Tracing immune reconstitution in the obese post-bariatric surgery through longitudinal single-cell RNA sequencing

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Impact of Obesity on the Immune System

- **Obesity Effects:**
  - Impairs immune function.
  - Triggers chronic low-grade inflammation.
  - Causes adipokine imbalance.
- **Post-Bariatric Surgery Observations:**
  - Positive changes in immune cells: NK cells, monocytes, B cells, T cells.
  - Focus of studies: Typically limited to specific immune cell types or general cell counts.
- **Research Gap:**
  - The detailed trajectory of immune cell landscapes at the single-cell level post-surgery remains underexplored.

1. Front Immunol. 2023; 14: 1131893.

2. Biomolecules. 2024; 14(2): 219.

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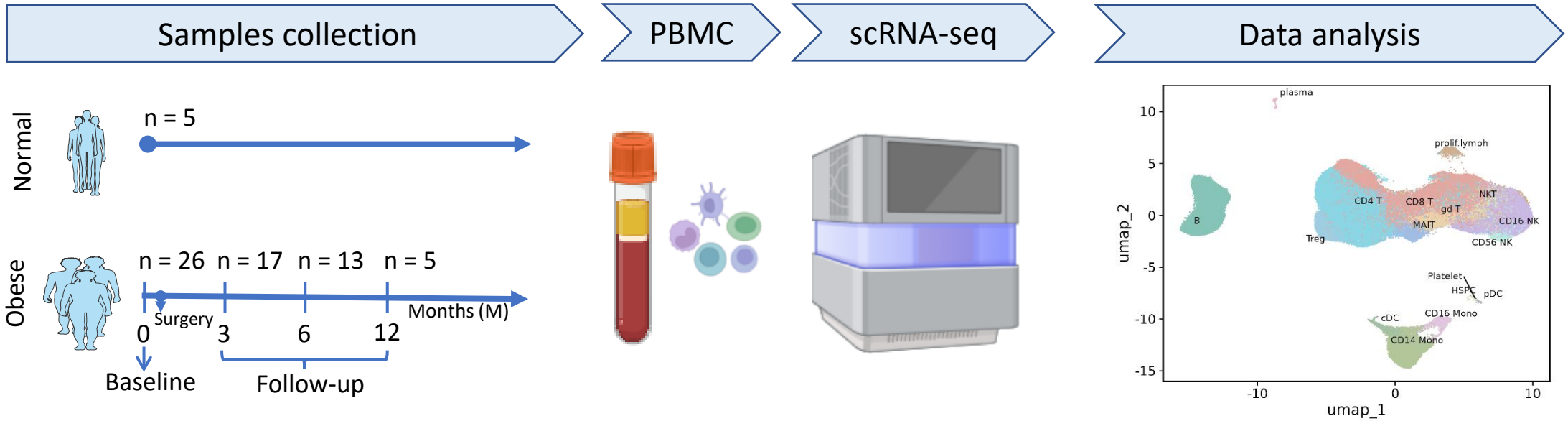
Research Methods



- Time-series scRNA-seq in a cohort of 59 obese samples.
- To investigate immune system modifications within the first year post-bariatric surgery.
- To understand the reversal process of obesity-induced immune dysregulation.

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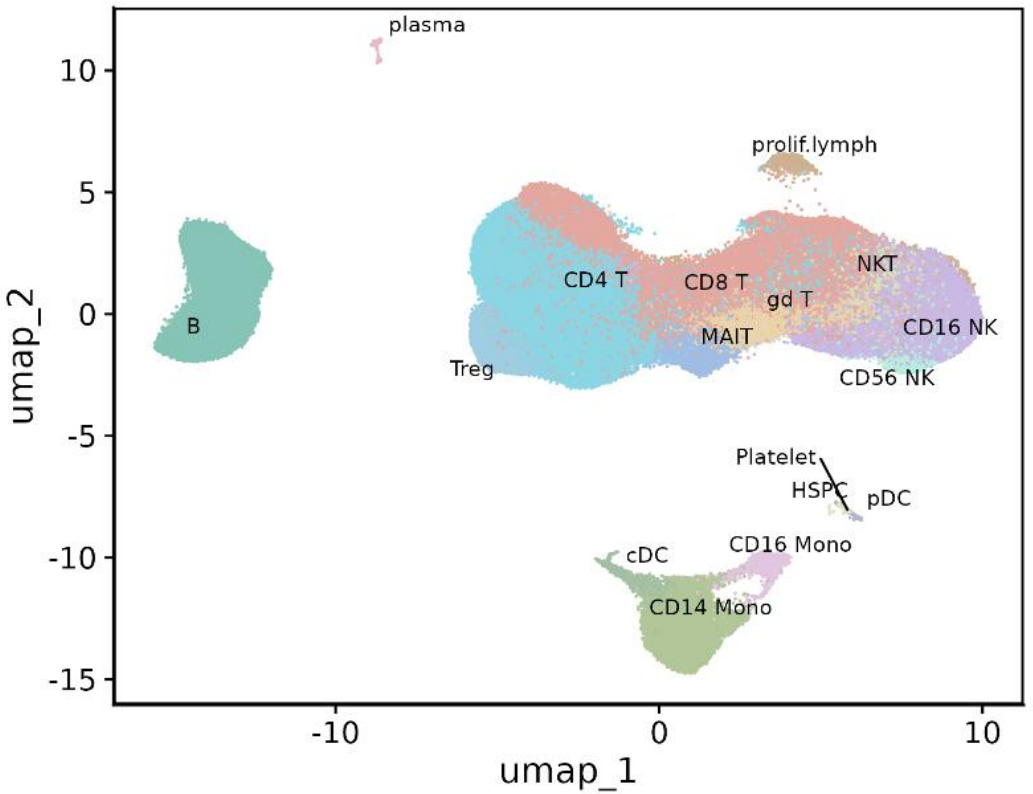
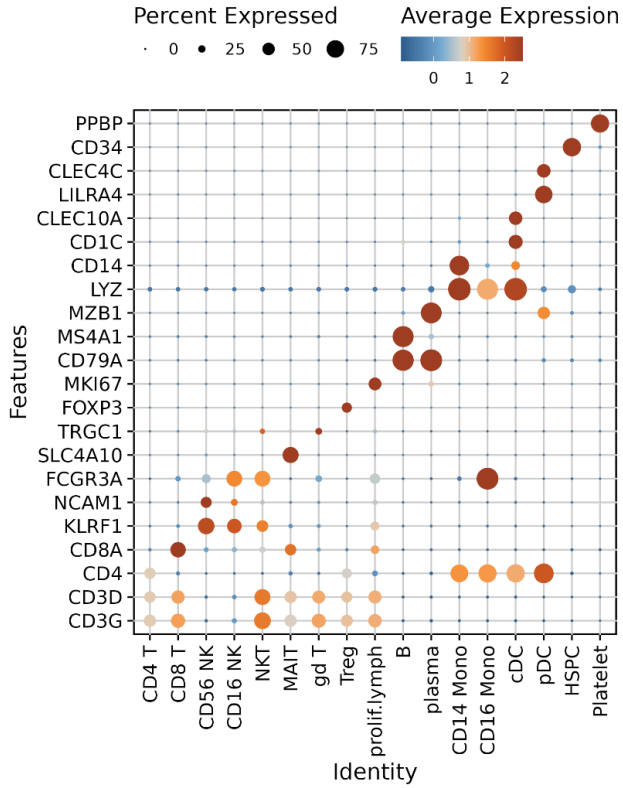
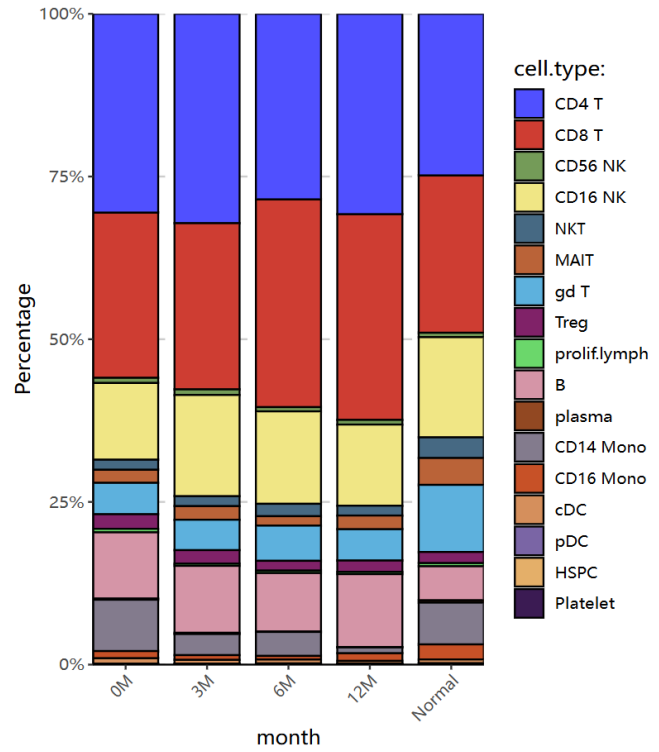
Cell type composition post-bariatric surgery



- UMAP plot of ~350,000 integrated cells from individuals with normal BMI and those post-bariatric surgery.



- Top-ranking marker gene expression levels across different immune cell subtypes.



- Relative abundance of immune cell subtypes across all donors at the indicated time points.

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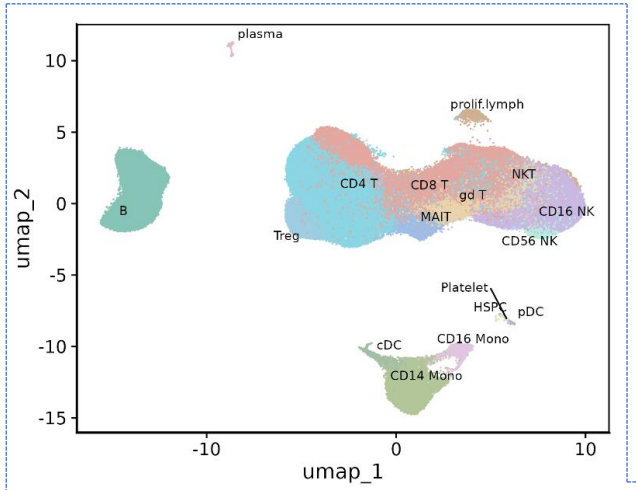
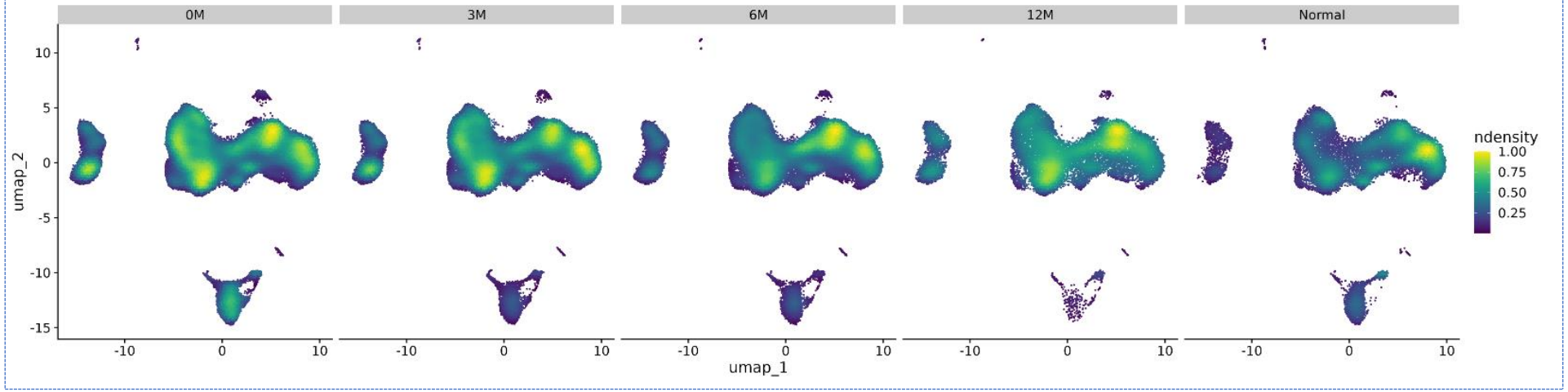
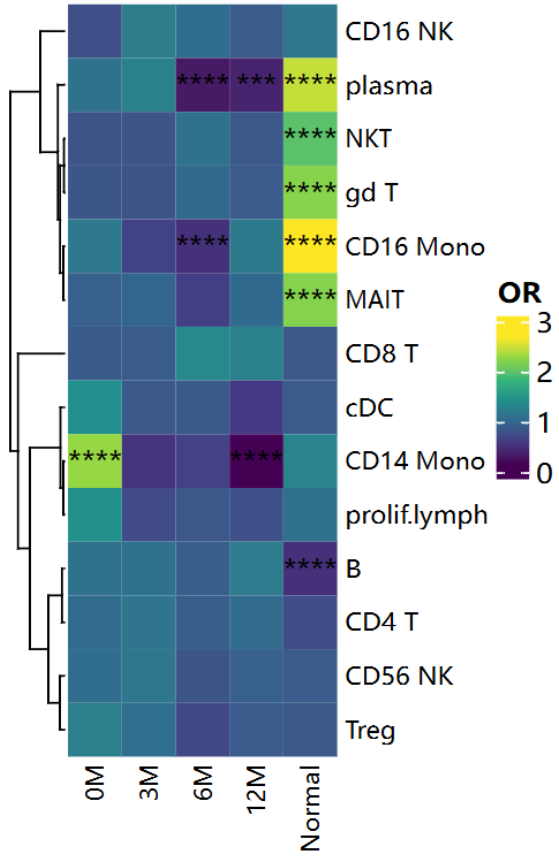
Cell type composition post-bariatric surgery



- Multiple immune cell subtypes, including B cells, NKT cells, monocytes/macrophages, and mucosal associated invariant T (MAIT) cells, exhibit dynamic changes in obese patients and after bariatric surgery.





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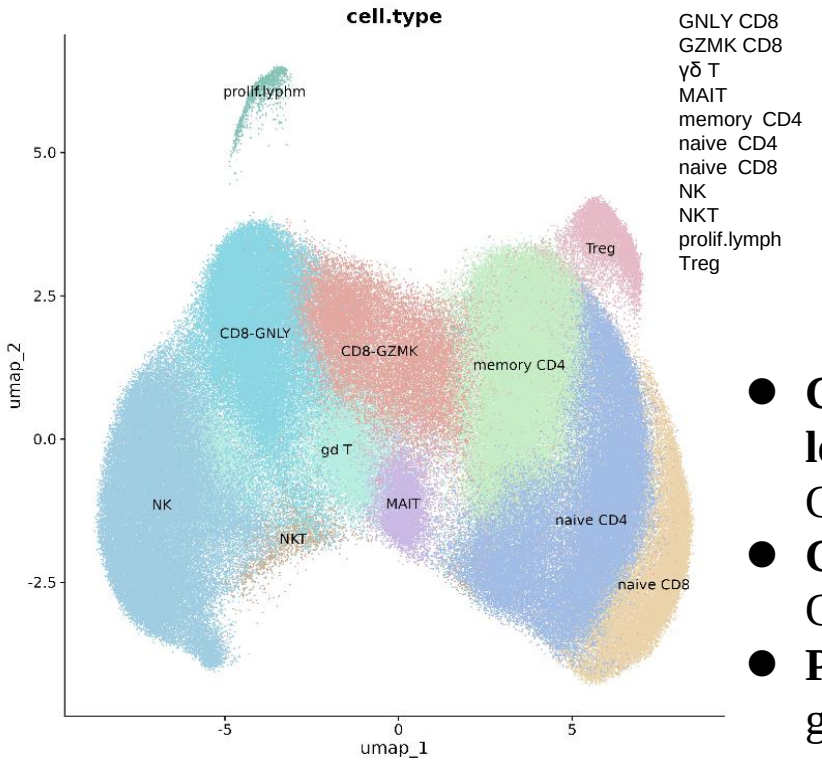
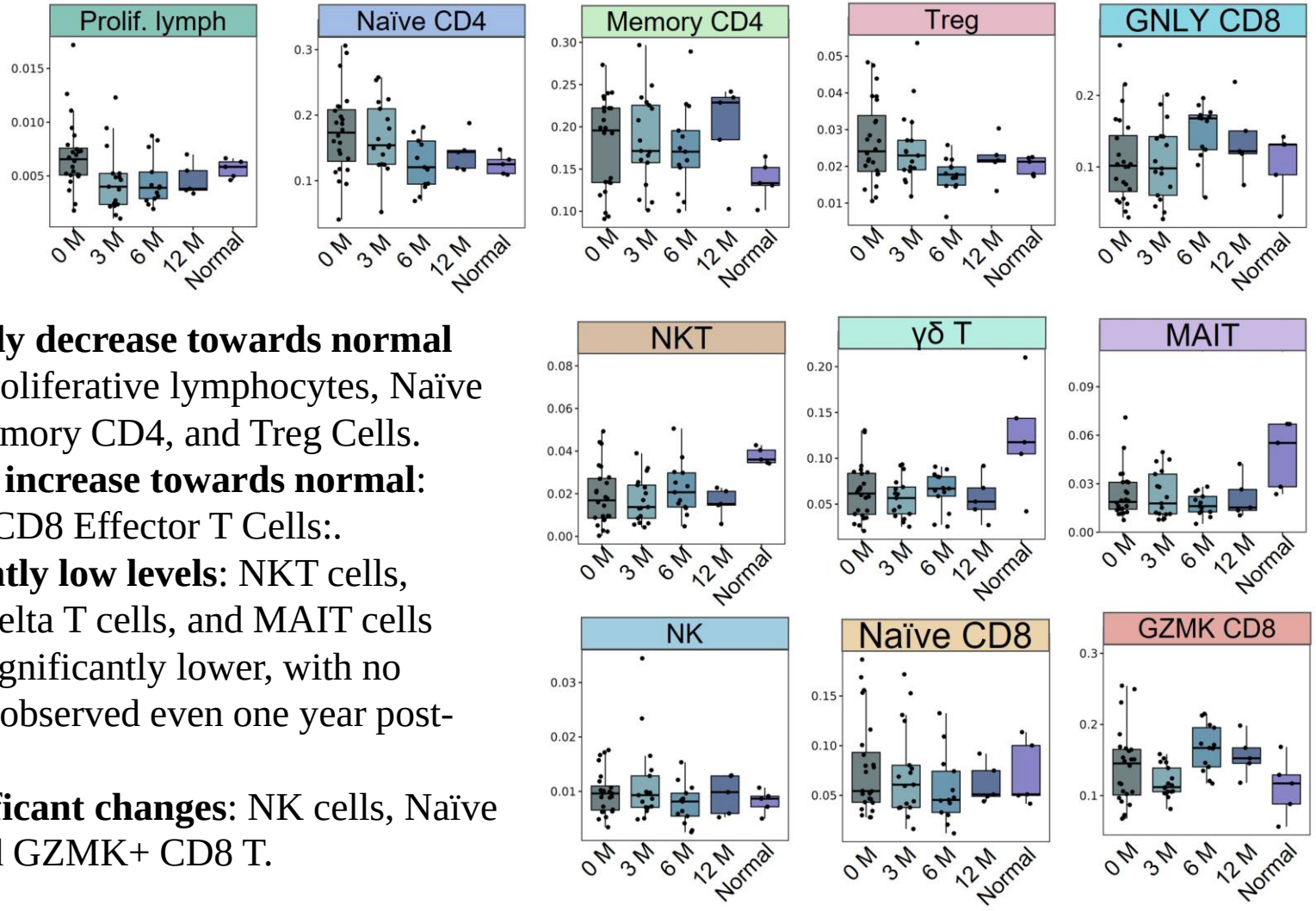
T/NK Cell Lineage Dynamics in Obesity and Post-Bariatric Surgery



GNLY CD8
GZMK CD8
γδ T
MAIT
memory CD4
naive CD4
naive CD8
NK
NKT
prolif.lymph
Treg

- Identified 11 distinct T/NK cell subtypes after reclustering the cells.



- **Gradually decrease towards normal levels**: Proliferative lymphocytes, Naïve CD4, Memory CD4, and Treg Cells.
- **Gradual increase towards normal**: GNLY+ CD8 Effector T Cells:.
- **Persistently low levels**: NKT cells, gamma delta T cells, and MAIT cells remain significantly lower, with no recovery observed even one year post-surgery.
- **No significant changes**: NK cells, Naïve CD8, and GZMK+ CD8 T.

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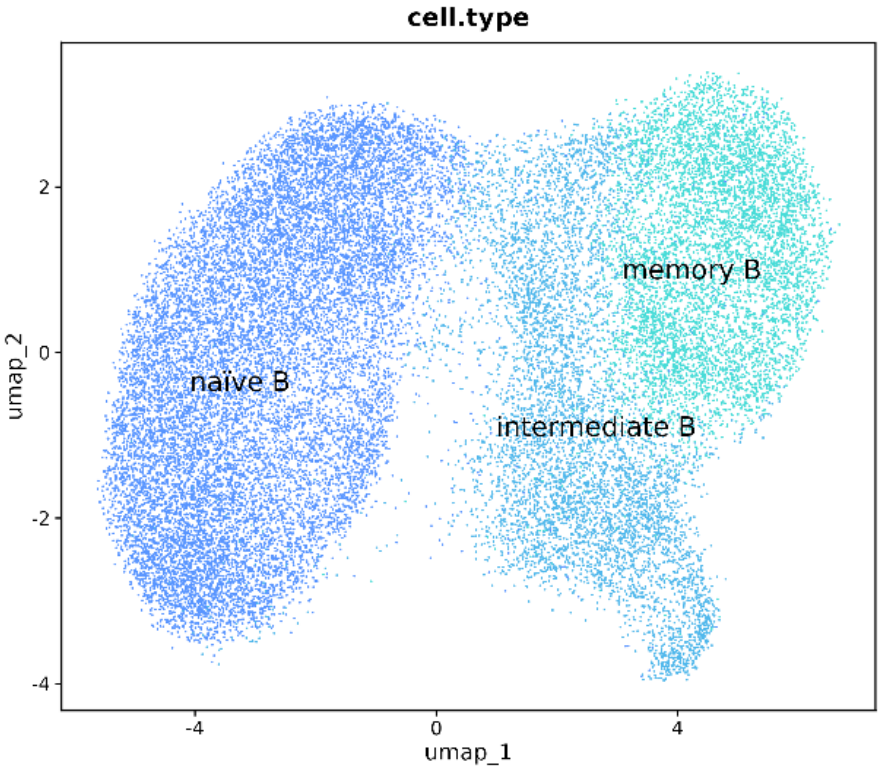
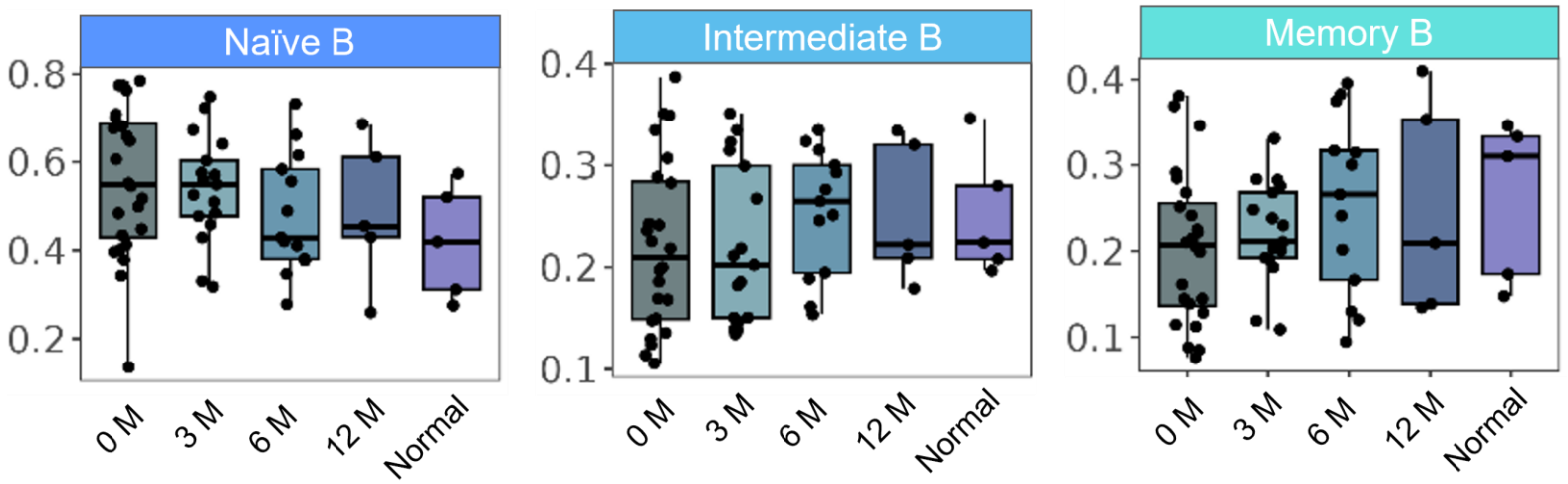
B Cell Lineage Dynamics in Obesity and Post-Bariatric Surgery



- Identified 3 distinct B cell subtypes after reclustering the cells.



- **Naïve B Cells:** Higher proportion in obese individuals compared to normal BMI.
- **Intermediate B Cells and Memory B Cells:** Show a transient increase post-surgery, followed by a return to pre-surgery levels.

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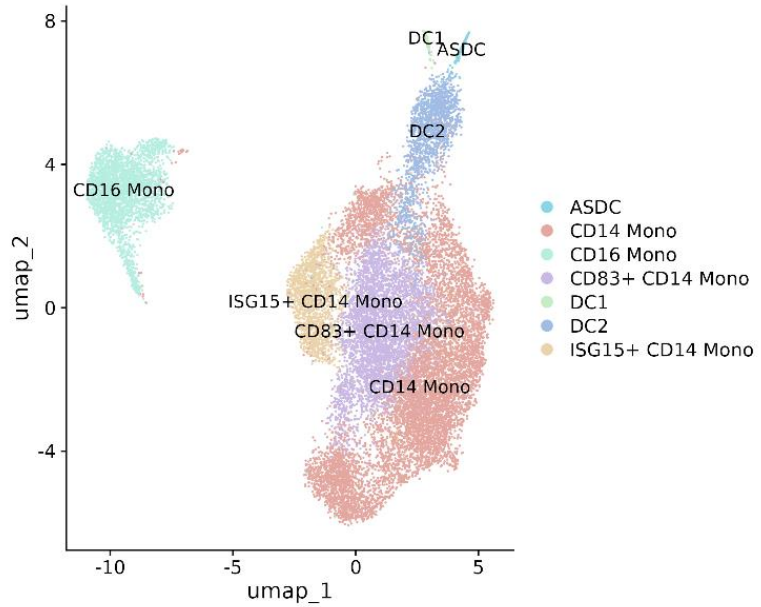
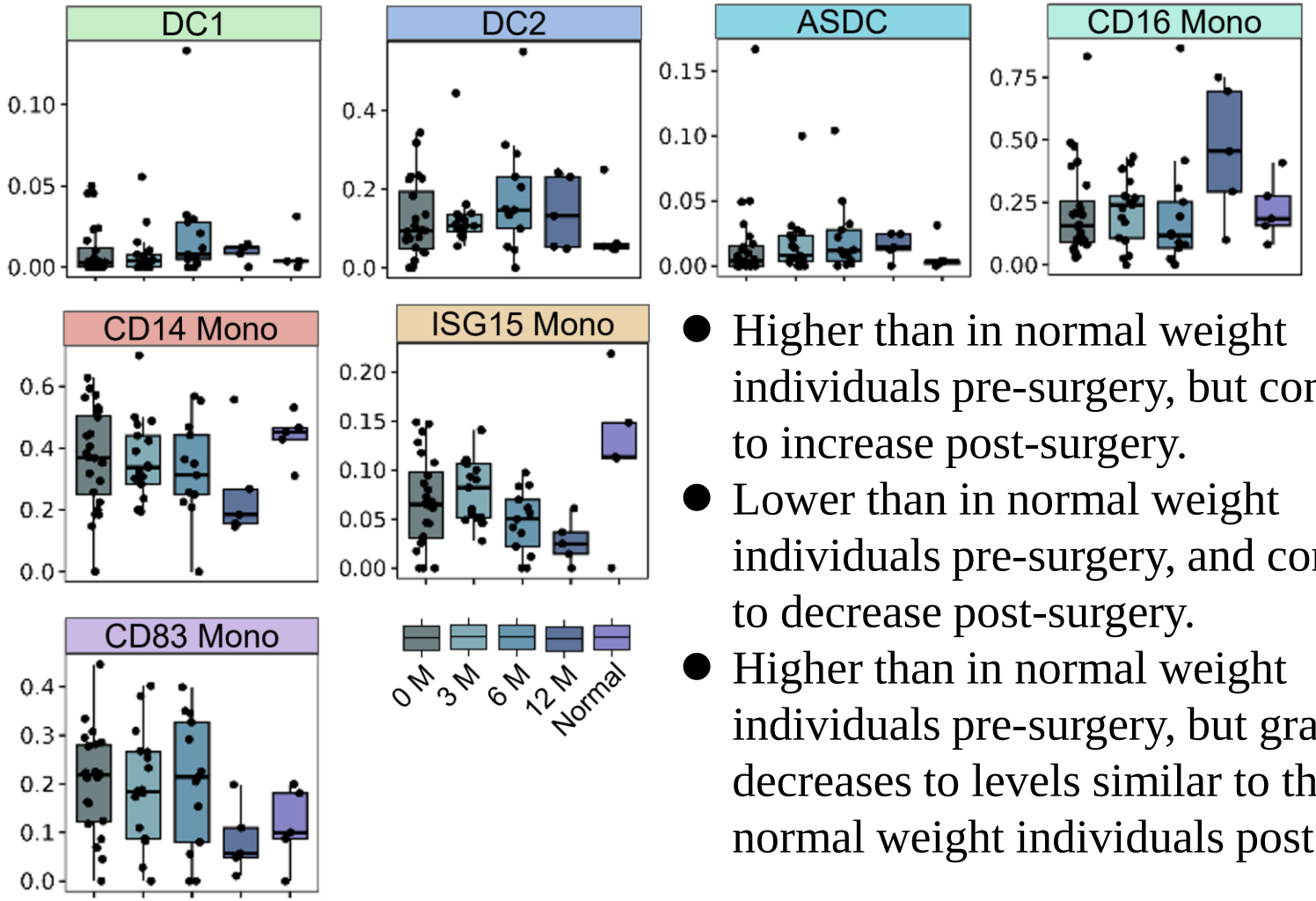
Mononuclear Phagocytes Lineage Dynamics in Obesity and Post-Bariatric Surgery



- Identified 7 distinct mononuclear phagocytes subtypes after reclustering the cells.



- Higher than in normal weight individuals pre-surgery, but continues to increase post-surgery.
- Lower than in normal weight individuals pre-surgery, and continues to decrease post-surgery.
- Higher than in normal weight individuals pre-surgery, but gradually decreases to levels similar to those of normal weight individuals post-surgery.

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Conclusions

- The immune system exhibits a phased recovery post-bariatric surgery, with both transient activations and gradual normalization.

- Certain immune functions, like NKT, γδT, MAIT cells,CD14 and ISG15+ monocytes show incomplete recovery, highlighting the persistent impact of obesity on immune health.

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CONFLICT OF INTEREST DISCLOSURE

- **I have NO potential conflict of interest to report**

➢ **Please do not post because these data have not been published!**

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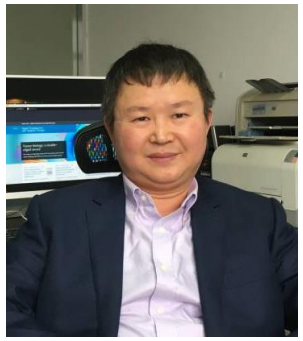

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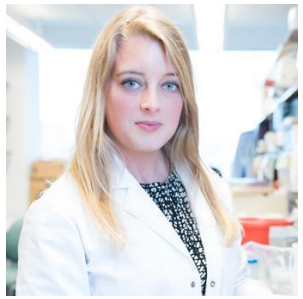

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Thanks for your attention!

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