# T cell type abundance and gene expression patterns in the context of clinical progression of treatment-naïve CLL/MBL patients from the OxPLoreD study

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## Introduction

Chronic lymphocytic leukaemia (CLL) is a B-cell neoplasm preceded by an asymptomatic precursor phase, monoclonal B-cell lymphocytosis (MBL). The Oxford Premalignant Lymphoproliferative Disorders (OxPLoreD) study (REC 19/SC/0065; NCT04023747) is a national prospective study of people with MBL/Stage A CLL or high-risk MGUS exploring the genomic and immunological features of progression to cancer. Malignancy progression may be mediated by the expansion of one or more subclones with distinct gene expression and/or mutation profile (1) as well as non-tumour cells in the peripheral blood (2). Utilising single cell multiomic (CITE-seq (3) & scTCR/BCR-seq) datasets, we aim to dissect the transcriptome and clonal architecture of T cells, known to be in a close cellular crosstalk with CLL tumour cells (4), in the context of MBL/CLL progression & highlight novel prognostic CLL markers.

For more details regarding the OxPLoreD study, please refer to poster abstract **1552313**.

## Single cell multiomic (CITE-seq & TCR/BCR-seq) datasets

| ID | Diagnostic | Clinical status | SHM status | Age | Sex | Tissue preparation | Source |
|---|---|---|---|---|---|---|---|
| A | MBL/CLL | non-progressor | mutated | 72 | M | unsorted PBMNCs | OxPLoreD |
| B | MBL/CLL | non-progressor | unmutated | 67 | M | unsorted PBMNCs | OxPLoreD |
| C | MBL/CLL | non-progressor | unmutated | 74 | M | unsorted PBMNCs | OxPLoreD |
| D | MBL/CLL | progressor | unmutated | 74 | M | unsorted PBMNCs | OxPLoreD |
| E | MBL/CLL | progressor | unmutated | 59 | F | sorted CD3+ & CD19+ 1:1 | OxPLoreD |
| F | MBL/CLL | progressor | unmutated | 59 | M | sorted CD3+ & CD19+ 1:1 | OxPLoreD |
| G | healthy | healthy old | NA | 66 | F | unsorted PBMNCs | Cartography |
| H | healthy | healthy young | NA | 24 | M | unsorted PBMNCs | Cartography |
| I | healthy | healthy old | NA | 60 | M | unsorted PBMNCs | Cartography |
| J | healthy | healthy young | NA | 47 | M | unsorted PBMNCs | Cartography |
| K | healthy | healthy old | NA | 71 | M | unsorted PBMNCs | Cartography |
| L | healthy | healthy young | NA | 23 | F | unsorted PBMNCs | Cartography |

## Acknowledgements & Contact

**Oxford Molecular Diagnostic Centre & The Oncology Clinical Trials Office, Department of Oncology, University of Oxford; Oxford University Hospitals NHS Foundation Trust; Cancer Research UK**

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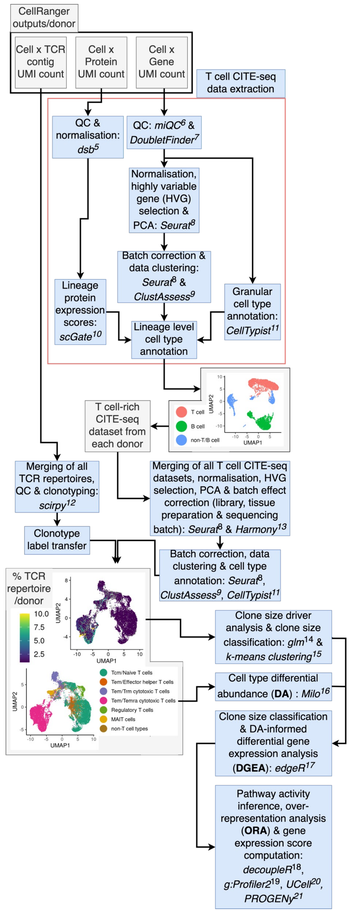
**Cartography** **OxPLoreD**

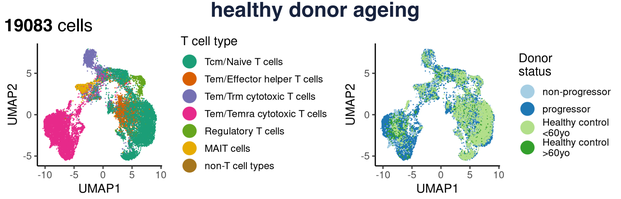
NB: QR codes to project partners' websites & not to electronic version of the poster

## Methods

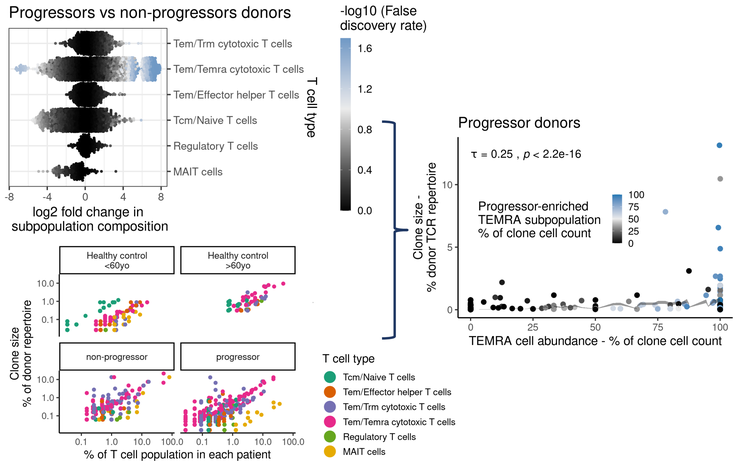



## Results

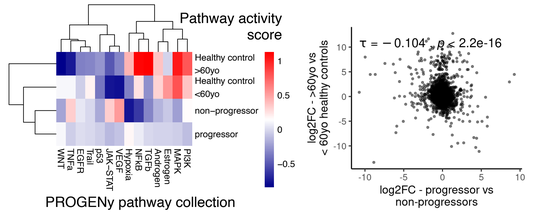
### The T cell differentiation landscape in the context of MBL/CLL & healthy donor ageing



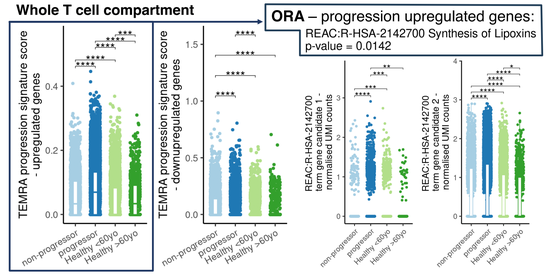

### CLL progression is associated with an expansion of TEMRA subpopulations in the context of clinical progression




### The transcriptomic profiles of the TEMRAs in expanded clones differ in healthy donor ageing vs CLL progression




### The TEMRA expanded clone progression transcriptomic signature highlights potential molecular correlates of CLL progression




## Discussions & questions addressed by ongoing work

TEMRAs are a potential T cell subtype relevant for CLL/MBL prognosis.

- Is CLL progression a function of the inflammatory status?
- Is there a CLL-driven T cell response localized in the TEMRA compartment?
- Is the SHM status of the CLL major clone affecting the CLL T cell ecosystem?
- Are the progression-associated TEMRA genes useful as a cost-effective prognostic marker?

## References

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