

Curriculum Vitae Prof. Gianluca MATTEOLI, DVM, PhD:

Research Statement: With over two decades of experience in mucosal immunology, I have dedicated my career to understanding the complex interplay between intestinal stromal cells and the innate immune system with the final aim to identify novel therapy to help patients suffering from inflammatory bowel disease.

- **Short CV**

January 2024 up to now: Chair of the Thesis Advisory Committee 5, Doctoral School Biomedical Sciences, KU Leuven.

October 2020 up to now: tenured Associate Professor of Mucosal Immunology at the Department of Chronic Diseases, Metabolism and Ageing, Faculty of Medicine, KU Leuven.

October 2015-September 2020: Assistant Professor Tenure track of Mucosal Immunology at the Department of Clinical and Experimental Medicine, Faculty of Medicine, KU Leuven.

October 2012-September 2015: Postdoctoral Fellowship from the Research Foundation Flanders (FWO) at the Translational Research Center for Gastrointestinal Disorders (TARGID), KU Leuven, Belgium, promoter Prof. dr. G.E. Boeckxstaens

January 2010-September 2012: Research Associate at the Translational Research Center for Gastrointestinal Disorders (TARGID), KU Leuven, Belgium, promoter Prof. dr. G.E. Boeckxstaens,

January 2006-December 2009: Postdoctoral scientist in the Immunobiology of dendritic cells and immunotherapy research group led by Dr. Maria Rescigno at the European Institute of Oncology, Milan, Italy; funded by AIRC fellowship (Italian association for cancer research)

January 2004-November 2005: Marie Curie Training Site at the Institute of Medical Microbiology, University of Tübingen, Germany; funded by Marie Curie fellowship (Contract QLK2-CT-2001-60035) and by DAAD fellowship (Deutscher Akademischer Austausch Dienst)

University degrees

November 2002-January 2006: PhD, thesis Department of Pathology and Animal Health; Faculty of Veterinary Medicine, University of Naples, Federico II, Italy and Institute of Medical Microbiology, University of Tübingen, Germany; funded by MIUR fellowship (Italian Ministry of University and Research)

September 1997-July 2002: Master in Veterinary Medicine, University of Naples, Federico II, Italy

- **Career path**

Throughout my career, I have been deeply committed to unraveling the molecular mechanisms that govern the maintenance of intestinal immune tolerance and their pivotal role in the prevention of inflammatory bowel disease. My research interests have revolved around molecular pathways that underlie the delicate balance between pro-inflammatory and anti-inflammatory processes in the intestine. We have explored the intricate interplay between different cell types, including epithelial cells, immune cells, and stromal cells, in the maintenance of a healthy intestinal microenvironment.

To gain insights into these complex processes, we have utilized a variety of cutting-edge techniques and technologies, including single-cell omics, advanced cell culture systems, preclinical models of intestinal inflammation, and analysis of patient samples. By combining these approaches, we have been able to identify novel molecular targets and pathways that are critical for the maintenance of intestinal immune tolerance and in resolution of inflammation.

As a result, I have been appointed as Associate Professor in 2020 and have successfully completed a Tenure professorship in Mucosal Immunology at the Faculty of Medicine, KU Leuven in October 2015. In Leuven, I further develop my research interest joining the Translational Research Center for Gastrointestinal Disorders (TARGID), where I could couple my expertise in preclinical models of intestinal inflammation with analysis of patient's samples to identify novel pathophysiological processes responsible for chronic intestinal inflammation. As recognition of my scientific achievements, I was able to collect more than 5 million euro of funding and build up an independent laboratory currently consisting of 4 post-doctoral research fellows, 6 PhD students, and a technician. As mentor, I have supported 10 PhD theses, and 4 postdocs to their independent career as leading scientists in biotech and in academia.

Five main publications

IL-1R signaling drives enteric glia-macrophage interactions in colorectal cancer. **Nat Commun.** 2024 Jul 19;15(1):6079. doi: 10.1038/s41467-024-50438-2

van Baarle L, De Simone V, Schneider L, Santhosh S, Abdurahiman S, Biscu F, Schneider R, Zanoletti L, Siqueira de Mello R, Verbandt S, Hu Z, Stakenborg M, Ke BJ, Stakenborg N, Salvador Laureano R, García-Reyes B, Henn J, Toma M, Vanmechelen M, Boeckxstaens G, De Smet F, Garg AD, Ibiza S, Tejpar S, Wehner S, **Matteoli G**.

Intercellular interaction between FAP+ fibroblasts and CD150+ inflammatory monocytes mediates fibrostenosis in Crohn's disease. **J Clin Invest.** 2024 Jul 23;134(16):e173835. doi: 10.1172/JCI173835.

Ke BJ, Abdurahiman S, Biscu F, Zanella G, Dragoni G, Santhosh S, De Simone V, Zouzaf A, van Baarle L, Stakenborg M, Bosáková V, Van Rymentant Y, Verhulst E, Verstockt S, Klein E, Bislenghi G, Wolthuis A, Frič J, Breyneart C, D'Hoore A, Van der Veken P, De Meester I, Lovisa S, Hawinkels LJ, Verstockt B, De Hertogh G, Vermeire S, **Matteoli G**.

Prostaglandin E2 receptor PTGER4-expressing macrophages promote intestinal epithelial barrier regeneration upon inflammation. **Gut.** 2021 Feb 7;gutjnl-2020-322146. doi: 10.1136/gutjnl-2020-322146. *Co-senior author. Na YR, Jung D, Stakenborg M, Jang H, Gu GJ, Jeong MR, Suh SY, Kim HJ, Kwon YH, Sung TS, Ryoo SB, Park KJ, Im JP, Park JY, Lee YS, Han H, Park B, Lee S, Kim D, Lee HS, Cleylen I, **Matteoli G***, Seok SH*.

Macrophages in intestinal inflammation and resolution: a potential therapeutic target in IBD. **Nature Reviews Gastroenterology & Hepatology.** June 2019 DOI : 10.1038/s41575-019-0172-4 . #Shared corresponding author Na YR, Stakenborg M, Seok SH[#], and **Matteoli G[#]**

CCR2-dependent monocyte-derived macrophages resolve inflammation and restore gut motility in postoperative ileus. **Gut.** 2017 Dec;66(12):2098-2109. doi: 10.1136/gutjnl-2016-313144. #Corresponding author Farro G, Stakenborg M, Gomez-Pinilla PJ, Labeeuw E, Goverse G, Di Giovangiulio M, Stakenborg N, Meroni E, D'Errico F, Elkrim Y, Laoui D, Lisowski ZM, Sauter KA, Hume DA, Van Ginderachter JA, Boeckxstaens GE, **Matteoli G[#]**.

Other scientific output and impact

In recent years, I have actively participated in various international consortia and initiatives aimed at defining the heterogeneity of myeloid cells in human diseases. Currently, I serve as a member of the managing committee for the European Cost action titled "Mye-Info-Bank," which focuses on converting molecular profiles of myeloid cells into biomarkers for inflammation and cancer. Previously, our lab was involved in the European Cost action "Mye-EUNITER," a network of investigators dedicated to exploratory research on myeloid regulatory cells. My team is also part of the international Human Immune and Gut Cell Atlas bionetworks. Within these initiatives, we provide support for sample collection and generation of single cell RNA sequencing data to characterize human intestinal immune and stromal cells, both in homeostasis and disease, including inflammatory bowel disease.

List of relevant research grants.

Helmsley Charitable Trust Grant 01/01/25-31/12/27 Targeting chronic inflammation and tissue remodelling in Crohn's disease with engineered T cells. (810,194 \$) Role: Coordinator

Helmsley Charitable Trust Grant 01/01/24-31/12/26 Fat as a villain in Crohn's disease. (2,723,404 \$) Role: Coordinator

WEAVE Grant by the Research Foundation-Flanders (FWO) and DFG - German Research Foundation 01/01/25-31/12/28 Uncovering enteric glia cells reactivity in the course of intestinal inflammation. (465.000 EUR) Role: Principal Investigator

Grant by the Research Foundation-Flanders (FWO) SBO (Strategisch Basis Onderzoek) 01/01/24-12/31/27 Druglike FAPs with maximal target residence time: from chemical discovery to preclinical evaluation in oncology and fibrosis theranostics. (1.798.406 EUR) Role: Co-promotor

HORIZON EUROPE grant 01/04/23-31/12/27 Validation of novel immunotherapeutic targets against fibrosis in inflammatory bowel diseases. Proposal acronym: FIBROTARGET. (6.000.000 EUR) Role: Co-coordinator

Grant Pioneer Award by the European Crohn's and Colitis Organisation (ECCO) 01/01/23-31/12/24
Unraveling the role of fibroblast subsets in fibro-stenotic Crohn's disease (300.000 EUR) Role: Co-promotor

Grant by the Research Foundation-Flanders (FWO) 01/01/21-31/12/24
Uncovering Enteric glia-macrophage communication in intestinal homeostasis and inflammation. (512.700 EUR)
Role: Principal Investigator

Grant by the VLAIO - Flanders Innovation & Entrepreneurship 01/07/2021-30/06/2023
Novel antibody-based IL-2 mimetics for the treatment of graft versus host and inflammatory bowel disease. (380.000 EUR) Role: Co-promotor

Grant by the Research Foundation-Flanders (FWO) 01/01/2019-31/12/2022 Crosstalk between the enteric nervous system and tumor-associated macrophages during colon cancer progression. (373.000 EUR) Role: Principal investigator

Faculty Resources Grant, University of Leuven, Belgium 01/10/21-30/09/24, Targeting intestinal macrophages as new treatment for Inflammatory Bowel Disease. (283.000 EUR) Role: Principal Investigator

Grant by the Research Foundation-Flanders (FWO) SBO (Strategisch Basis Onderzoek) 01/01/19-12/31/22
Exploration and preclinical validation of myeloid cell pathways as novel targets and biomarkers for fibrosis development in IBD. (1.783.000 EUR) Role: Co-promotor

Faculty Resources Grant, University of Leuven, Belgium 01/10/17-30/09/21
The role of innate immunity in chronic intestinal inflammation and fibrosis. (882.000 EUR) Role: Co-Investigator

Grant by the Research Foundation-Flanders (FWO) 01/01/17-12/31/22
Monocyte-derived macrophages as crucial players in the resolution of inflammation and tissue repair in Inflammatory Bowel Disease (464.000 EUR); Role: Principal investigator

Leuven, 28th February 2025

