



Giuditta Clerici

Correlation of PRS with cell type composition after ILR transformation provides new insights into the relationship between immune-related diseases and PBMCs cell type proportions

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1. Motivation

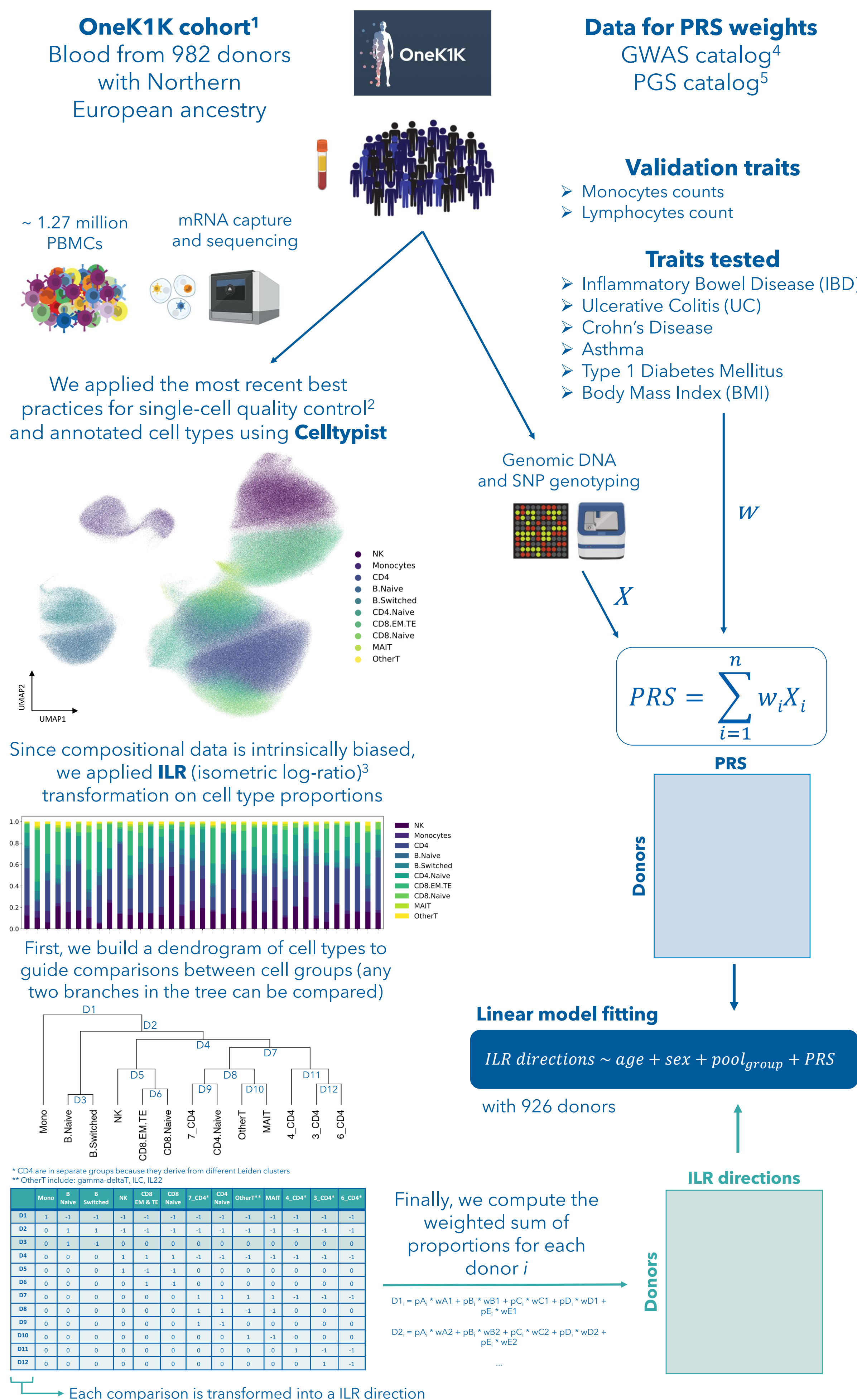
Many diseases, such as Obesity, Type 1 Diabetes Mellitus, Asthma, Inflammatory Bowel Disease, show immune-related alterations. These alterations can result in an imbalanced composition of Peripheral Blood Mononuclear Cell (PBMCs) that can be measured by scRNA-seq experiments.

For most of these disorders, the involvement of specific PBMC types remains unclear.

2. Aims of the project

- Provide a **novel and robust method** to study the relationship between PRS and cell type composition estimated from scRNA-seq experiments
- Study the influence of **genetic predisposition to inflammatory traits** on PBMCs compositions

3. Data & Methods



4. Results

Validation traits

$ILR\ directions \sim age + sex + pool_group + PRS_{Lymphocyte\ count}$

The PRS for **lymphocyte** count is **negatively** related to **D1**
(p.val = 0.040, t.val = -2.05)

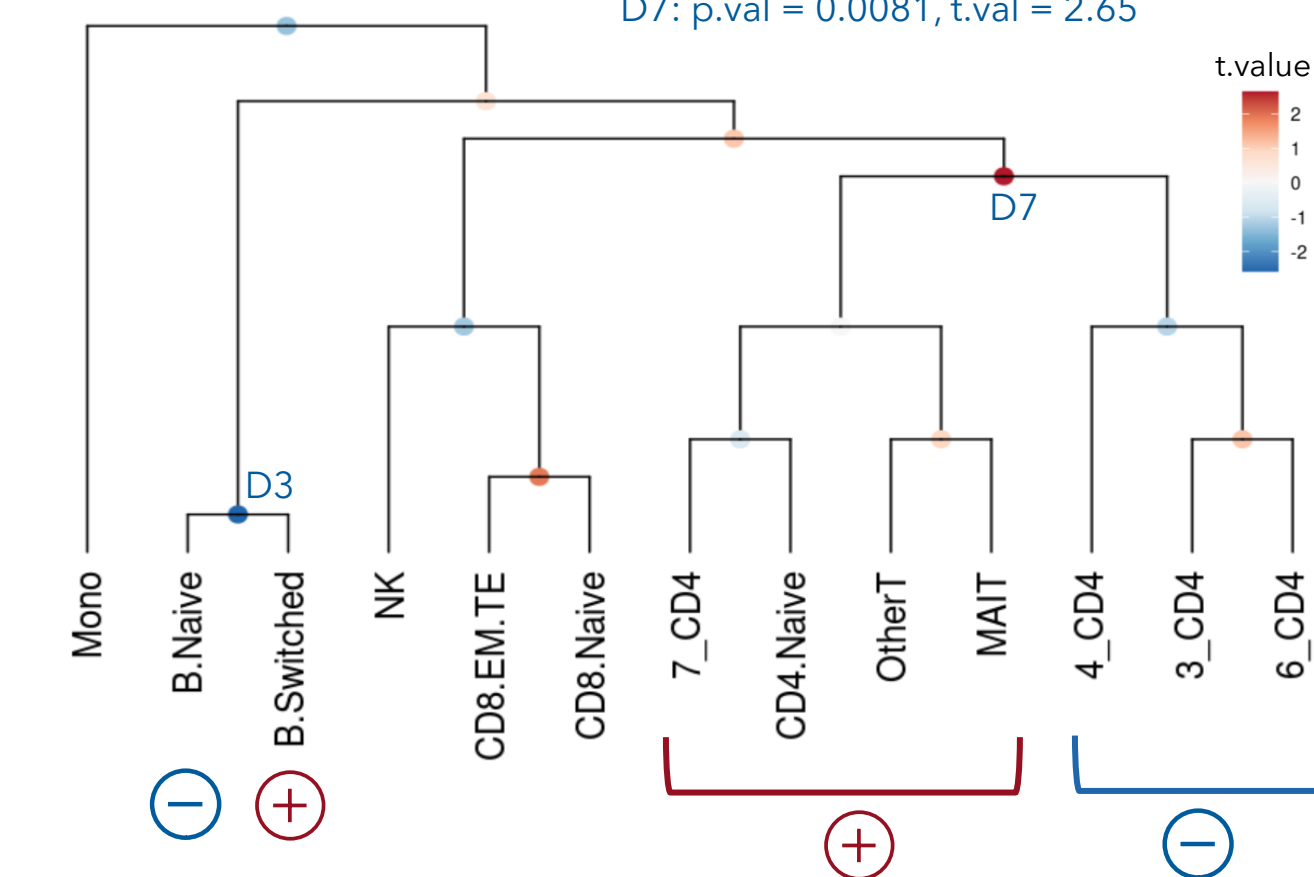
$ILR\ directions \sim age + sex + pool_group + PRS_{Monocyte\ count}$

The PRS monocyte count is **positively** related to the ratio monocytes/lymphocytes (p.val = 0.05, t.val = 1.94)

Traits tested

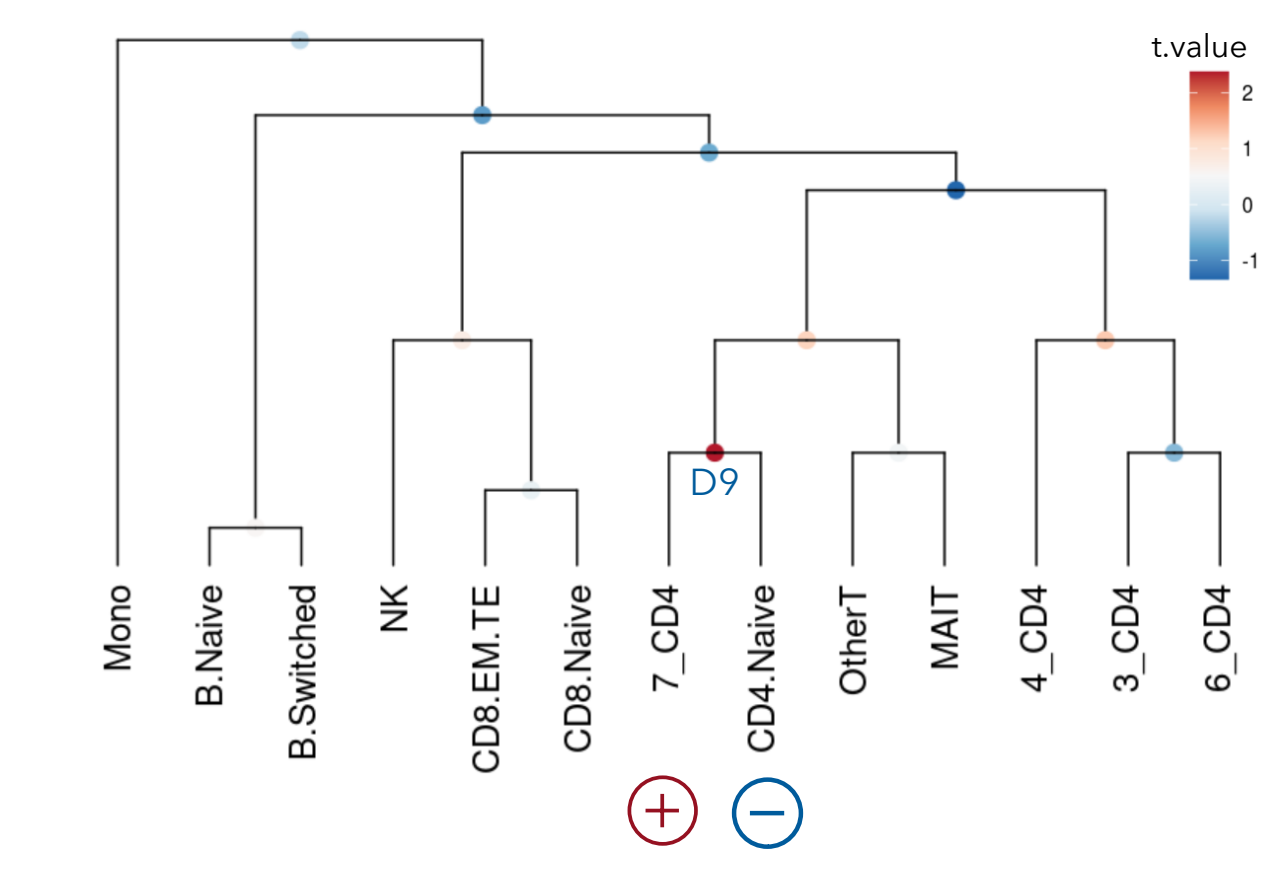
$ILR\ directions \sim age + sex + pool_group + PRS_{BMI}$

D3: p.val = 0.0098, t.val = -2.58
D7: p.val = 0.0081, t.val = 2.65



$ILR\ directions \sim age + sex + pool_group + PRS_{IBD}$

D9: p.val = 0.02, t.val = 2.4



How to read the plots

Each dot (**node**) on the dendrogram represent a **contrast or direction** between two groups of cells. The colors represent the **t.value** of the association between that ILR Direction and the PRS for the trait of interest, with red for positive and blue for negative. If there is a **positive relationship** (red dot), then you can assume that the cell type on the left of that node increase (respect to the one on the right) together with the increase in PRS for the trait tested.

5. Conclusions and future perspectives

In summary, our approach provides a novel and robust method to correlate a phenotype of interest and cell-type composition. We discovered some interesting associations between disease PRS and alteration in specific cell type proportions. This can lead to new insights into the immune-related component of these diseases and the mechanisms of immune dysregulation.

Future perspectives

- Test our method on a bigger dataset
- Extend the analysis to other phenotypes
- Wrap the method in a package

- Human Technopole, Milan, Italy
- Wellcome Sanger Institute, Hinxton, UK
- University of Cambridge, Cambridge, UK

- Yazar S. et al, Single-cell eQTL mapping identifies cell type-specific genetic control of autoimmune disease (2022)
- Lukas Heumos et al, Best practices for single-cell analysis across modalities (2023)
- Vera Pawlowsky-Glahn, Juan José Egozcue, Raimon Tolosana-Delgado, Modeling and Analysis of Compositional Data (2015)
- GWAS catalog GCST90002393 and GCST90002388
- PGS catalog PGS003981, PGS002066, PGS001331, PGS002727, PGS002025,

