, Grout J, Rafiei A, Lin H, Manz M, Baccarini A, Poulikakos P, Brown B, Gnjatic S, Lujambio A, McClain M, Picarsic J, Allen C, Merad M, BRAFV600E-induced senescence drives Langerhans Cell Histiocytosis pathophysiology, **Nat Medicine 2021** May;27(5):851-861