Short Curriculum Vitae

2015 - Msc in Biochemistry and Biotechnology
Ghent University
2013 - Bridge Program to the Master of Science
in Biochemistry and Biotechnology
Ghent University
2011 - Bachelor in Agro-and Biotechnology
KATHO Roeselare

Publications

Integrated scRNA-Seq Identifies Human Postnatal Thymus Seeding Progenitors and Regulatory Dynamics of Differentiating Immature Thymocytes
Immunity - 2020

Conventional and Computational Flow Cytometry Analyses Reveal Sustained Human Intrathymic T Cell Development From Birth Until Puberty
Frontiers in Immunology - 2020

Promotor
Professor Tom Taghon, PhD
Ghent University, Belgium

Guidance comittee
Professor Jo Vandesompele, PhD
Professor Georges Leclercq, PhD

Examination committee chair

Professor Peter Van Eenoo, PhD
Ghent University, Belgium

Examination committee members

Professor Filip Van Nieuwerburgh, PhD
Ghent University, Belgium

Professor Martin Guilliams, PhD
Ghent University, Belgium

Professor Vanessa Vermeirssen, PhD
Ghent University, Belgium

Professor Jules Meijerink, PhD
Princes Maxima Centrum, The Netherlands

Professor Adrian Liston, PhD
Babraham institute, United Kingdom

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FACULTY OF MEDICINE AND HEALTH SCIENCES

Molecular and functional dissection of early T lymphocyte development in human at the single cell level

Marieke Lavaert

Department of Diagnostic Sciences
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BRIEF OVERVIEW

All blood cells in human develop in the bone marrow (BM) microenvironment from hematopoietic stem cells (HSC). One exception to this are the T cells which require that a thymus seeding precursor (TSP) migrates from the BM into the thymus since only this gland supports T cell development. These TSPs give rise to an abundance of functionally diverse T cells, which protect us from disease through their T cell receptor (TCR). However, the thymus undergoes involution early during life, thereby gradually limiting T cell development. Consequently, restrictions in the TCR repertoire diversity either due to old age or due to illness leave patients vulnerable to infections. Thus, understanding how these TSPs give rise to mature T cells in the thymus and how T cell development is affected during life holds significant clinical potential.

To address this missing link in hematopoiesis we performed single cell RNA sequencing (scRNA-seq) to profile the initial stages of human T cell development. This allowed us to identify two distinct populations of TSPs in the human thymus, peripheral blood and BM, rather than a single multipotent population as was proposed in literature. Both populations were observed to give rise to T cells in vitro, while only one was predicted to give rise to dendritic cells in vivo. Using this dataset, we were able to dissect the transcriptional landscape underlying early human T cell development. Finally, we leveraged algorithms, initially used to analyse scRNAseq data, now to analyse flow cytometry data obtained from pediatric thymus samples ranging in age from birth to puberty and benchmarked our pipeline to state-of-the-art methods revealing equal or better performance.

SUMMARY

The onset of single cell sequencing has not only resulted in novel biological insights, but also the development of new algorithms for the analysis of this data. Despite these innovations, the precise nature of the TSPs and their progeny has remained enigmatic. To address this, we performed scRNAseq to profile up to 70.000 $CD34^+$ immature human thymocytes. We integrated our thymocyte dataset with publicly available peripheral blood mononuclear cell (PBMC) and BM datasets. This not only allowed the identification of several non-T-lineage progenitors within the human thymus, but also revealed the existence of two distinct seeding populations in these tissues. Both TSP populations were found to support T cell development in vitro, whereas only one was predicted by the STEMNET algorithm to generate plasmacytoid dendritic cells. In addition, we were able to discern distinct T-lineage developmental intermediates which had remained enigmatic in human. Subsequently, we inferred a trajectory starting from the TSPs through these developmental intermediates, which we validated using our CITEseq data. In combination with gene regulatory networks, this inferred trajectory allowed the dissection of the transcriptional landscape underlying early human T cell development.

While many algorithms have been developed to analyse scRNAseq data, their impact on the analysis of other data types is unclear. Hence, we applied these algorithms on flow cytometry data that was used to profile T cell progenitors, mature T cells and non-T-lineage immune cells in pediatric thymus samples ranging in age from birth to puberty. We benchmarked our pipeline to current state-of-the-art analysis pipelines and found our approach to be at least as performant.

In conclusion, using innovative methods, we were capable of resolving a missing link in human hematopoiesis by identifying the TSPs and we were able to dissect the initial stages of human T cell development and the changes in their transcriptional landscape underlying their development. We also applied algorithms commonly used in scRNAseq data analysis on flow cytometry data and found this approach to be as or more performant compared to current state-of-the-art methods.