Mapping human myeloid cell maturation from bone marrow to peripheral blood to tissues

Kyra van der Pan[1], Enrique De La Rosa[3#], Indu Khatri[1,2#], Sara Kassem[1], Anniek L de Jager[1], Brigitta AE Naber[1], Inge F de Laat[1], Alesha Louis[1], Marjolijn Hameetman[4], YK Onno Teng[5], Meta Roestenberg[6], Stijn Crobach[7], Wouter BL van den Bossche[8], Daniela Damasceno[9], José Manuel Sánchez-Santos[10], Alberto Orfao[9], Javier De Las Rivas[3], Jacques JM van Dongen[1,9], Cristina Teodosio[1,9†], Paula Díez[1,9,11†]

[1] Department of Immunology, Leiden University Medical Center (LUMC), Leiden, The Netherlands

[2] Cancer Research Center (CiC-IBMCC, CSIC/USAL and IBSAL), Consejo Superior de Investigaciones Científicas (CSIC), University of Salamanca (USAL) and Instituto de Investigación Biomédica de Salamanca (IBSAL), Salamanca, Spain

[3] Leiden Computational Biology Center, LUMC, Leiden, The Netherlands

[4] Flow cytometry Core Facility, LUMC, Leiden, the Netherlands

[5] Department of Nephrology, LUMC, Leiden, The Netherlands

[6] Department of Parasitology, LUMC, Leiden, The Netherlands

[7] Department of Pathology, LUMC, Leiden, The Netherlands

[8] Department of Neurosurgery, Brain Tumor Center, Erasmus Medical Center, Rotterdam, The Netherlands

[9] Translational and Clinical Research Program, Cancer Research Center (IBMCC; University of Salamanca - CSIC); Cytometry Service, NUCLEUS; Department of Medicine, University of Salamanca and Institute of Biomedical Research of Salamanca (IBSAL), Salamanca, Spain

[10] Department of Statistics, University of Salamanca, Salamanca, Spain

[11] Department of Functional Biology (Immunology area), Faculty of Medicine, University of Oviedo, Oviedo, Spain

[#] Both authors contributed equally to this work and must be considered as second authors

[†] Both authors contributed equally to this work and must be considered as senior authors

Presenting author

Monocytes, macrophages and dendritic cells (DC) are crucial in maintaining homeostasis, regulating inflammation, and orchestrating immune responses. Despite the existing knowledge about these cells, their plasticity, functional heterogeneity, and the discovery of new subsets currently hamper the definition of their exact maturational relationship. In this study, we characterized human monocyte, macrophage and DC populations across five human tissues (bone marrow, peripheral blood, peritoneal dialysate, colon, and skin) to better define their role via innovative single-cell trajectory analysis of mass cytometry (CyTOF) combined with quantitative mass spectrometry (MS) of highly purified myeloid cell populations.

A panel of 33 heavy-metal-labelled antibodies was carefully selected from an initial screen of over 100 protein markers, enabling the identification of 75 distinct innate myeloid cell populations across the five examined tissues. This approach enabled the detection and characterization of rare cell populations (frequency <0.1%) and supported the evaluation of single-cell trajectories across different populations and tissues.

Furthermore, 16 subsets were isolated and subjected to tandem mass tag (TMT)-quantitative MS-based analysis, providing an unbiased proteome atlas of these myeloid cell subsets. By integrating CyTOF and MS data, we delineated the human monocyte-macrophage maturation trajectory from bone marrow to peripheral blood and subsequently to the other three tissues.

This study offers unprecedented insights into the phenotypic and functional interconnections between monocyte, macrophage and DC populations across different human tissues. Our findings contribute to a deeper understanding of myeloid cell heterogeneity and maturation, with the potential to guide future research on innate immune responses and targeted therapeutic strategies.