NAME, QUALIFICATIONS AND CONTACT DETAILS

Jérôme Martin, PharmD; PhD
Board certification in Clinical Pathology

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EDUCATION AND EMPOYMENT

2019 to present: Associate Professor of Immunology (MCU-PH) – Université de Nantes, Nantes, France

2016 to 2019: Postdoctoral fellow – Dr Miriam Merad's lab – Icahn School of Medicine at Mount Sinai, New York, NY

2012-2016: Assistant Professor of Immunology (AHU) – Université de Nantes, Nantes, France

2011 to 2012: Chief Resident – CHU de Nantes, Nantes, France

2006 to 2011: Resident in Clinical Pathology – CHU de Nantes, Nantes, France

2014: PhD in Immunology Faculté de Médecine, Université de Nantes, Nantes, France

2011: Clinical pathology certification, Faculté de Pharmacie, Université de Nantes, Nantes, France

2011: PharmD Faculté de Pharmacie, Université de Nante, Nantes, France

2010: Master of Advanced Studies in Immunology, Institut Pasteur et Faculté de Médecine Paris V, Paris, France

2009: Interuniversity degree in medical toxicology, Université d'Angers.

AWARDS AND HONOURS:

2009-2010: "Année recherche" - Research fellowship for excellence in Medicine during residency; **2011-2012**: Chief resident (« médaille d'or ») CHU de Nantes; **2016**: Fondation Bettencourt-Schueller – "Prix pour les jeunes chercheurs" (€ 25,000); **2018**: Philippe Foundation ($12,000); **2018**: Rising Star in Immunology (FOCIS 2018 - San Francisco; $ 750)

5 SELECTED PUBLICATIONS (from 28 in peer-review journals)

Total citations in September 2019: 526; H-index: 10.

1**. 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** 178(6):1493-1508.e20. doi: 10.1016/j.cell.2019.08.008. (IF : 36.216) (1 cite – Google scholar)

2. **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. Limited Presence of IL-22 Binding Protein, a Natural IL-22 Inhibitor, Strengthens Psoriatic Skin Inflammation. **J Immunol. 2017** 198(9):3671-3678 (IF:4.92). (IF:4.86) (25 cites – Google scholar)

3. **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, IL-22BP is produced by eosinophils in human gut and blocks IL-22 protective actions during colitis. **Mucosal Immunol. 2016** 9(2):539-49. (IF: 7.48) (45 cites – Google scholar)

4. **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. Interleukin-22 binding protein (IL-22BP) is constitutively expressed by a subset of conventional dendritic cells and is strongly induced by retinoic acid. **Mucosal Immunol. 2014** 7(1):101-113 (IF 7.54) (112 cites – Google scholar)

5. **Martin JC**, Baeten DL and Josien R. Emerging role of IL-17 and Th17 cells in systemic lupus erythematosus. **Clin. Immunol. 2014** 154 (1):1-12 (IF 3.99) (105 cites – Google scholar)

RESEARCH

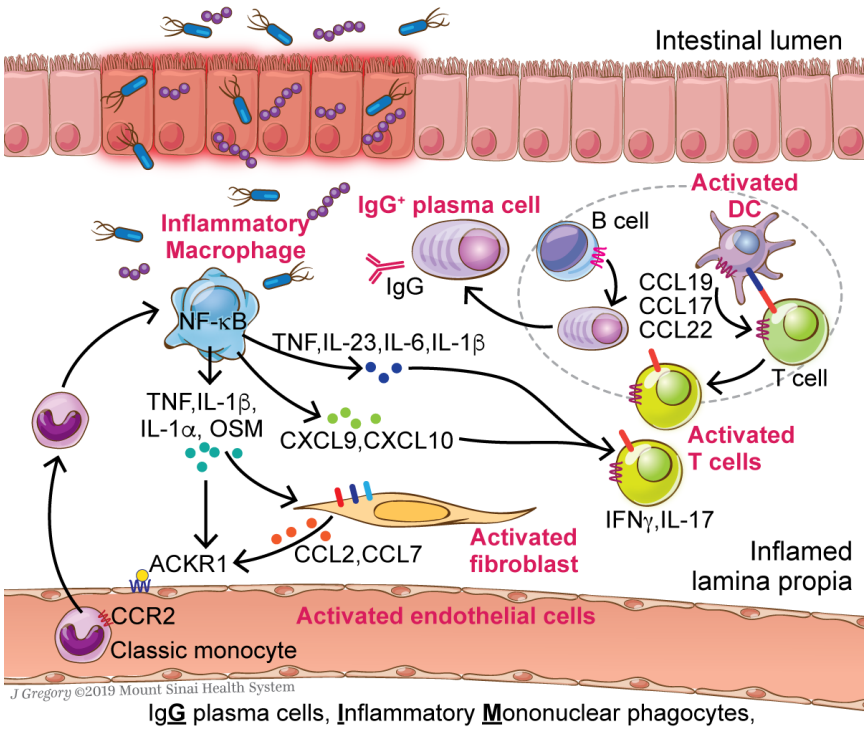
Our objective is to harness the power offered by new single-cell technologies to deconvolute immunopathogenic responses and their heterogeneity in tissues of patients affected by immune-mediated inflammatory diseases (IMIDs) in order enhance the rational for future drug and biomarker discovery. **Immune-mediated inflammatory diseases (IMIDs)** encompass a group of chronic disorders of the immune system with unknown etiologies and a continuously rising incidence in Western countries over the past 70 years (Bach, 2002). IMIDs can severely **impacts the quality of life** of patients. Pain and discomfort, which can complicate daily activities and lower performance at work, are frequently observed in most IMIDs. Besides, patients suffering from IMIDs are prone to **develop severe cardiovascular, metabolic and psychological comorbidities**. By affecting about **70 million people**, IMIDs represent a **major public health issue in Europe** (Cooper et al., 2009). Despite important success, however, the **clinical benefit** of targeted **immunotherapy** in polygenic IMIDs has remained **limited to a subset of patients** and the use of standard of care imaging and/or histological diagnostic assays has failed to stratify potential responders from non-responders. Immunopathological heterogeneity across clinically and histologically identical lesions has long been recognized and it is now clear that clinical and histological diagnoses are not sufficient to predict the clinical response to most immunotherapies. Accordingly, none of the targeted immunotherapy approved to treat patients affected by polygenic IMIDs are provided with decision algorithms to maximize

therapeutic responses. **Diseases** are caused by **dysfunctional cell types** that populate the **organ affected**. Yet there is little understanding of the cellular diversity in normal or diseased organs. There is therefore an **urgent need to gain a better understanding of the cellular programs** in **normal and lesional human tissues**, as the poor understanding of disease pathophysiology significantly limits the identification of relevant targets.

Project:

Our current project aims at characterizing the **pathogenic role of mononuclear phagocytes (MNP) in Crohn's disease**. In a previous study, we optimized a pipeline for the analysis of gut tissue resections and endoscopic biopsies with high-resolution single cell technologies (scRNAseq, high-dimensional cytometry, multiplex imaging). We identified a cellular module, which we named the **GIMATS module** (IgG-plasma cells, inflammatory MNP, activated T and stromal cells). The GIMATS organization appeared driven by a unique **MNP-dependent cytokine/chemokine network**. The GIMATS module was present in inflamed ileums of a **subset of patients** and its presence at diagnosis correlated with **failure** to achieve durable corticosteroid-free **clinical remission** upon **anti-TNF therapy** (Martin JC, Cell, 2019). We now want to better characterize the cellular and molecular drivers of the **MNP-driven GIMATS module** to identify new therapeutic targets tailored to non-responders to anti-TNF therapy. To this end we apply state-of-the-art technologies to the characterization of MNP and interacting partners in normal and inflamed tissues of CD patients. This allows the generation of patient-driven hypotheses that we test in optimized pre-clinical reductionist approaches including in-vitro culture systems and rodent colitis models.

GIMATS^{high} in Crohn's disease inflamed ileums associates with resistance to anti-TNF



IgG plasma cells, Inflammatory Mononuclear phagocytes, Activated T cells and Stromal cells

Significance for Crohn's disease:

CD represents a major burden that impacts negatively the patients' quality of life and progressively leads to high disability altering daily life and work productivity. Besides, the incidence of CD has dramatically increased worldwide over the past 50 years and, with 505 per 100,000 inhabitants, Europe has the highest prevalence rate of CD. CD cumulative relapse rate is 90 % within the first ten years of the disease and 40% of the patients experience a first surgery within ten years after diagnosis. While new therapeutic strategies have decreased the need for surgery as compared to older cohorts, the rate of second surgery has remained unchanged. Incomplete control of mucosal inflammation in CD lesions represents a significant risk factor for progressive bowel damage and surgical resection (Pariente et al., 2011). However, up to 40% of CD patients never respond to anti-TNF antibodies and despite enormous dedication to research and development, the pharmaceutical industry continues to struggle to identify novel drug targets that ultimately meet clinical endpoints in IBD trials. These failures represent an enormous economic burden and a distraction for physicians and scientists that adversely impact clinical care. With this project, we will provide a comprehensive network of the cellular and molecular basis for resistance to anti-TNF blockade as well as novel therapeutic opportunities tailored for combination with anti-TNF antibody blockade