Tumor immune microenvironment (TIME) is associated with the survival outcome and progression in triple negative breast cancer

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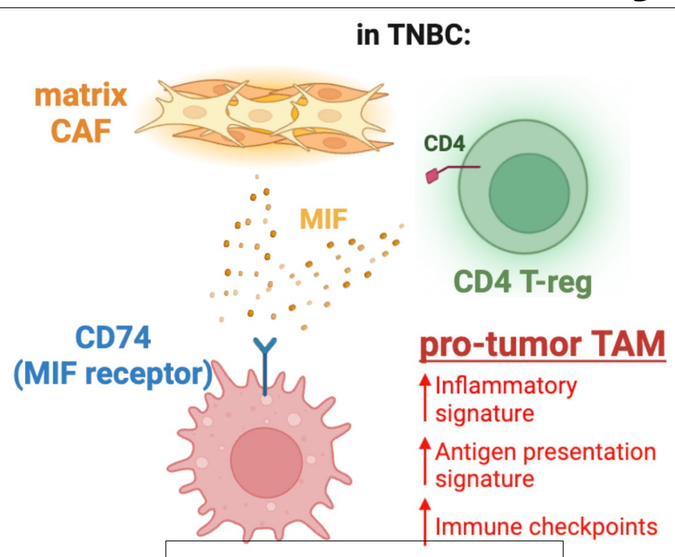
Abstract / summary

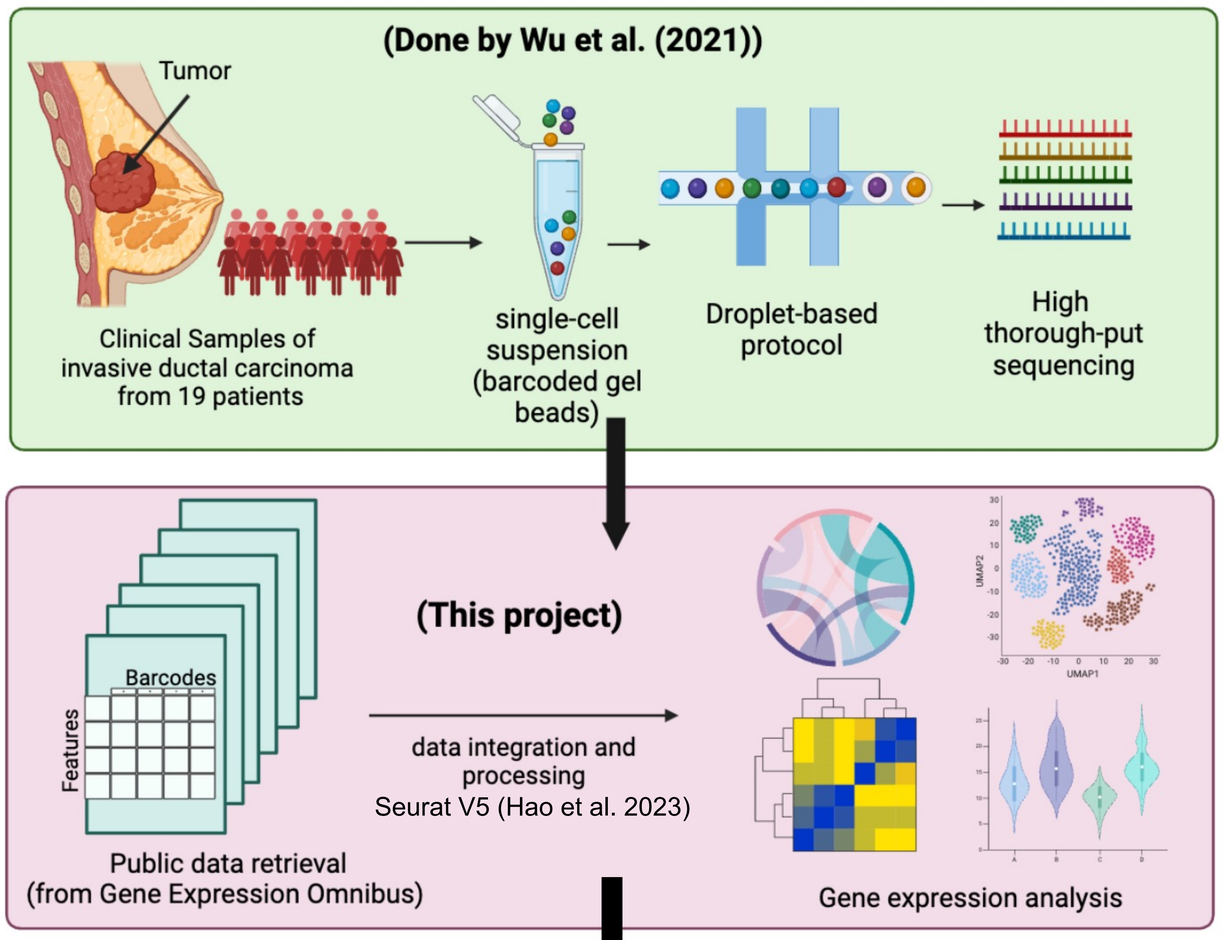
in TNBC:



Introduction

- Severity: breast cancer is a chronic disease that **severely affect the world population** (2022: 2.3 million women with breast cancer) (World Health Organization, 2024)
- Breast cancer: broadly divided into different clinical subtypes, including **ER+, PR+, HER2+ breast cancer and TNBC**
- TNBC is the **most aggressive** and deadly subtype of breast cancer
- **Tumor-immune micro-environment (TIME)** has been found to be crucial in determining the survival outcome of the patients
- Aim: characterize the crucial subtypes of tumor-associated cells that may potentially affect the **survival outcome** and **tumor progression in TNBC**

Materials and Methods

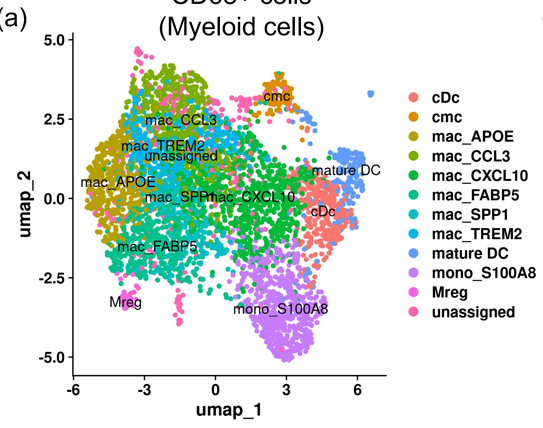


Independent Validation by bulk RNA seq data (TCGA-BRCA cohort)

TCGA

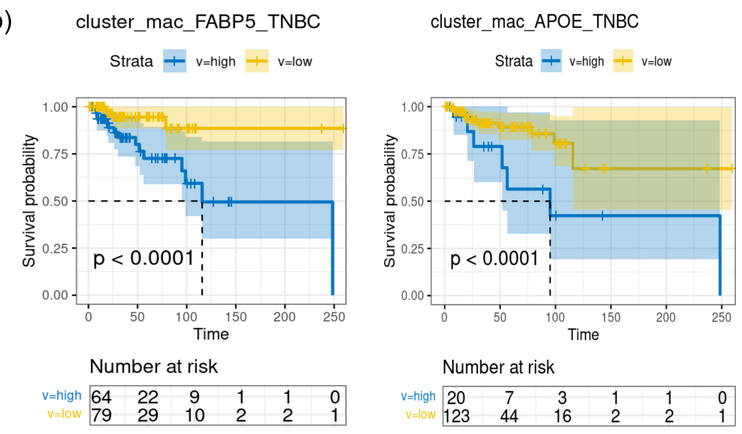
Results

(a) CD68+ cells (Myeloid cells)



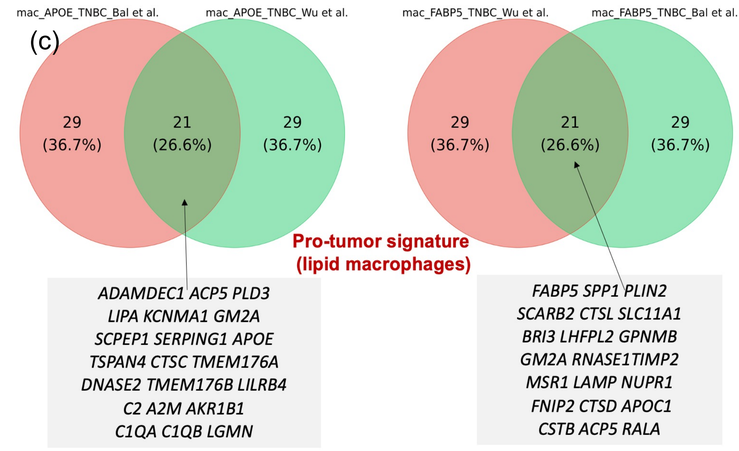
UMAP visualization of myeloid cells (CD68+)

(b)



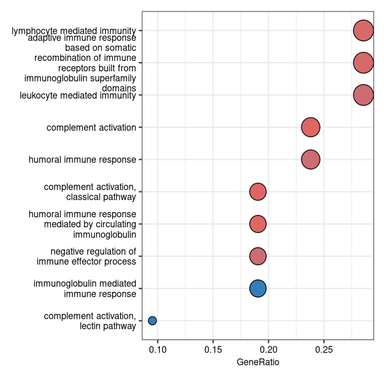
Kapien-Meier surivival analysis of lipid-associated macrophages

(c)

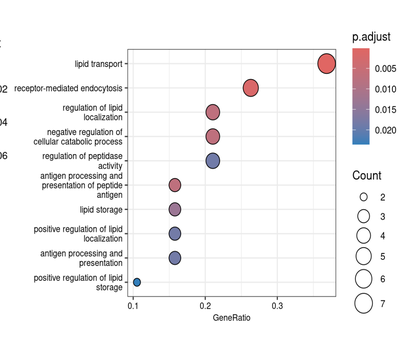


Independent validation of lipid macrophage signature using another set of **single-cell RNA seq** data from Bal et al. (2021)

(d) mac_APOE's gene signature



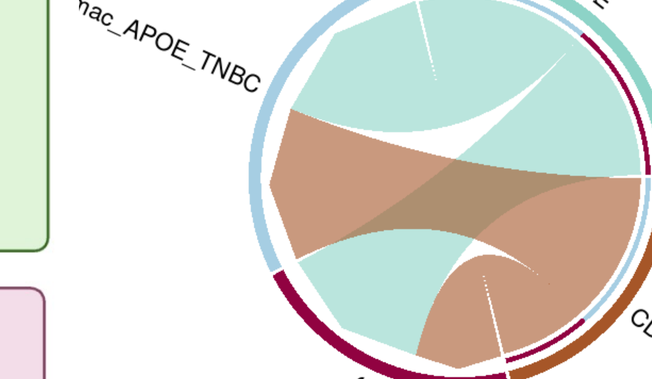
mac_FABP5 gene signature



Gene ontology (GO) analysis of co-expressed lipid-mac signature

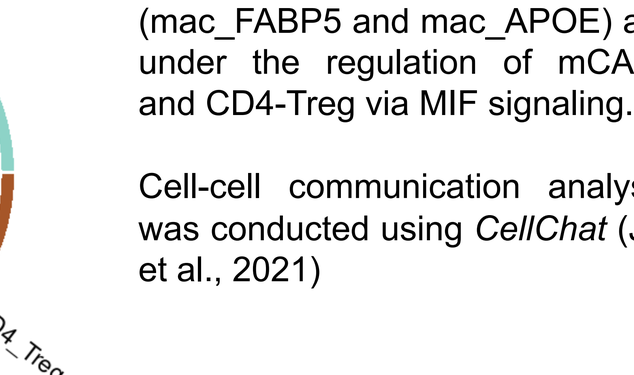
(e)

Gene signature	Related Genes	Identifier
Pro-inflammatory / Antigen presentation signature	*CCL11 IFNG CCL3 CCL4 IL1B TNF IL1R2 CD80 CD86 TLR2 HIF1A CSF2 IL6 CCL2 CCL8 CCL5 CD68 HLA-DPA1 HLA-DQA1 HLA-DQB1 HLA-DRA HLA-DRB1 IRF5 TLR4*	Zhang et al. (Cancer cell, 2021)



- **Strong positive correlation** between pro-inflammatory signature and gene signature of lipid macrophage signature

(f)



Independent validation by TCGA-BRCA cohort

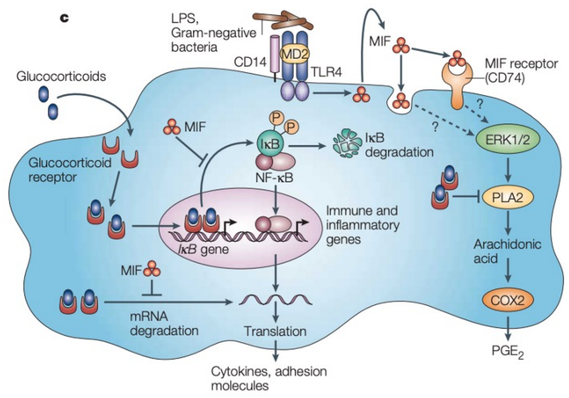
- **Strong positive correlation** between some well-known myeloid immune checkpoints and gene signature of lipid macrophage signature.

(e) MIF signaling pathway network

Lipid associated macrophage (mac_FABP5 and mac_APOE) are under the regulation of mCAFs and CD4-Treg via MIF signaling.

Cell-cell communication analysis was conducted using *CellChat* (Jin et al., 2021)

Discussion



(Calandra & Roger, 2003)

MIF signaling

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inflammatory phenotype in myeloid cells

↓

- mCAF and CD4-Treg: potential **source of MIF signaling**

↓

- Association with **immuno-suppression** in myeloid cells

↓

- Tuned down **anti-cancer immunity** by macrophage

- **Future research directions:**

- study the correlations between MIF signaling, lipid macrophage signature and other T cell signature (e.g. T-cell dysfunction in effector T cells)

Reference:
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