Application of Machine Learning to Analyze Immune Cellular Compartments in a Pre-Transplant Cohort

Franz Fenninger, Vivian Wu, Karen Sherwood, Oliver Günther, Davide Cina, Jenny Tran, Krishna Anuj Dwarka, Paaskum Wong, Lenka Allen, Jason Wong, and Paul Keown for the Genome Canada Transplant Consortium

Introduction: Kidney disease causes complex alterations in the immune system, including changes in cell frequencies, alterations of surface antigen expression levels and impaired cell function. We sought to quantify these immune parameters in a pre-transplant patient cohort and compare them to healthy control references.

Cohort

- Blood samples were collected from
  - **35 pre-tx** patients
    - Chronic kidney disease
    - End stage renal disease
  - **12 healthy** controls

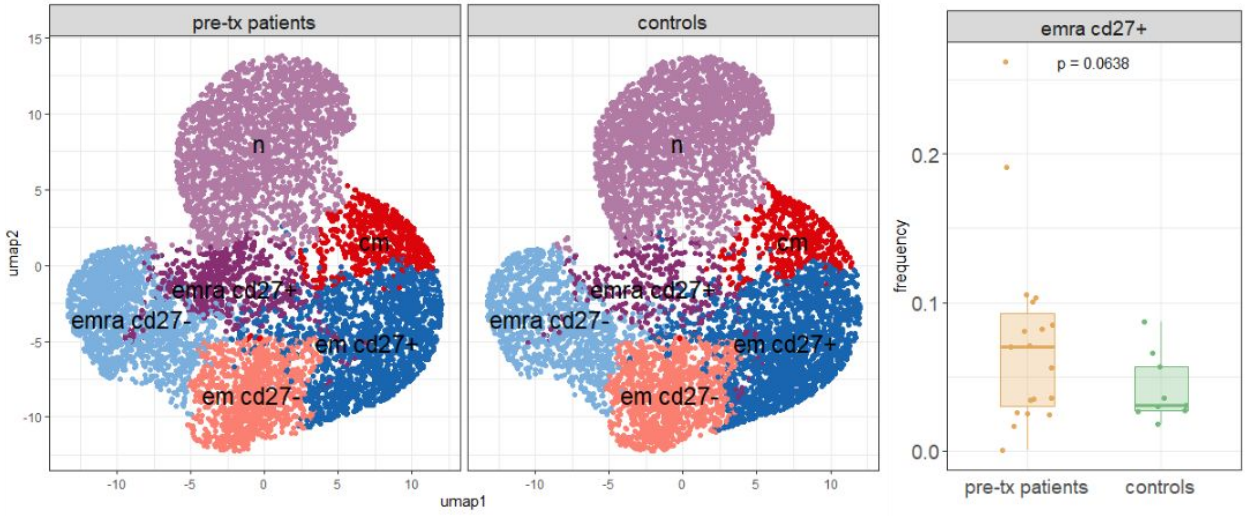
Immunophenotyping

- Flow cytometry using **5 different panels**
  - CD8 / CD4 T cells
  - B cells
  - NK cells
  - Monocytes

Analysis pipeline

- Custom **R/Bioconductor** script
- Integration of machine learning tools
  - Cell clustering using **FlowSOM**
  - Dimensionality reduction and visualization by **uMAP**

Results: Increased CD8 TEMRA CD27+ cell frequency



Conclusions:

- Data give insights into dysregulation of immune system during kidney disease
- Serve as baseline for longitudinal transplant analysis
- **Machine Learning reduces complexity of immunophenotyping panels**
- Provides automatic gating procedure and allows more intuitive visualization
- Allows design of more targeted immunophenotyping panels
- Guide future biomarker discovery

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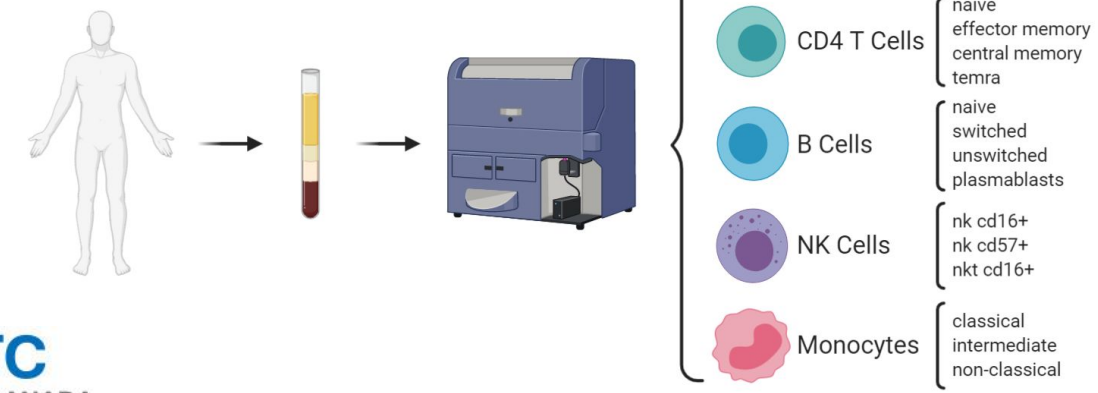

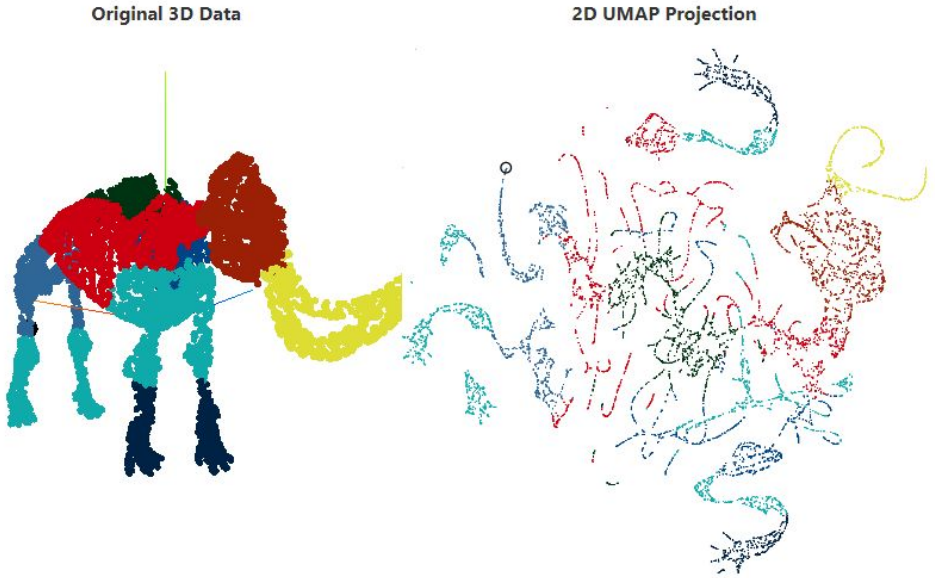

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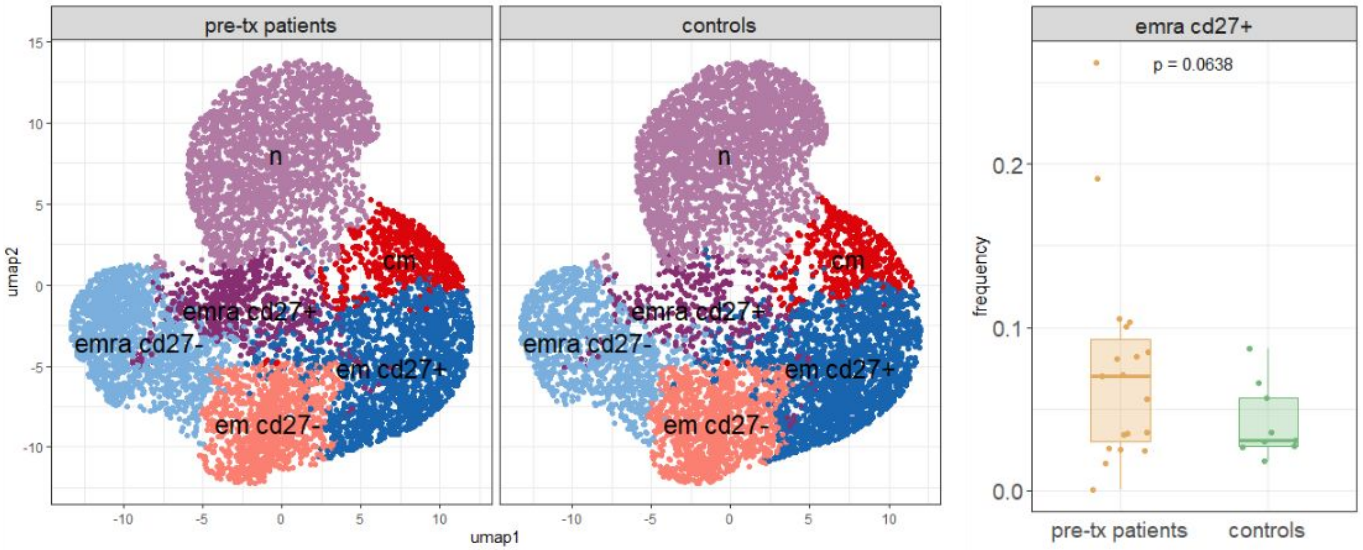
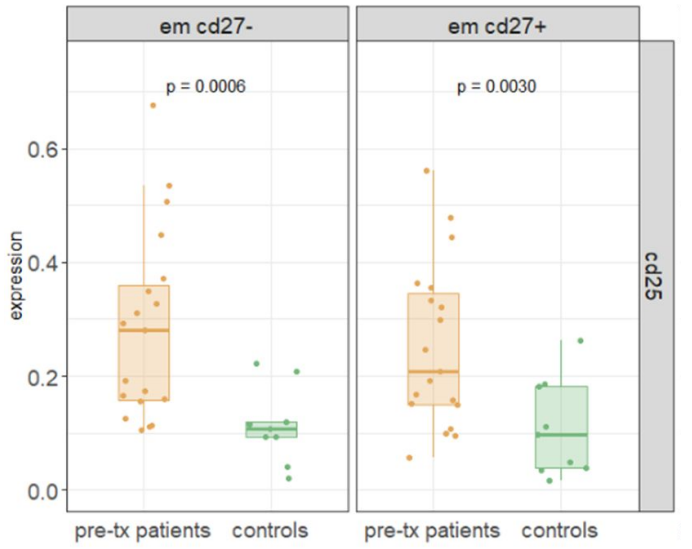
CD8 T Lymphocyte Flow Panel Results and Conclusions

CD8 T lymphocytes of pre-tx patients exhibit an increased differentiation status and elevated activation markers as in systemic inflammation.

Increased CD8 TEMRA CD27+ cell frequency



Elevated IL-2Ra (CD25) levels on CD8 EM cells



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References

- Figure created with BioRender.com
- Understanding UMAP, Coenen & Pearce | Google PAIR

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