Single-Cell Genomic Characterization Reveals the Cellular Reprogramming of the Gastric Tumor Microenvironment
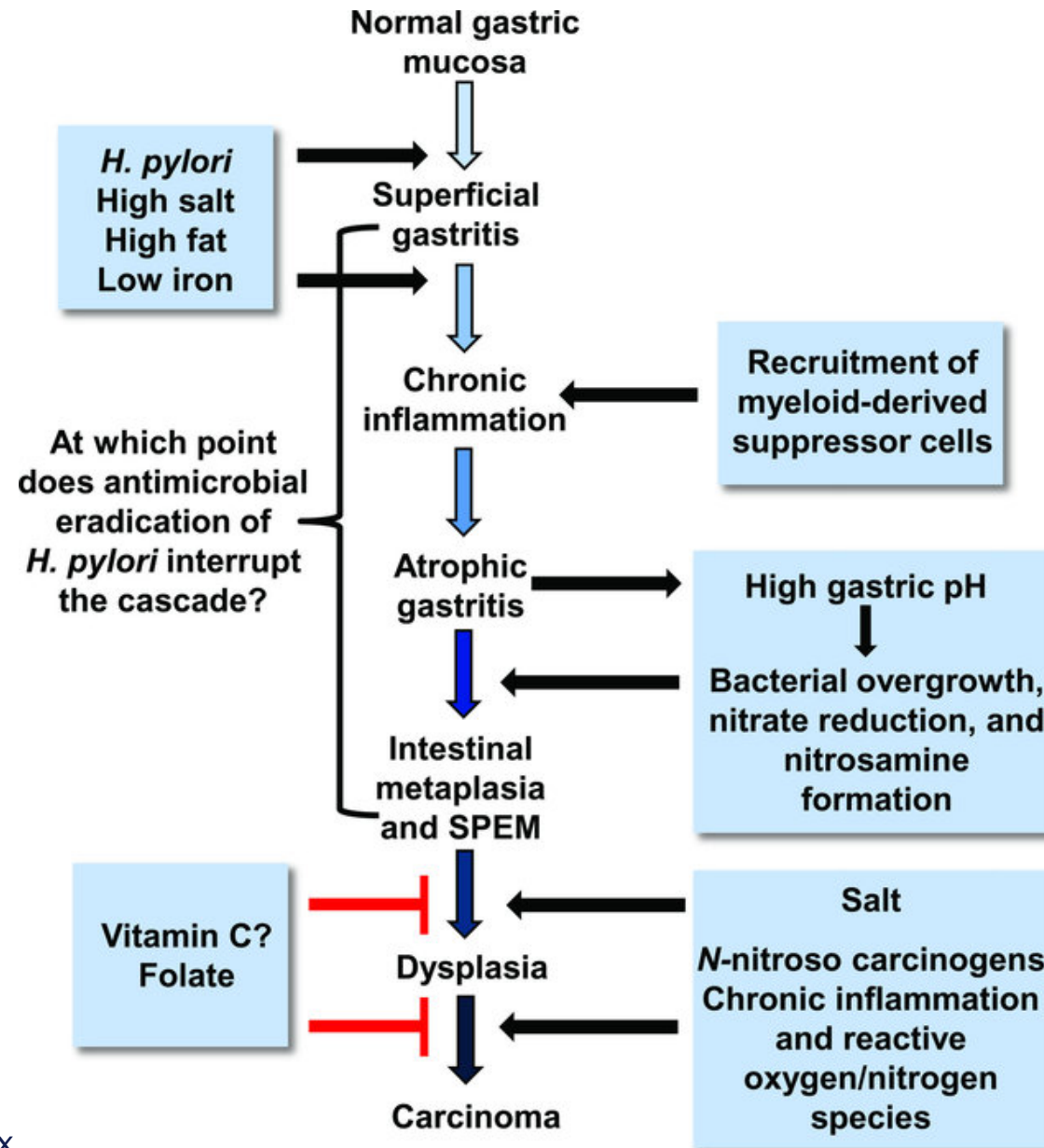
Sathe et al.

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JC_23112021

Jonas Bauer

Gastric cancer

Correa Cascade

Background: H.pylori

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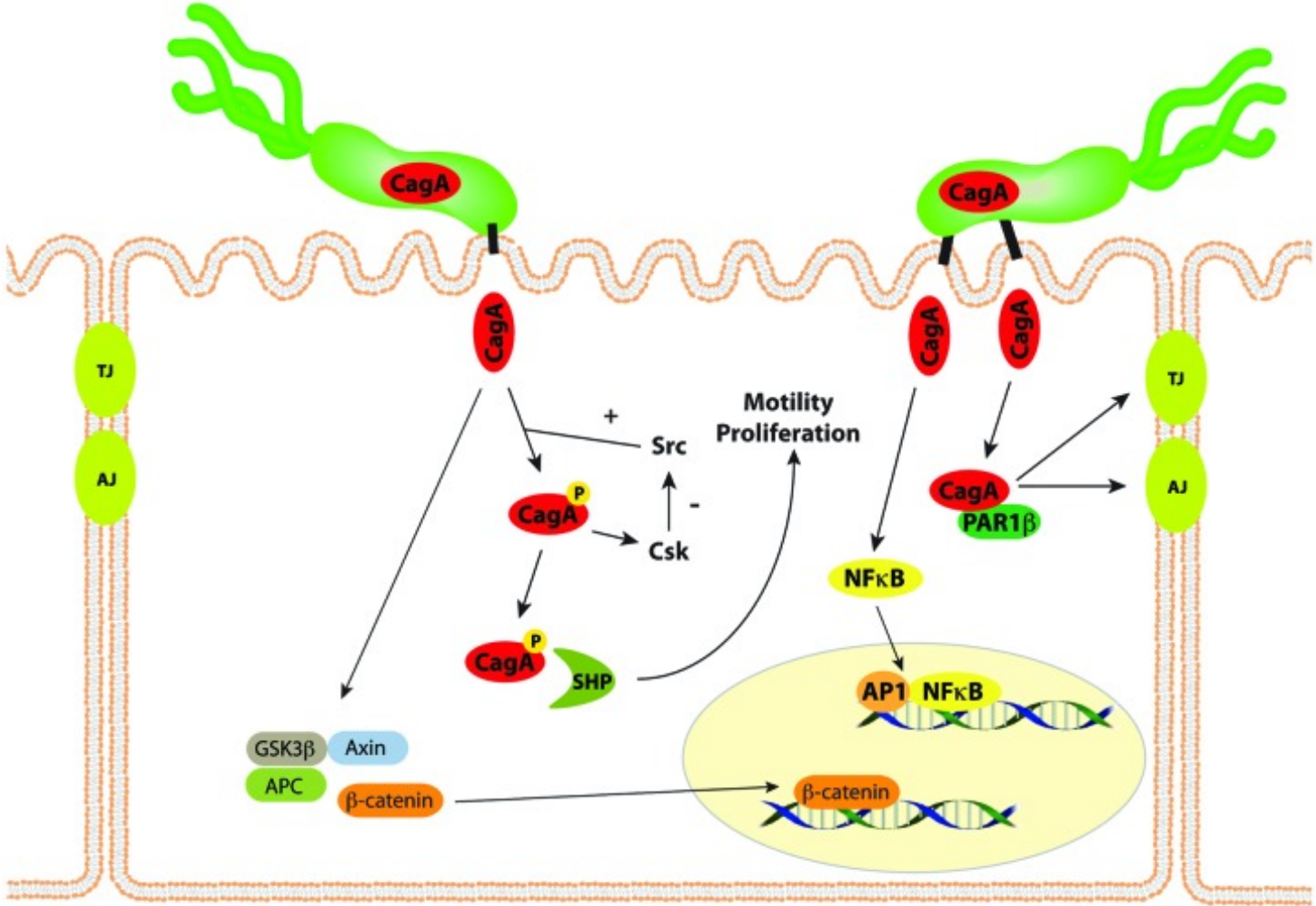
Background: H.pylori
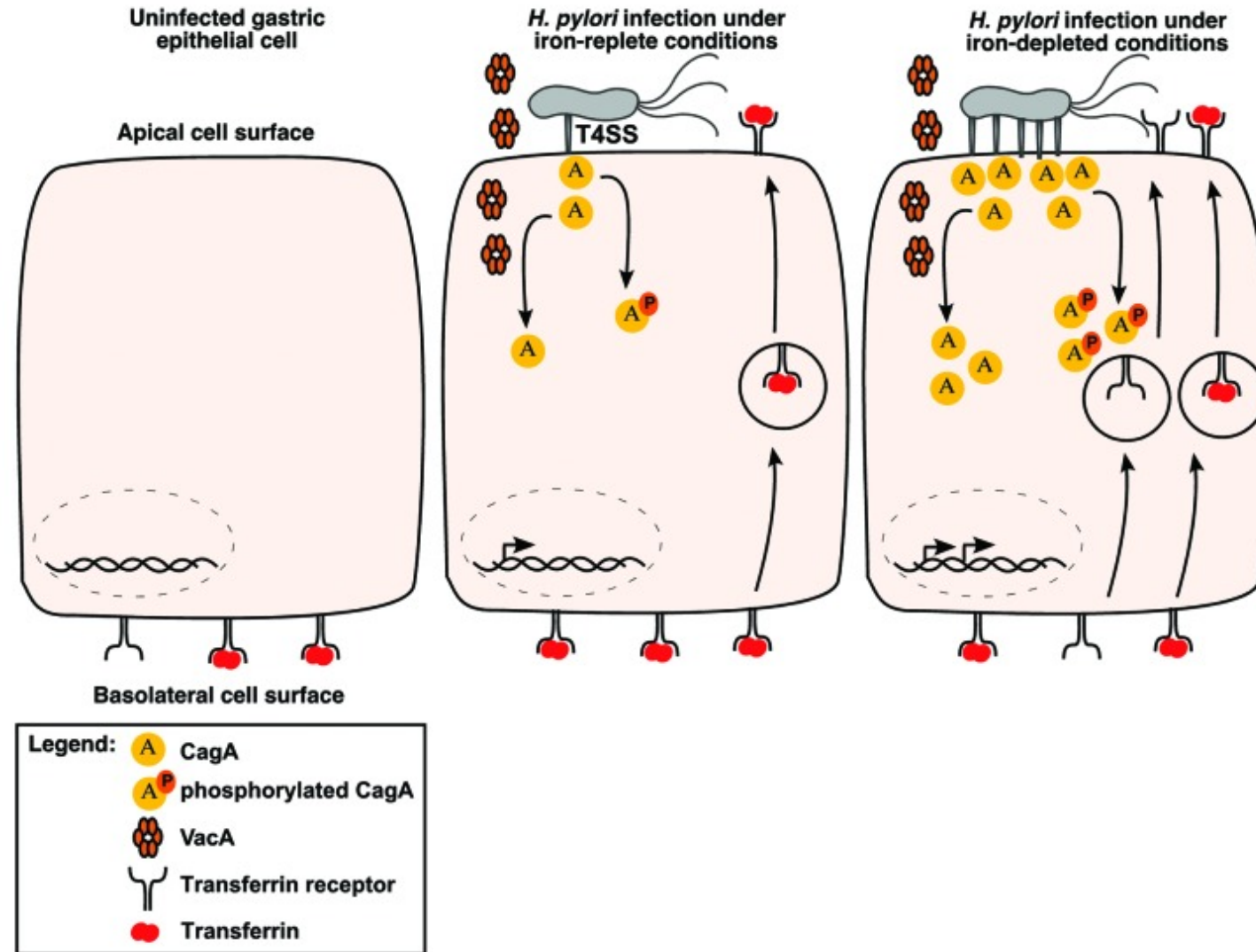
Gastric cancer

- diffuse seborrheic keratoses in combination with acanthosis nigricans: Leser-Trélat-syndrome
- Most patients are symptomatic, with weight loss and abdominal pain

Gastric cancer

Biomarkers
- CEA, CA 125, CA 19-9, and CA 72-4
- Alpha-fetoprotein
- Pepsinogen

- Helicobacter pylori infection in 65–80%
- 2% of people with H. pylori develop stomach cancer
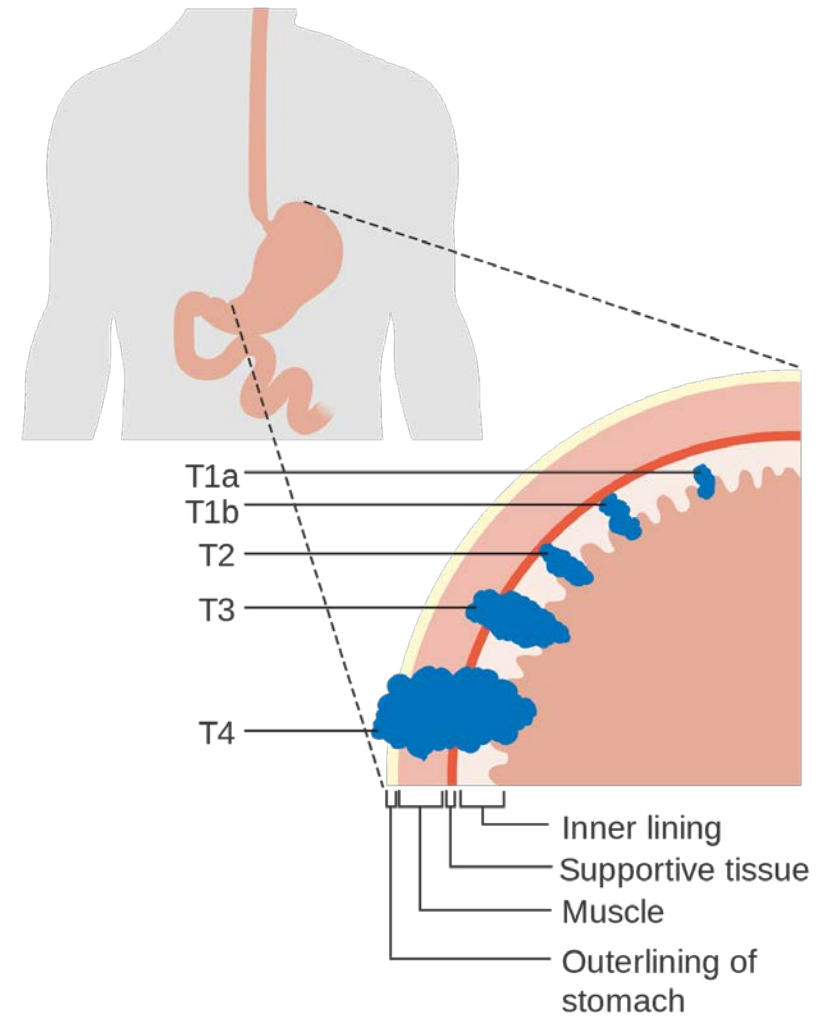
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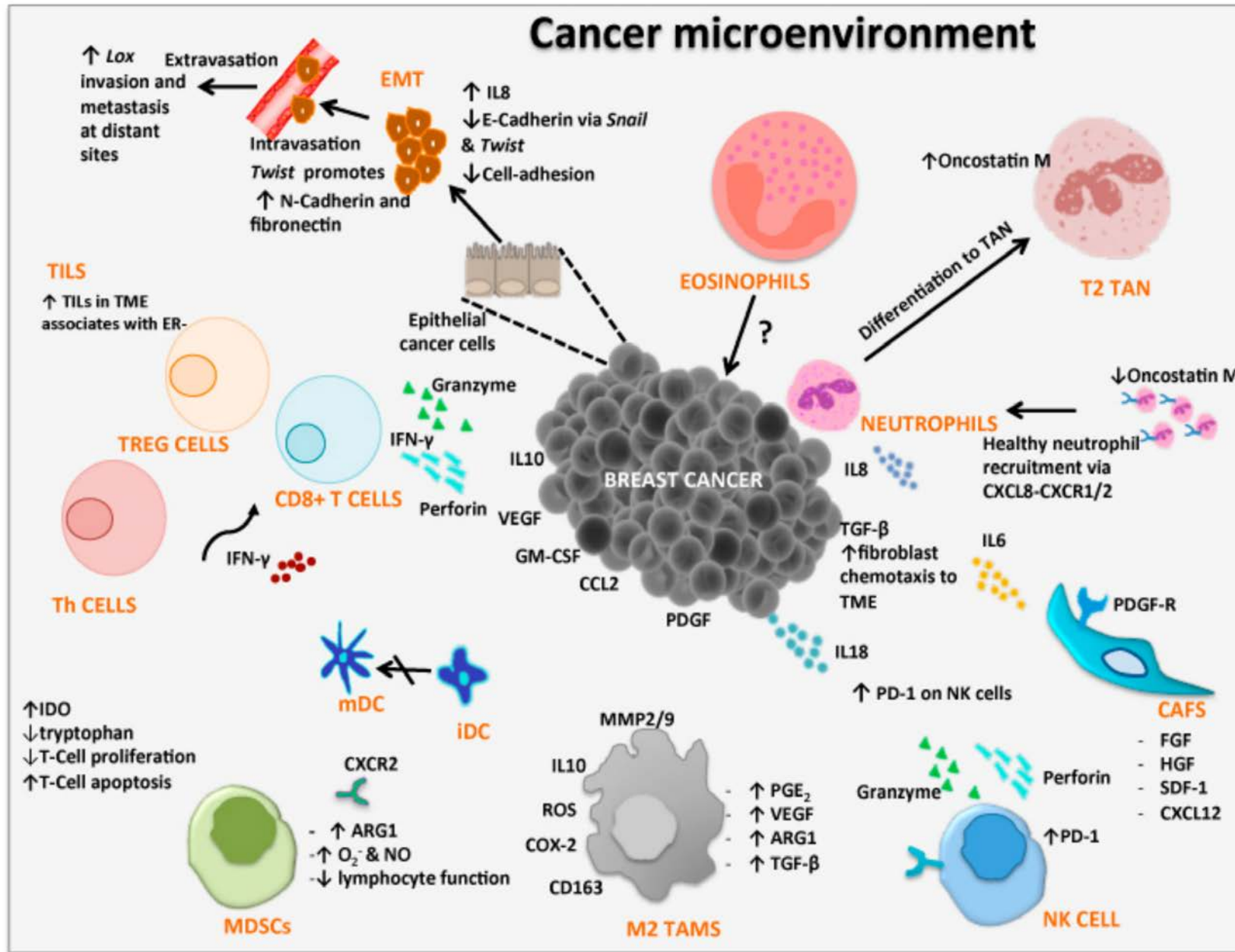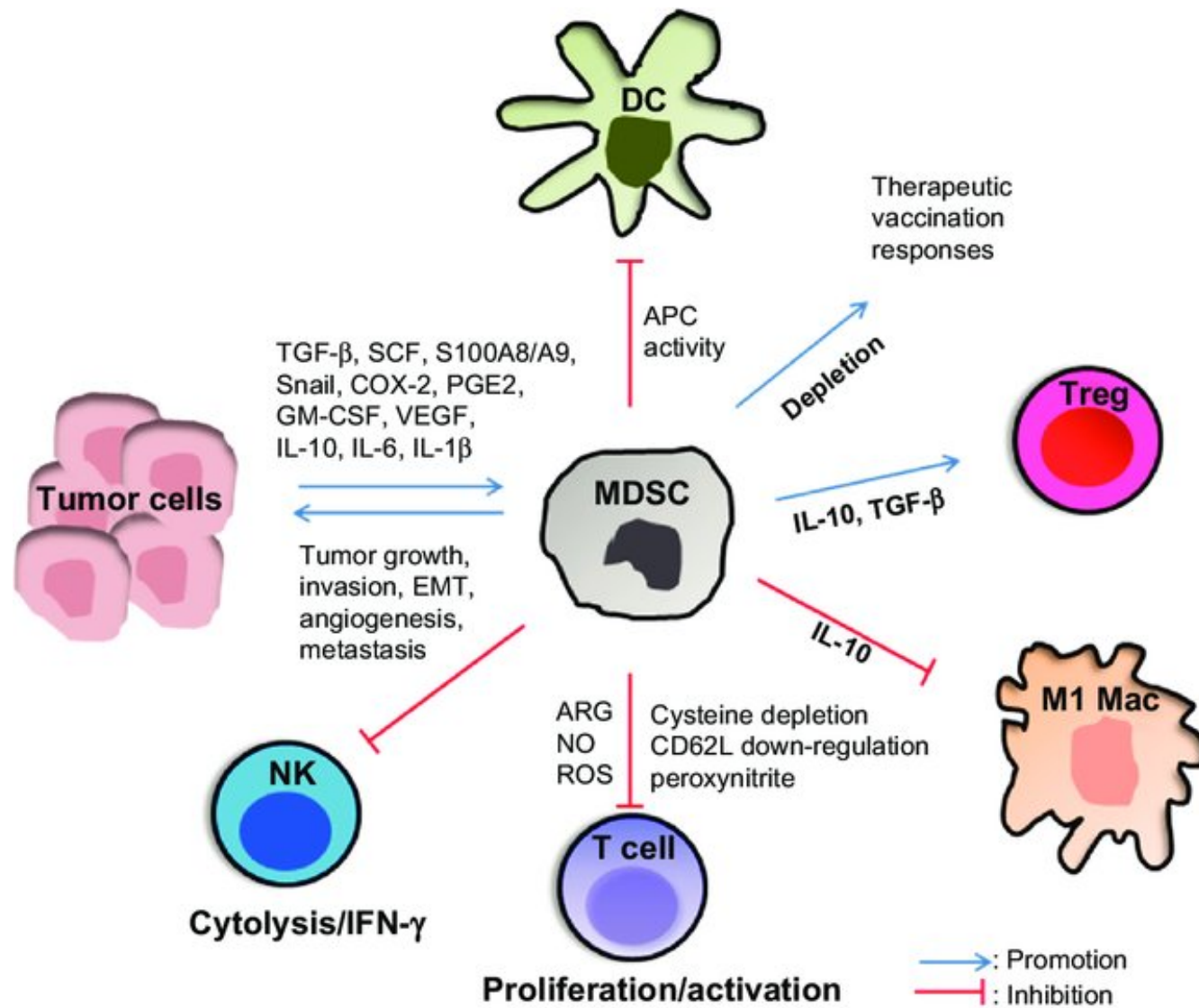# Gastric cancer

Laurén and World Health Organization classification

| Laurén classification	World Health Organization classification
Intestinal type	Papillary adenocarcinoma
	Tubular adenocarcinoma
	Mucinous adenocarcinoma
Diffuse type	Signet-ring cell carcinoma and other poorly cohesive carcinomas
Indeterminate type	Mixed carcinoma
	Adenosquamous Carcinoma
	Squamous cell carcinoma
	Hepatoid adenocarcinoma
	Carcinoma with lymphoid stroma
	Choriocarcinoma
	Carcinosarcoma
	Parietal cell carcinoma
	Malignant rhabdoid tumor
	Mucoepidermoid carcinoma
	Paneth cell carcinoma
	Undifferentiated carcinoma
	Mixed adeno-neuroendocrine carcinoma
	Endodermal sinus tumor
	Embryonal carcinoma
	Pure gastric yolk sac tumor
	Oncocytic adenocarcinoma

Cancer microenvironment
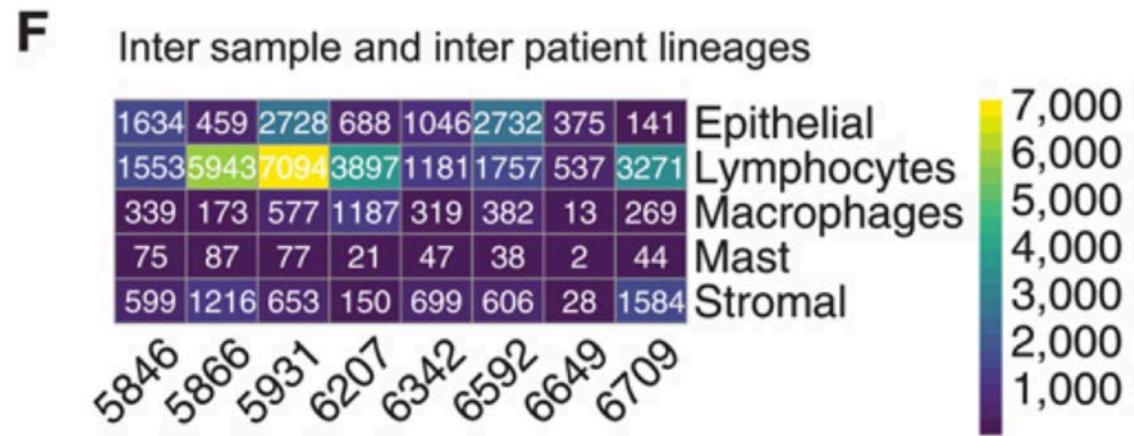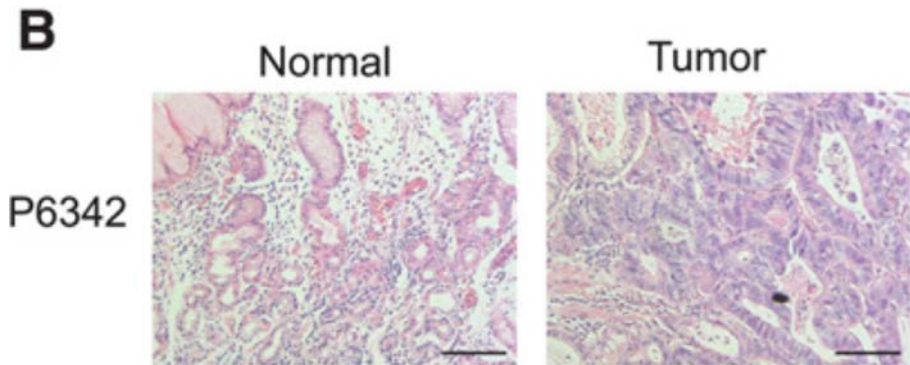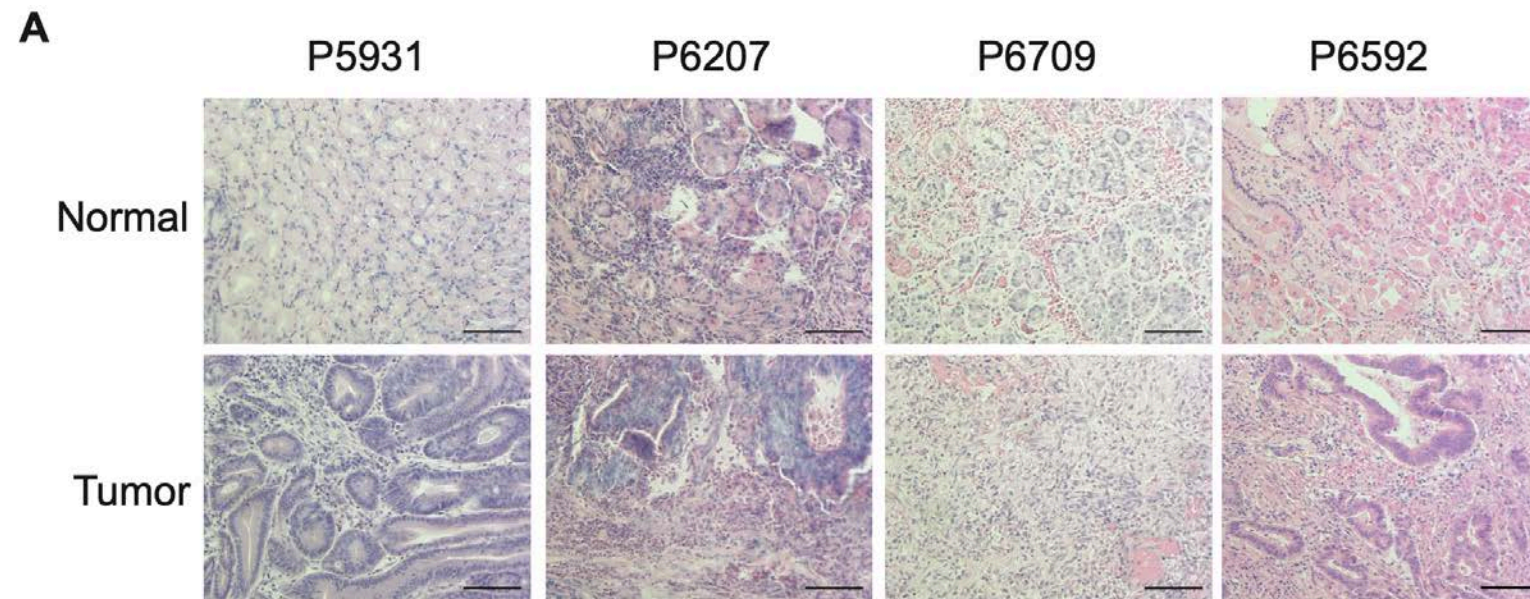
Targeting myeloid-derived suppressor cells augments antitumor activity against lung cancer; ImmunoTargets and Therapy 2012(1):7-12

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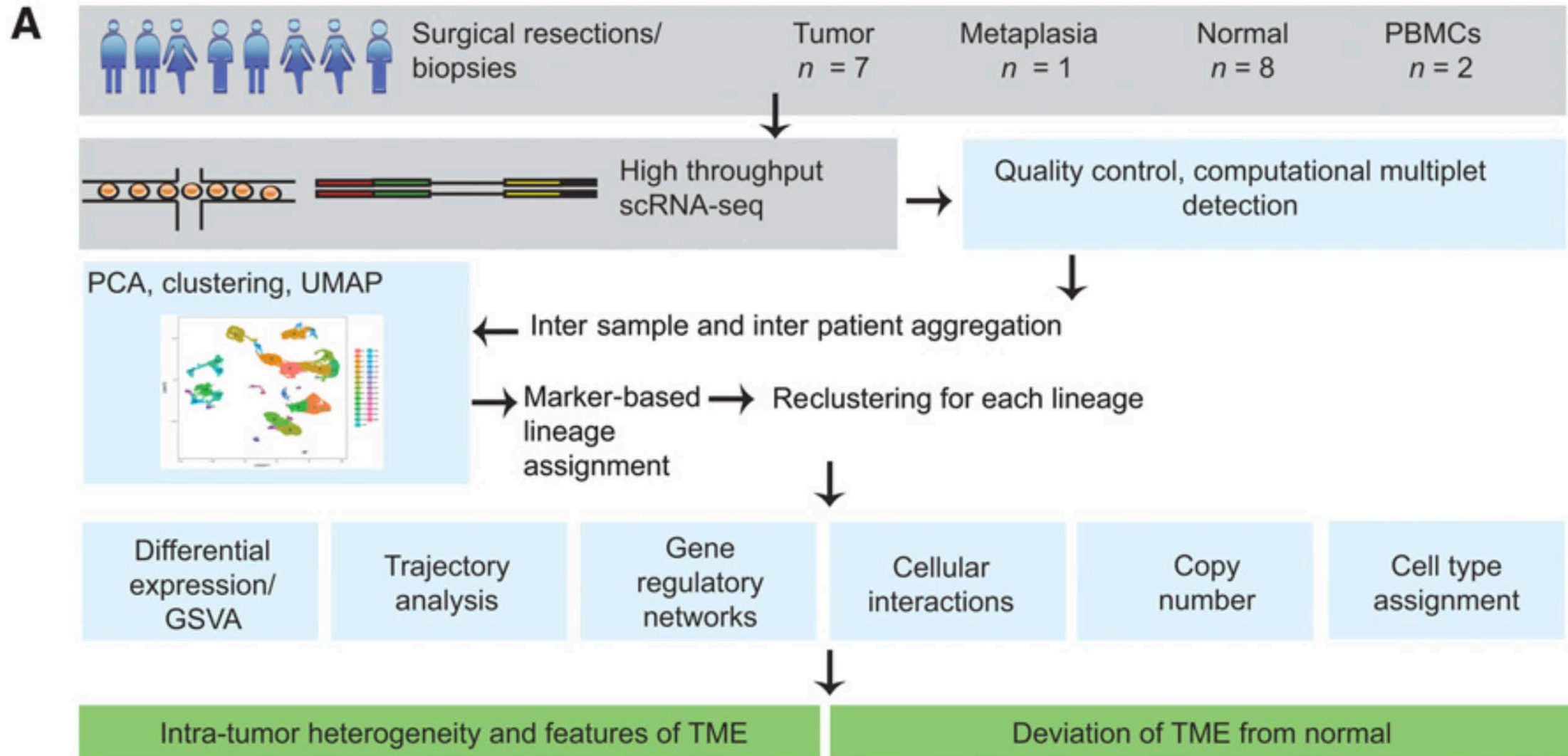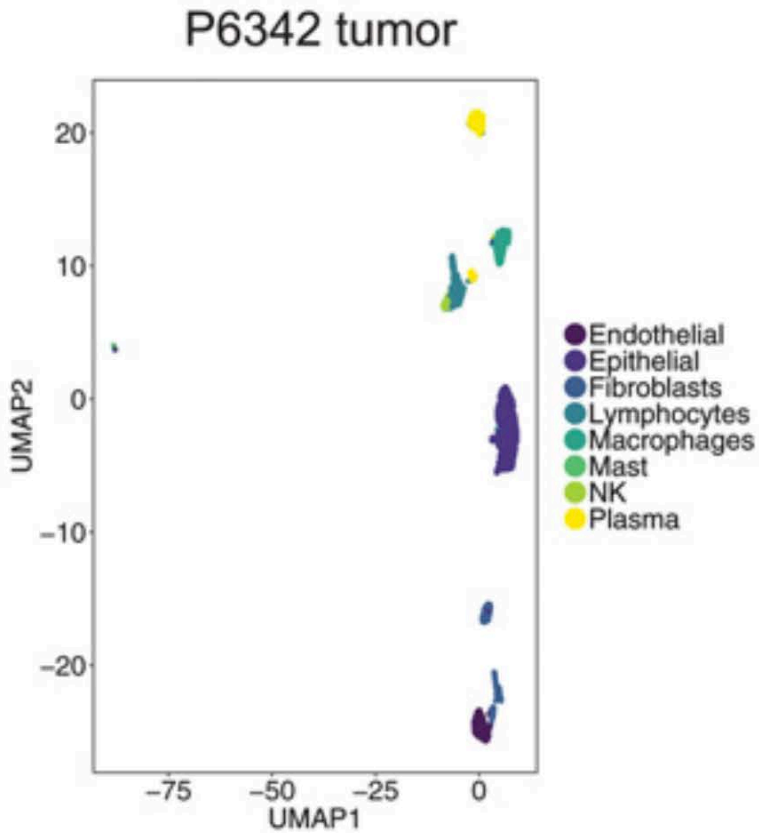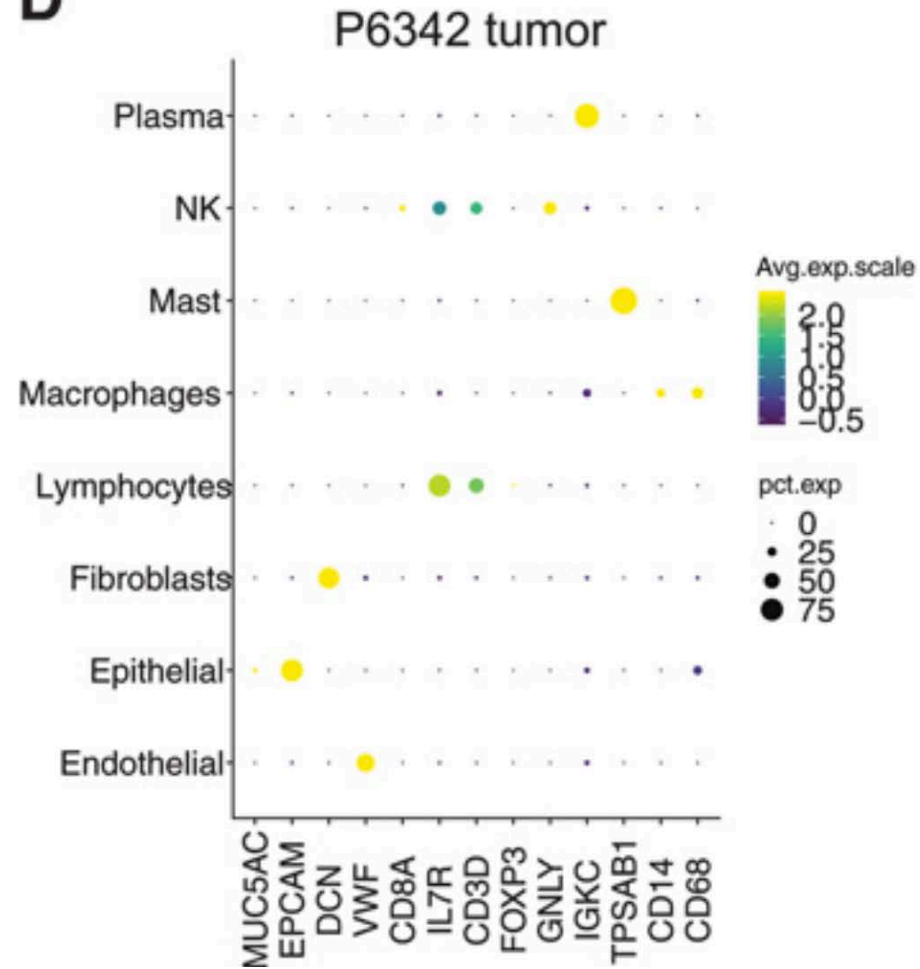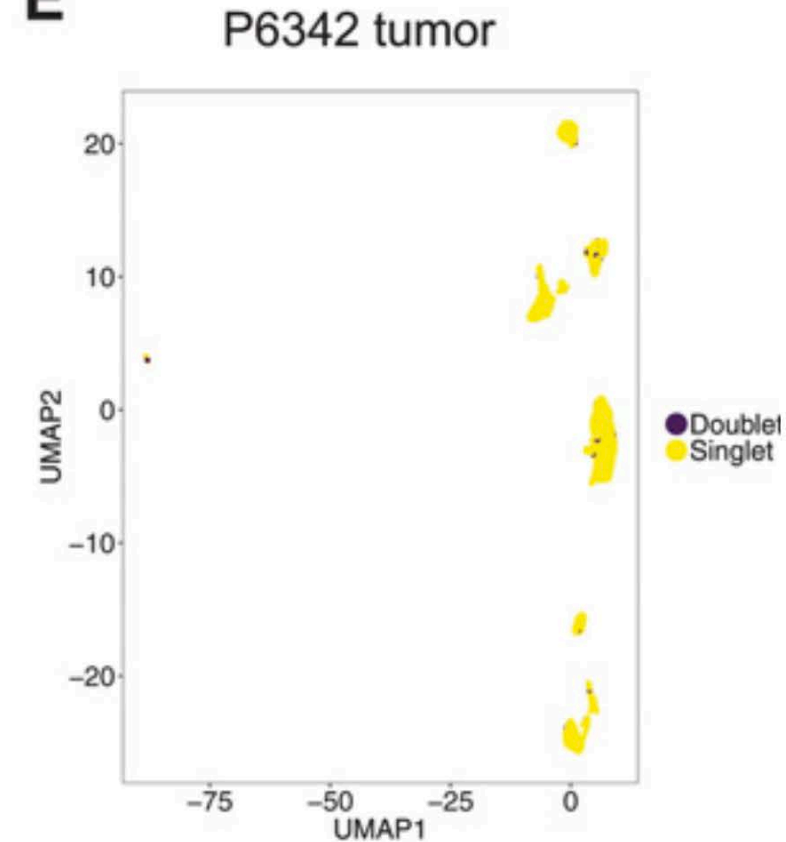
Methods

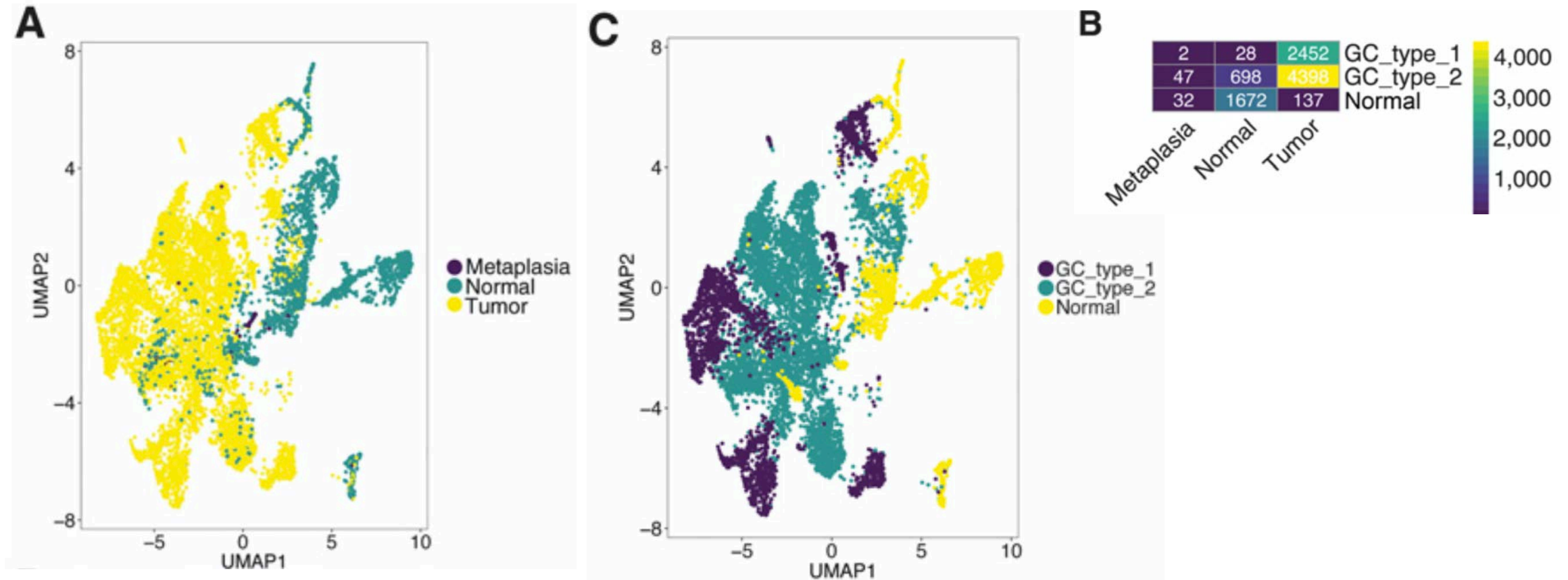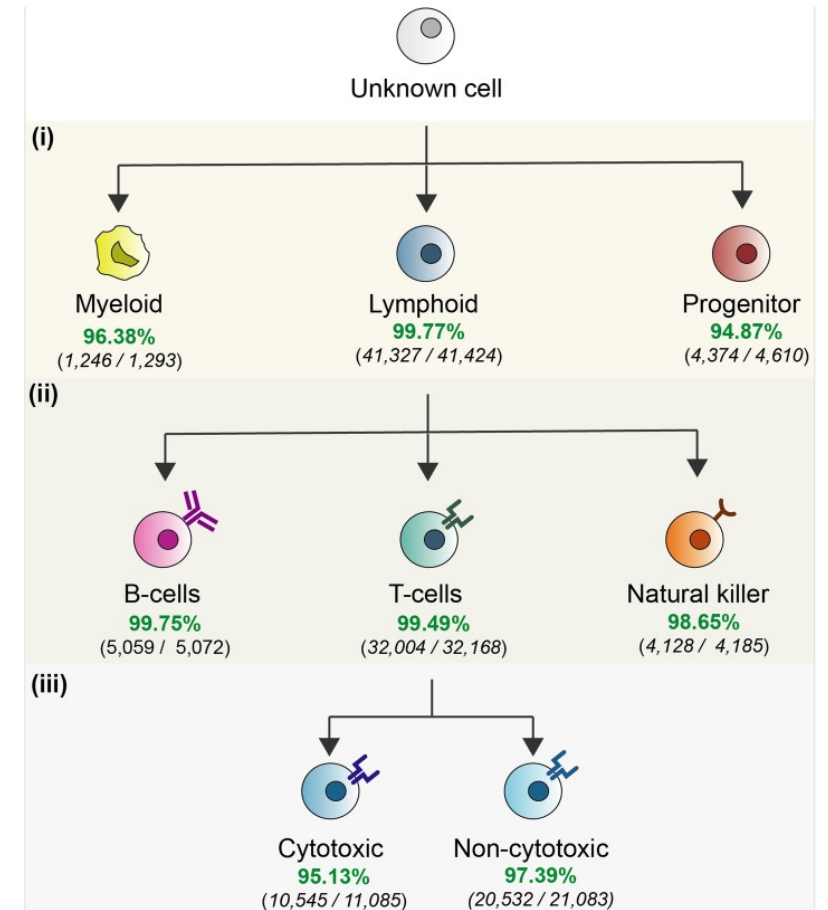# Results

Results
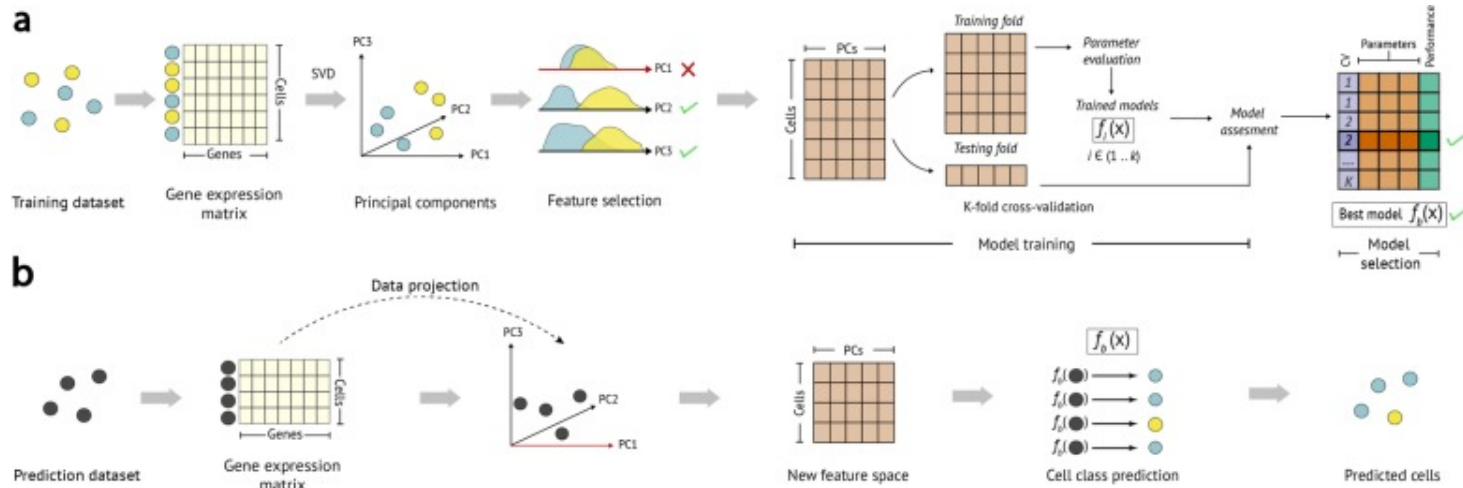# Single-cell profiling of gastric cancer
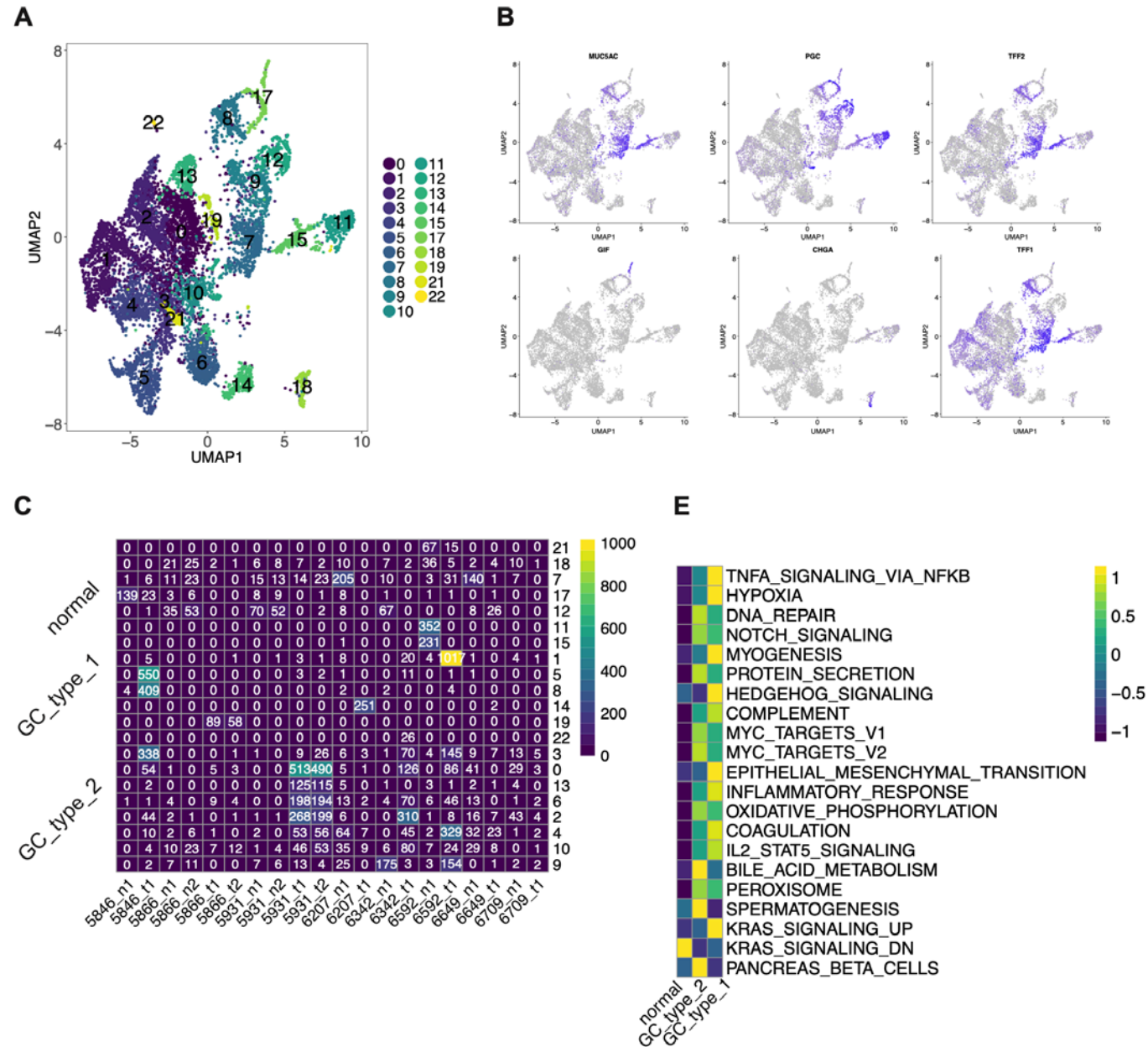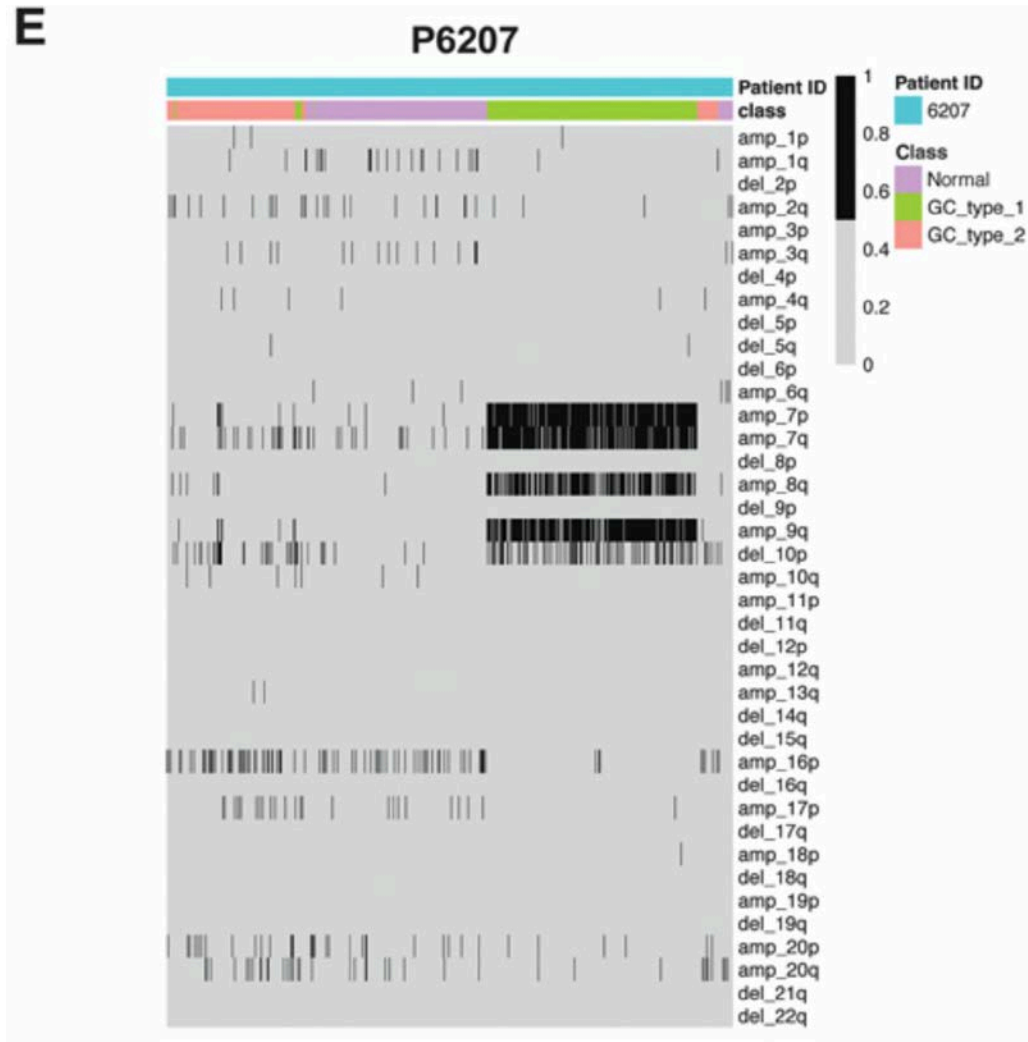
Results
Epithelial cells

scPred

scPred: accurate supervised method for cell-type classification from single-cell RNA-seq data; Jose Alquicira-Hernandez et al.
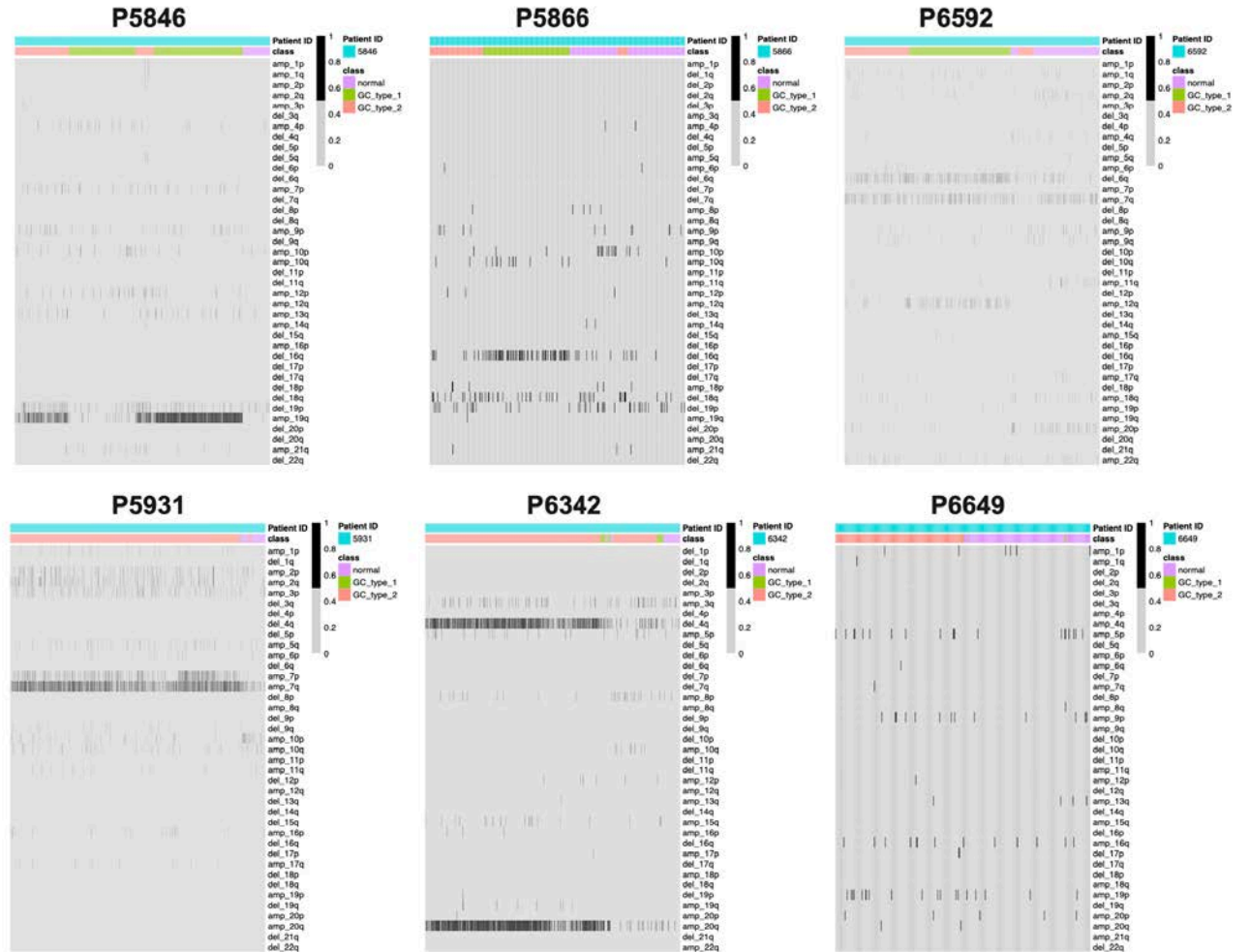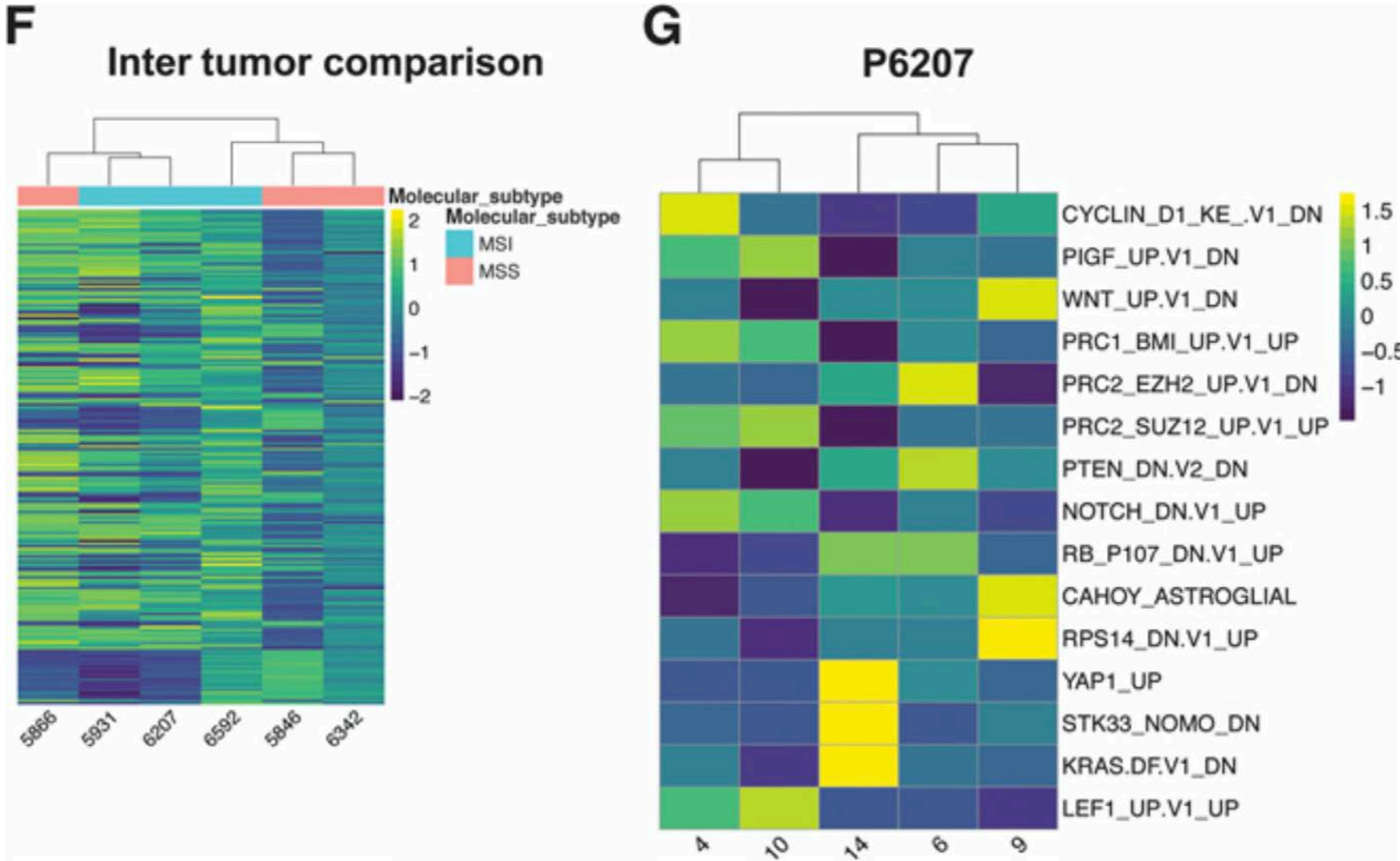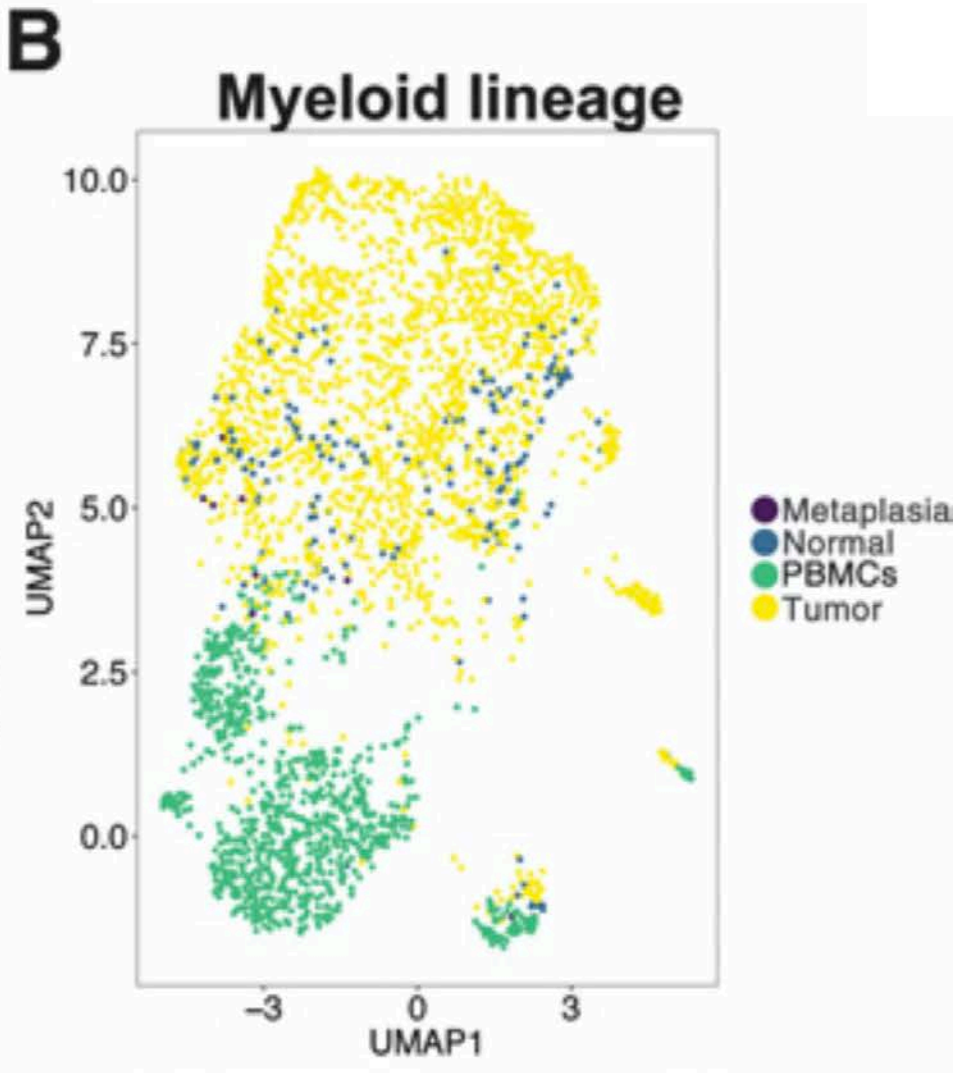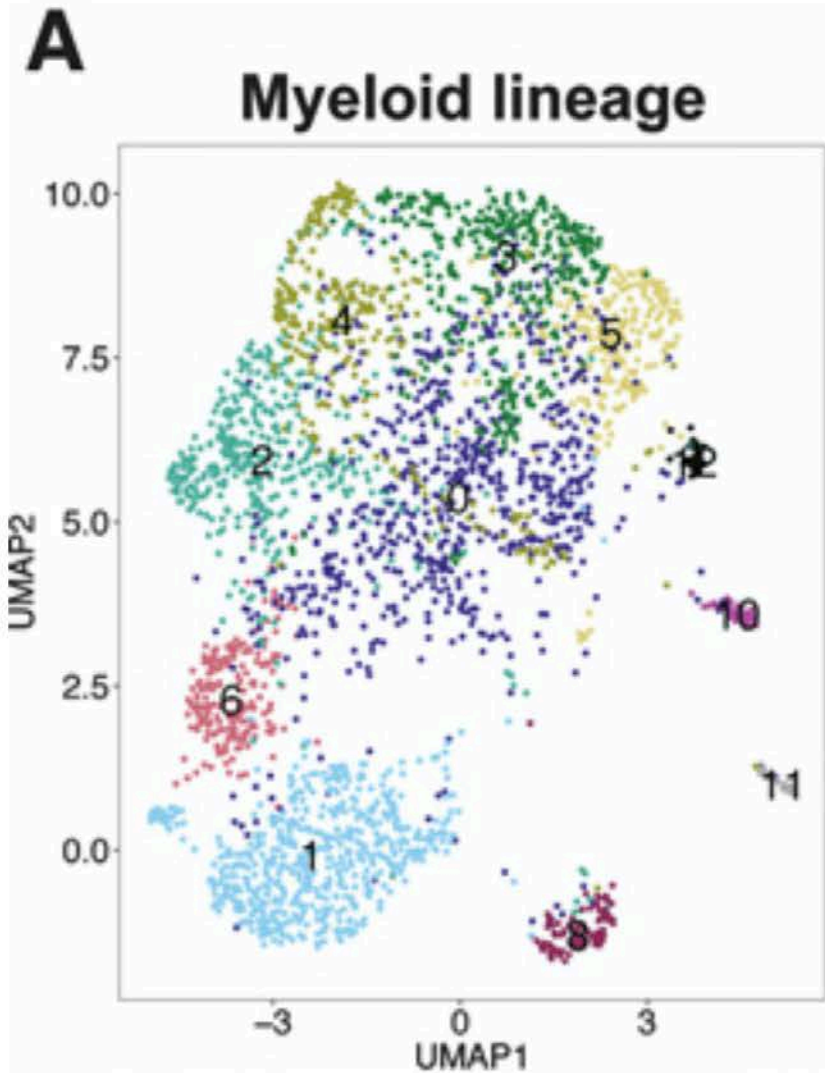
Results

Results

Results

Results

Results

Results

Results

Results

B Cytotoxic T lymphocytes

A
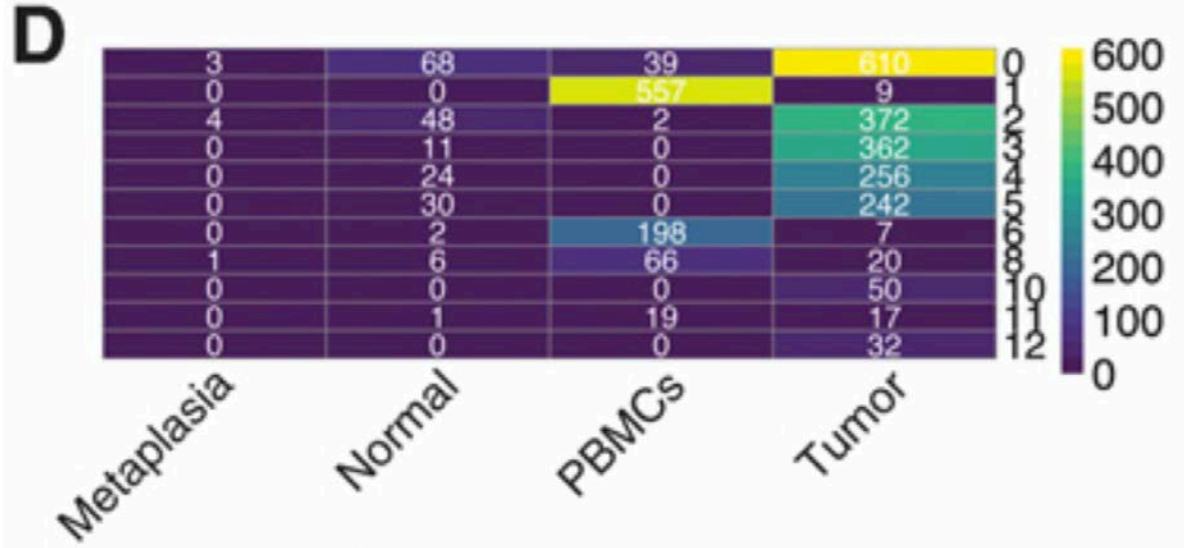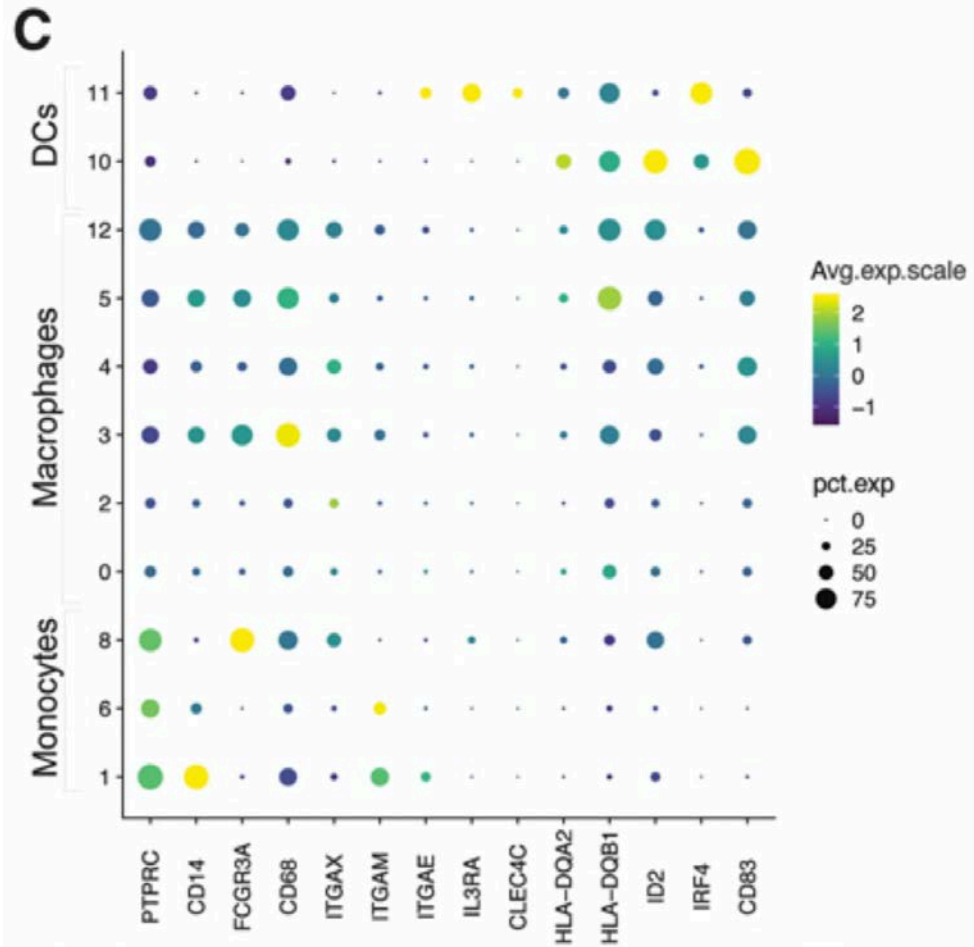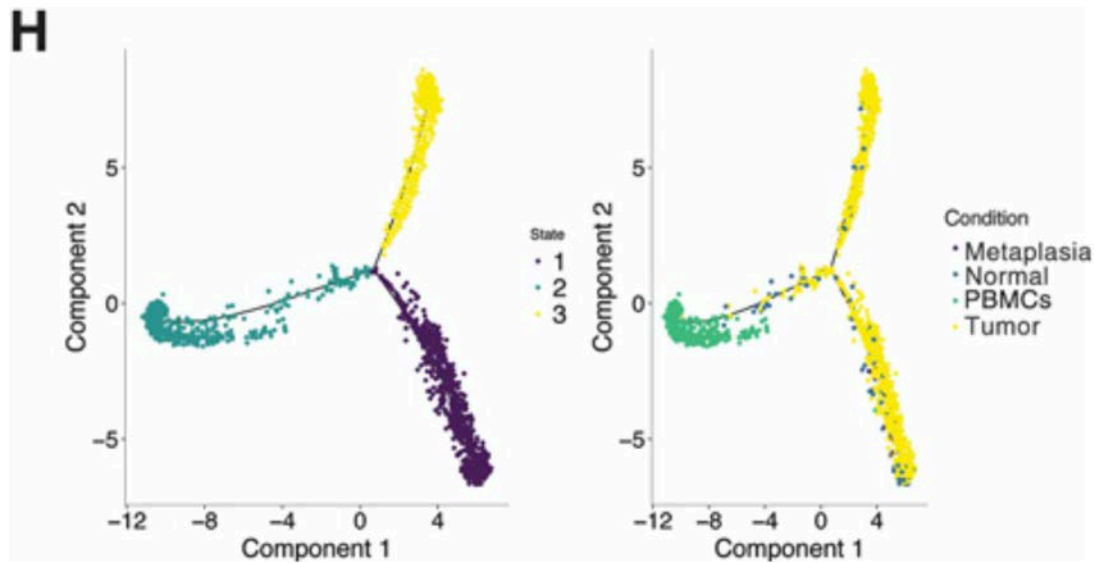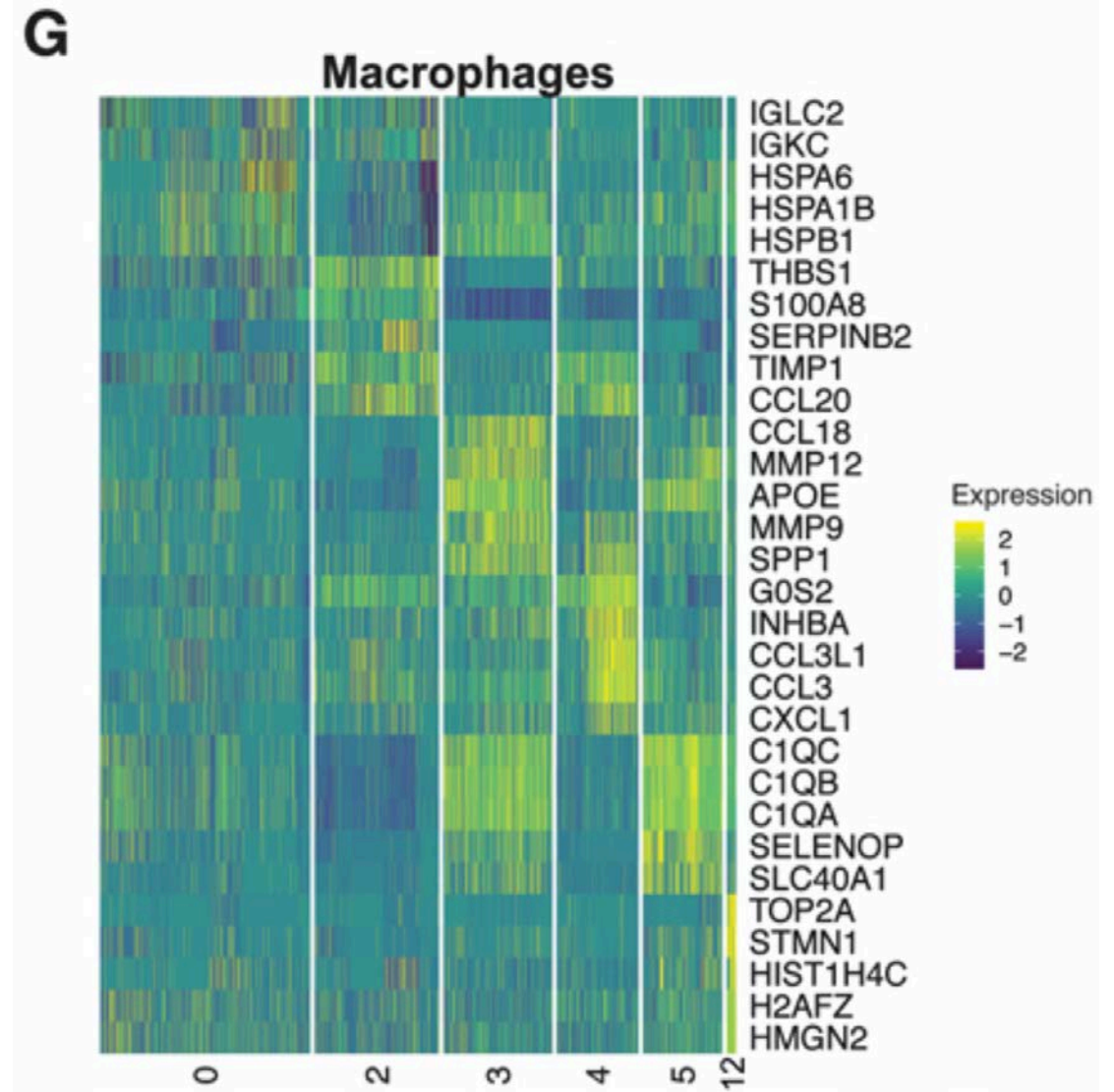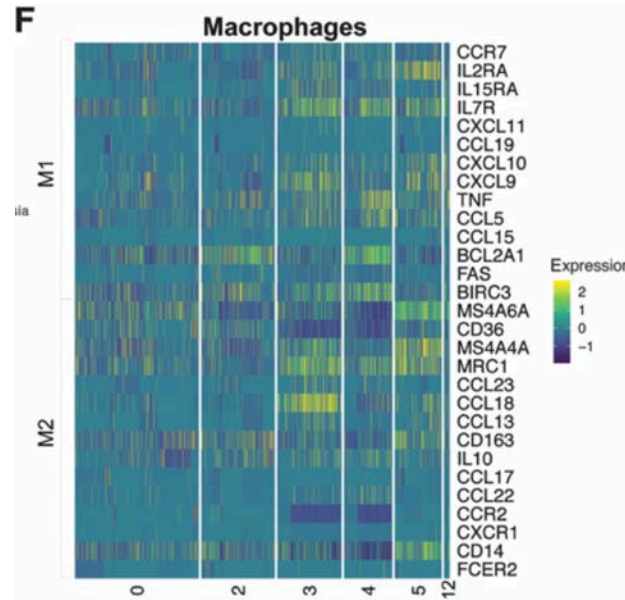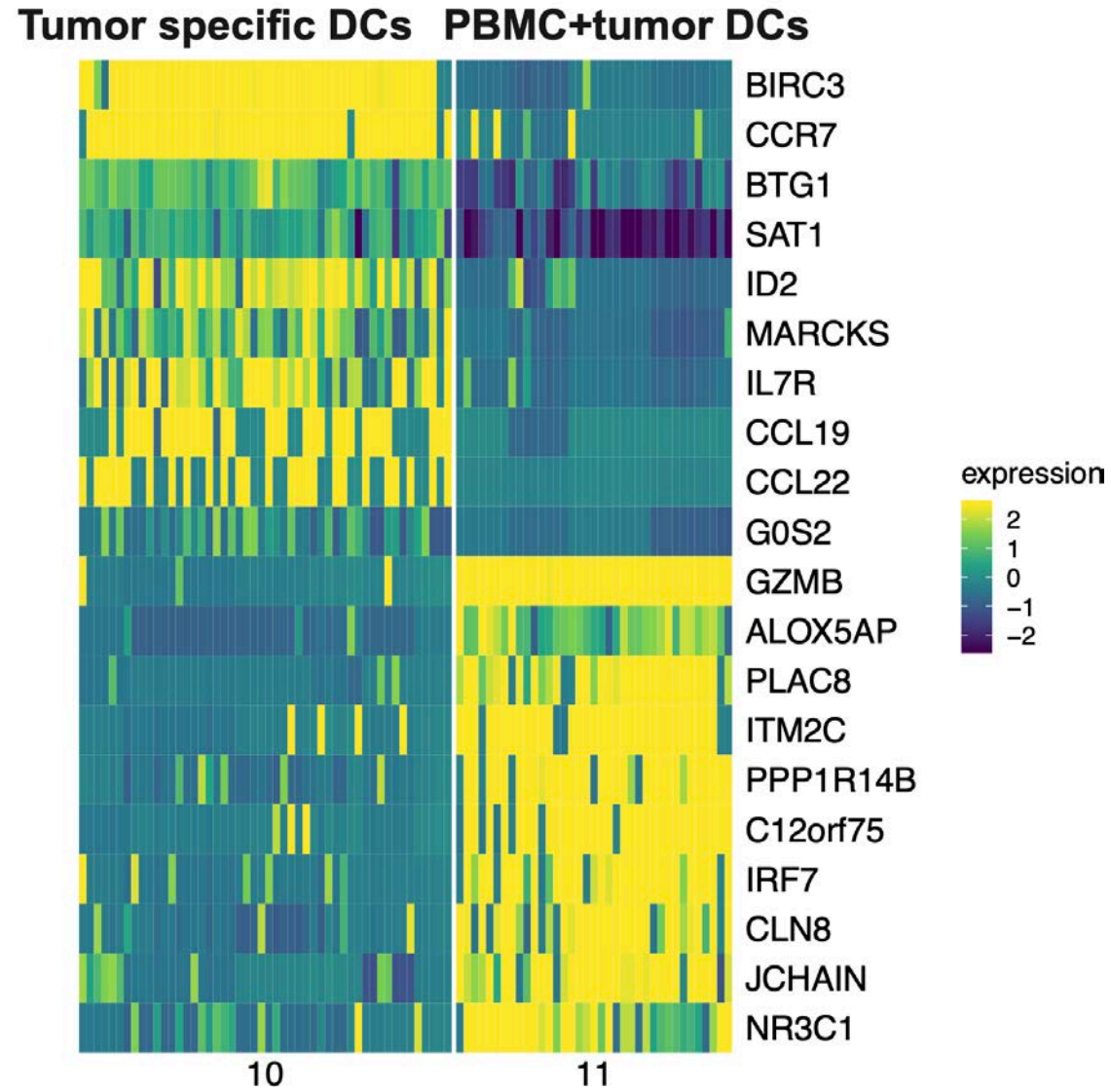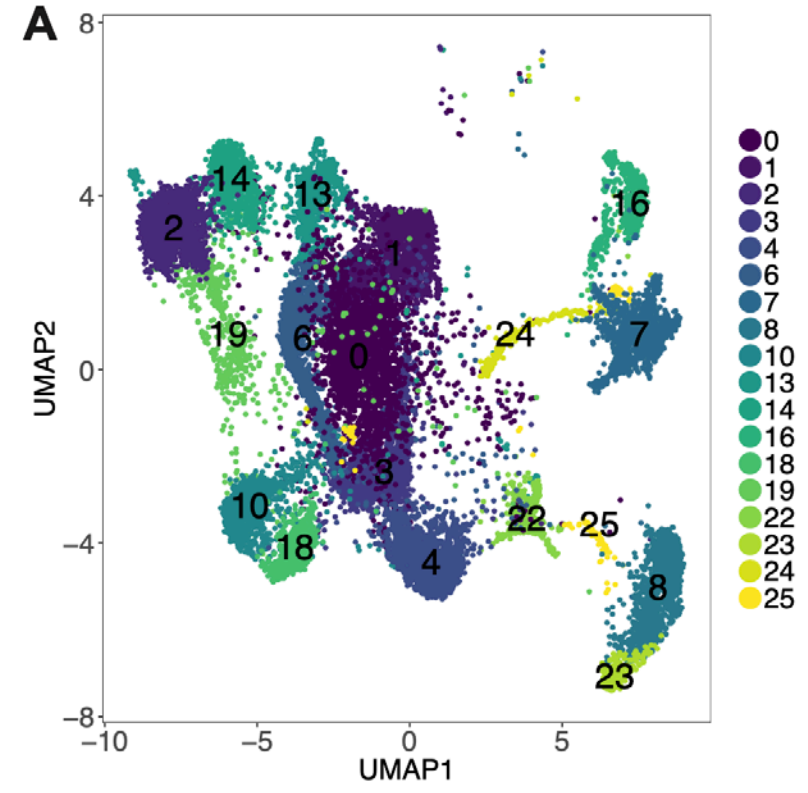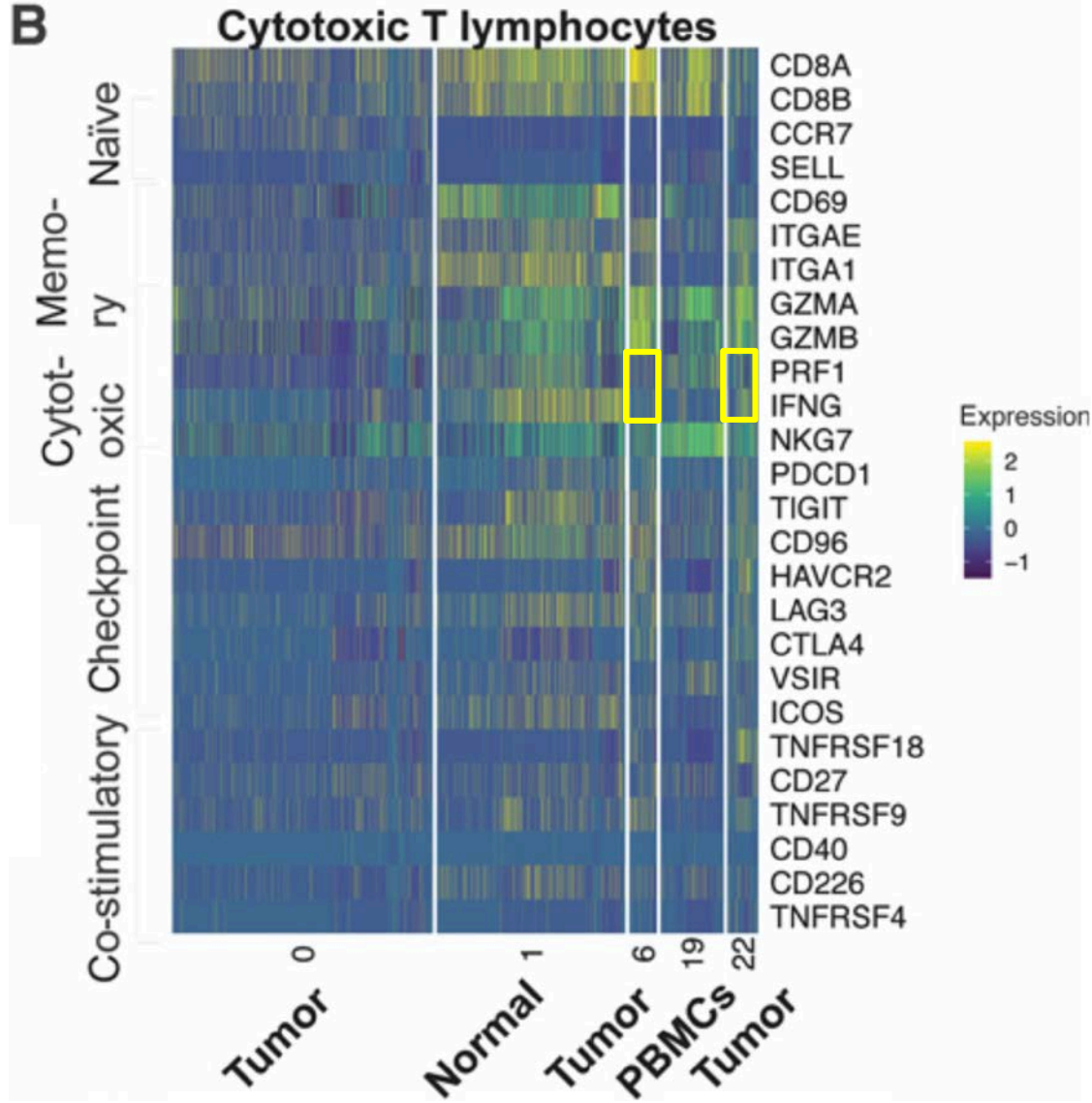
B

Cell type	Cluster number
CD8	0,1,6,19,22
CD4	3,6,10,18
NK	2,13,14
B	8,22,23
Plasma	7,16,24,25
Treg	4,22

Results

Results

Results

Results

A **Treg**

metaplasia	normal	pbmc	tumor	
3	119	9	1218	4
0	6	2	42	22

B **Treg**

p=1.99E-67

D **CD4 T lymphocytes**

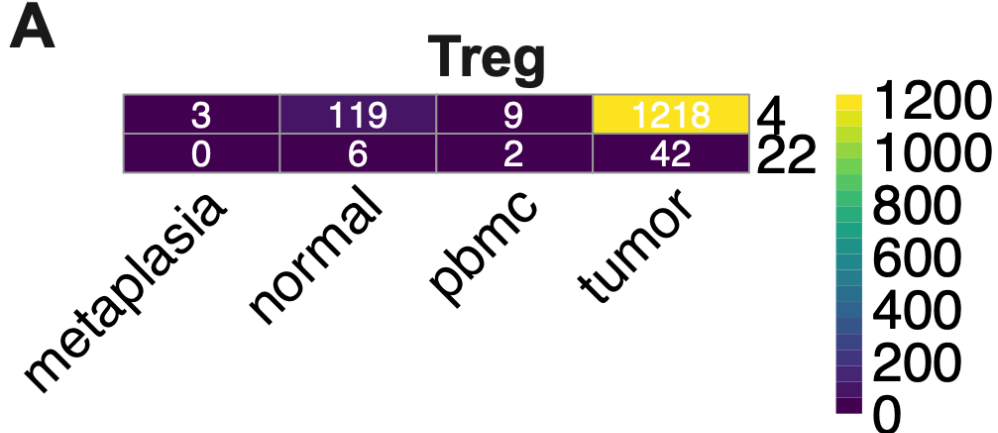| metaplasia	normal	pbmc	tumor	
3	687	4	711	3
0	52	0	78	6
1	14	1037	78	10
0	3	636	3	18
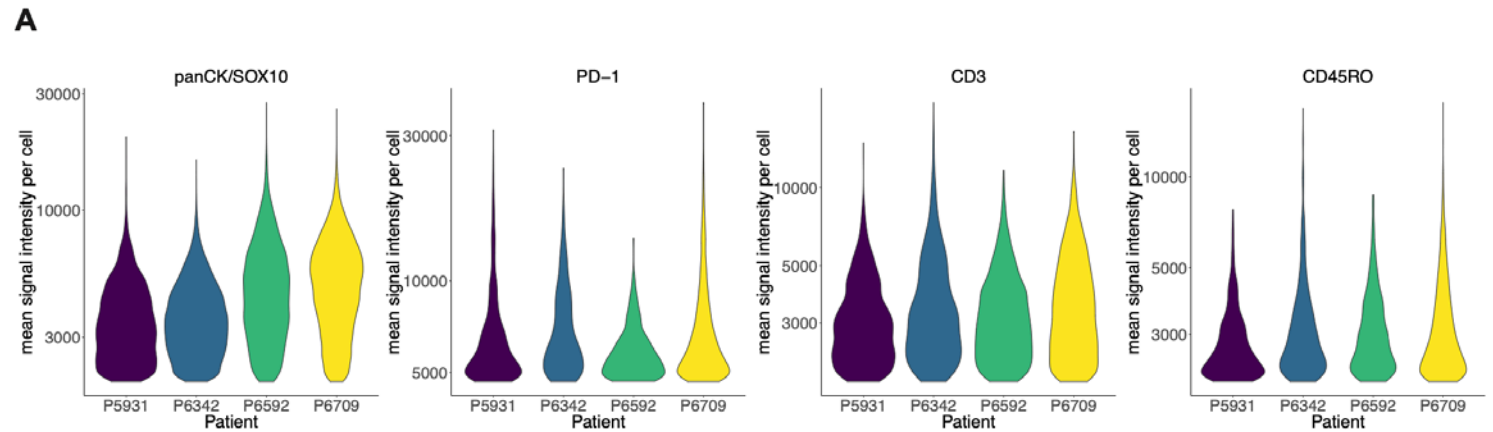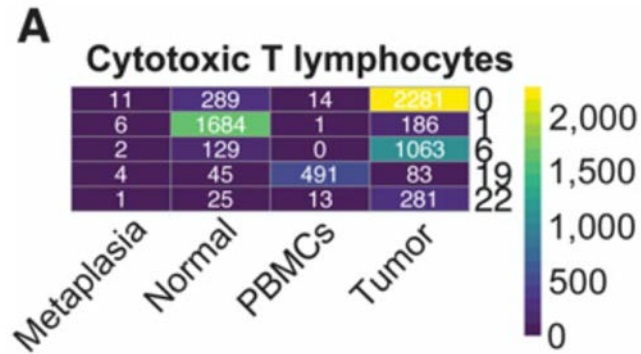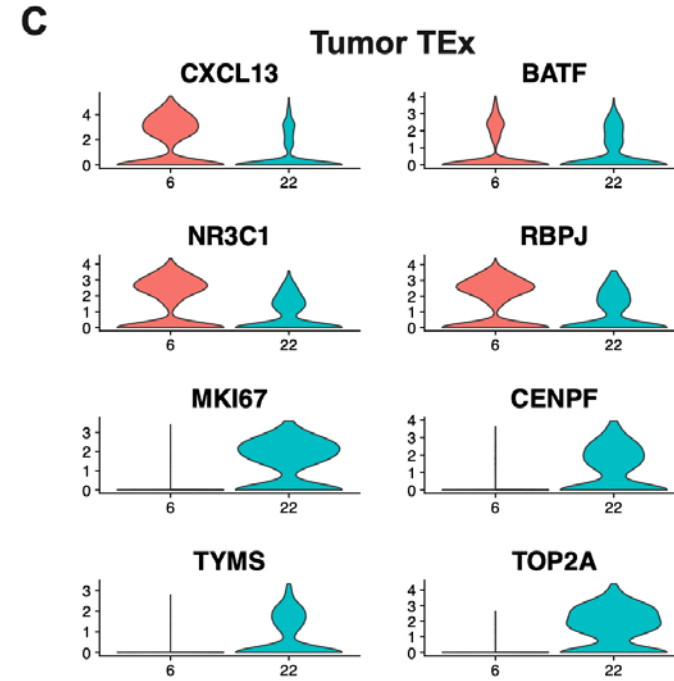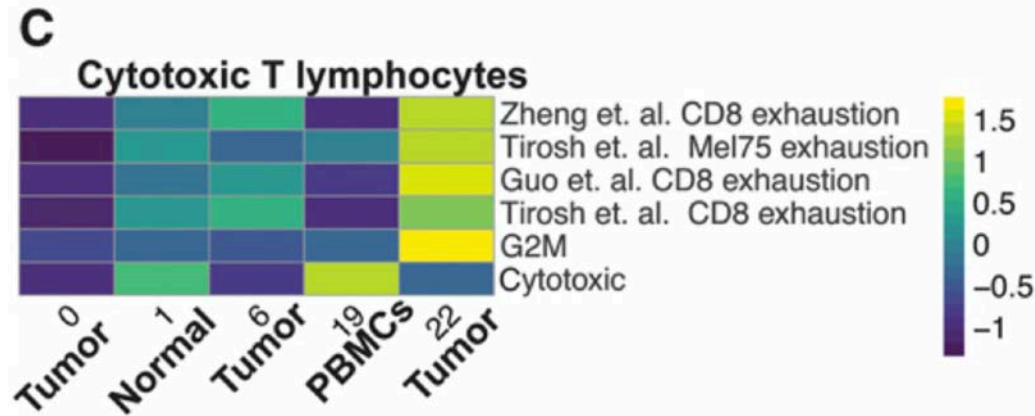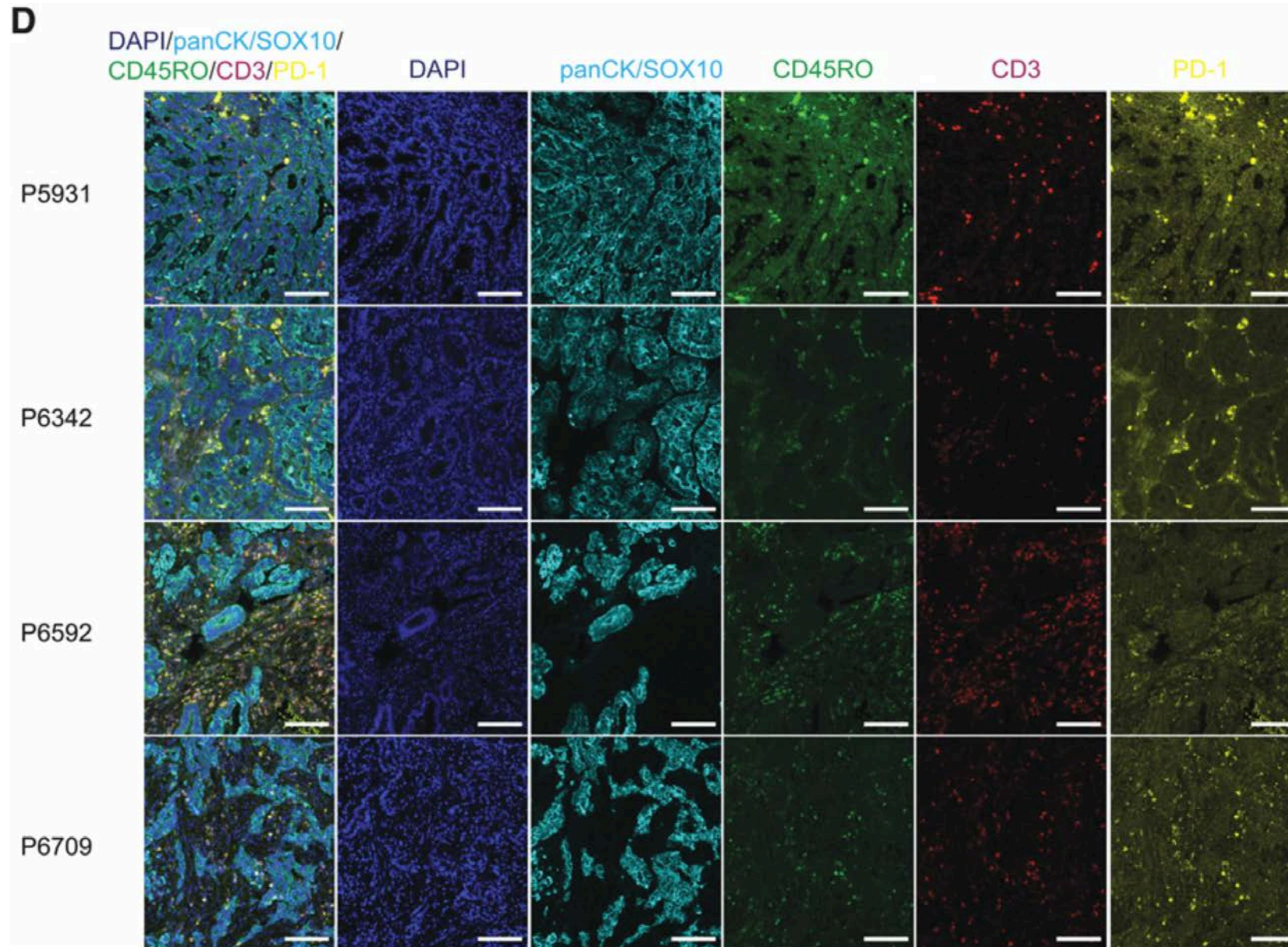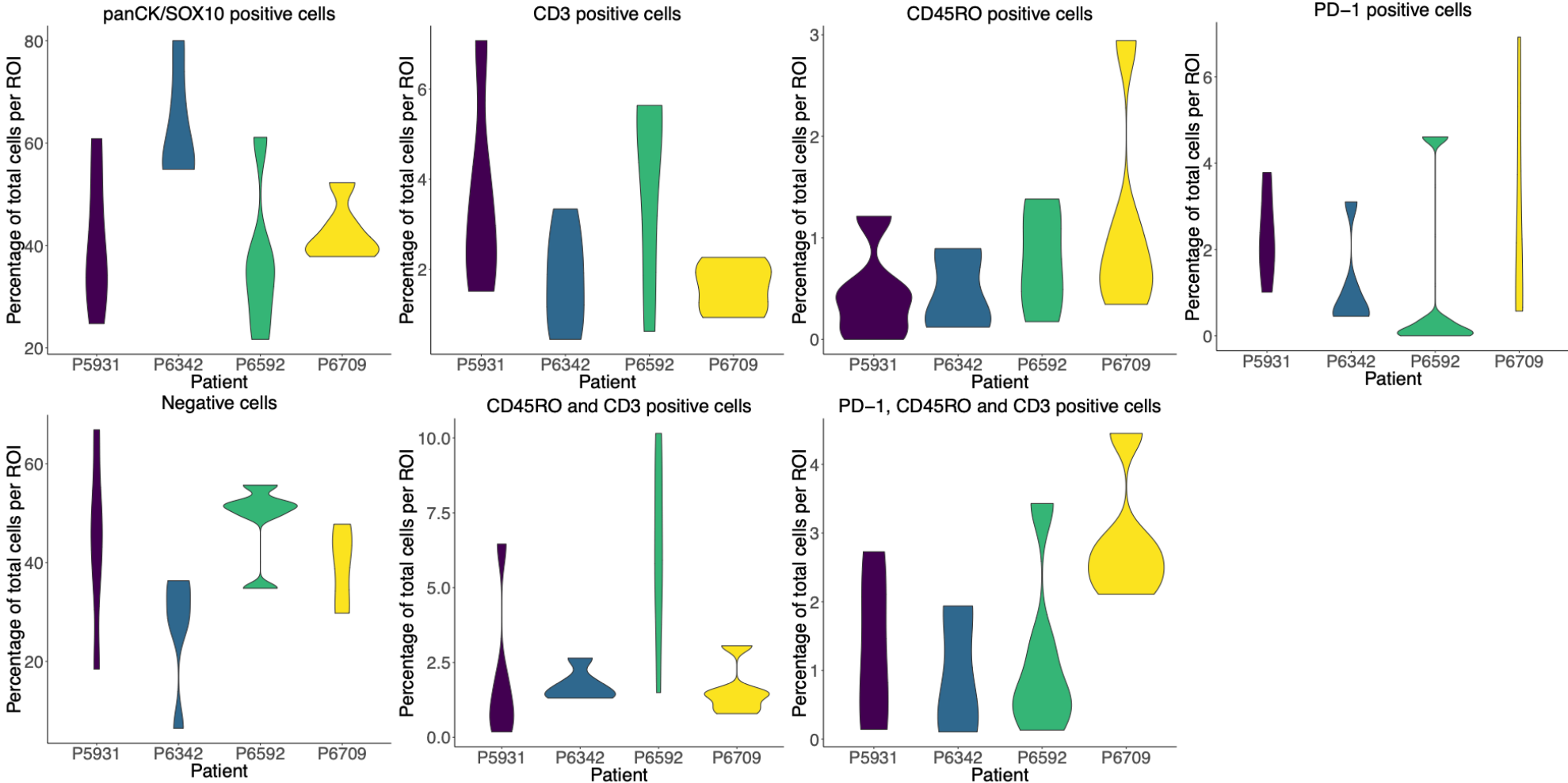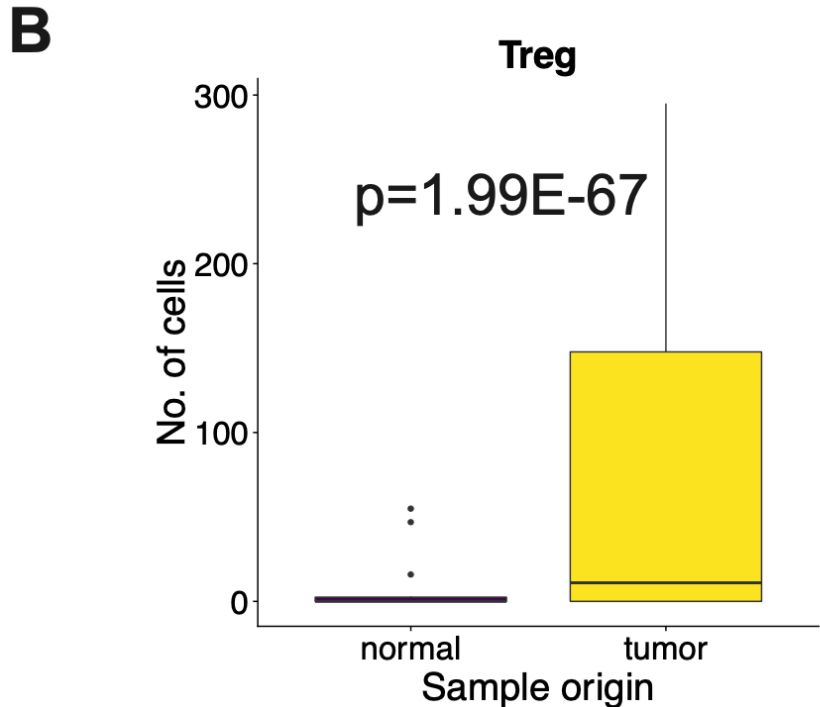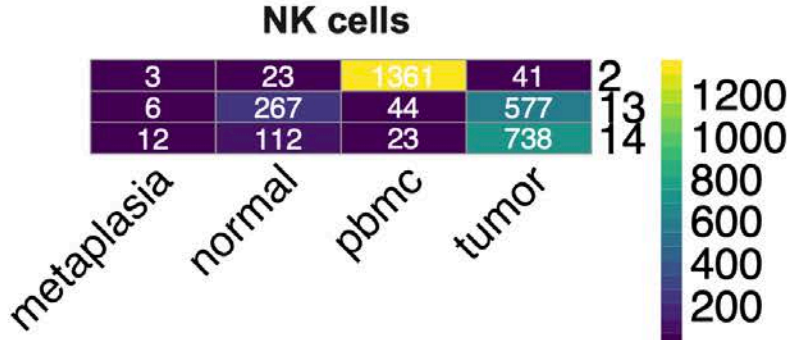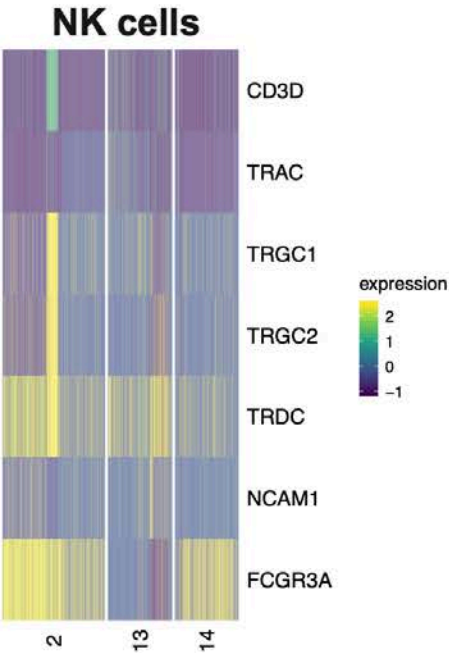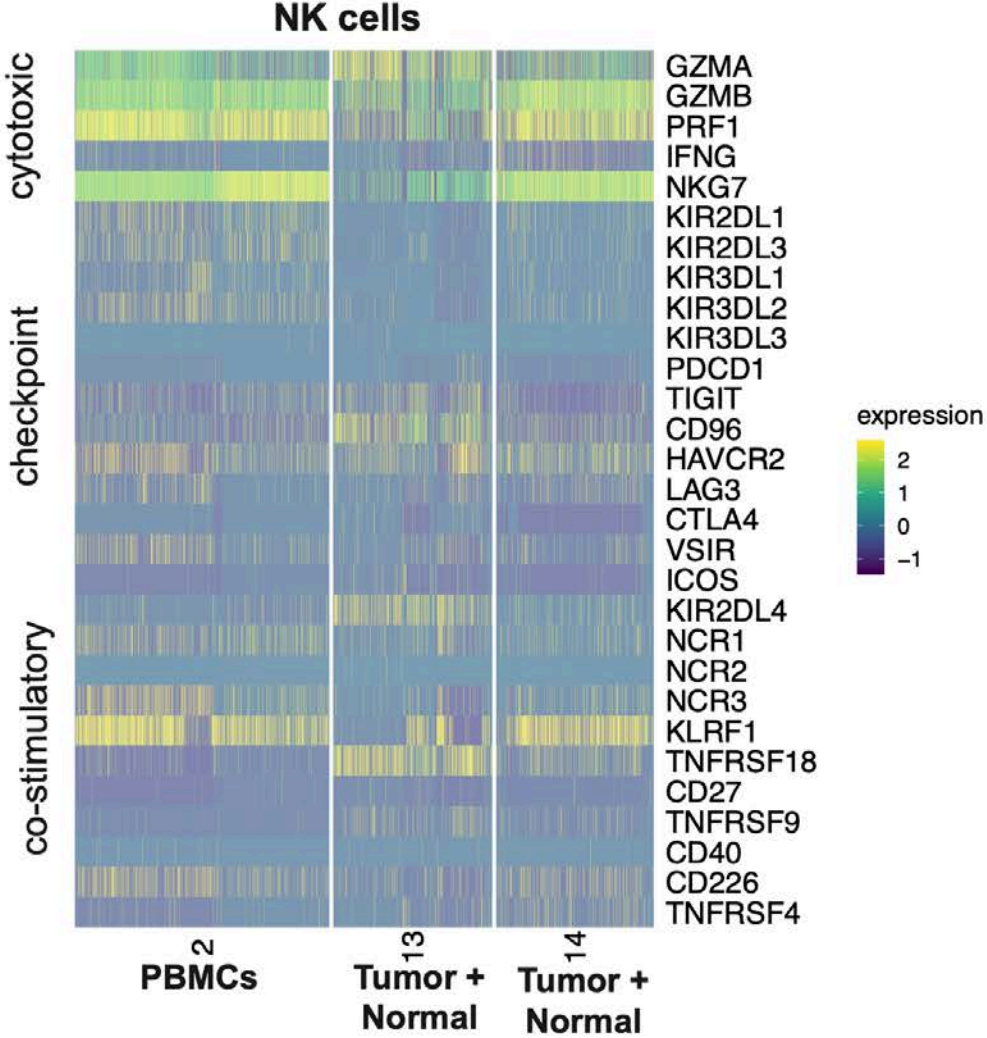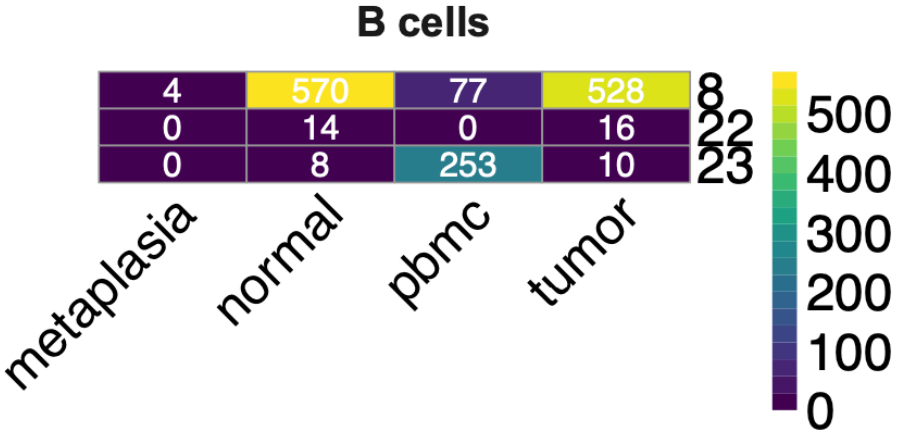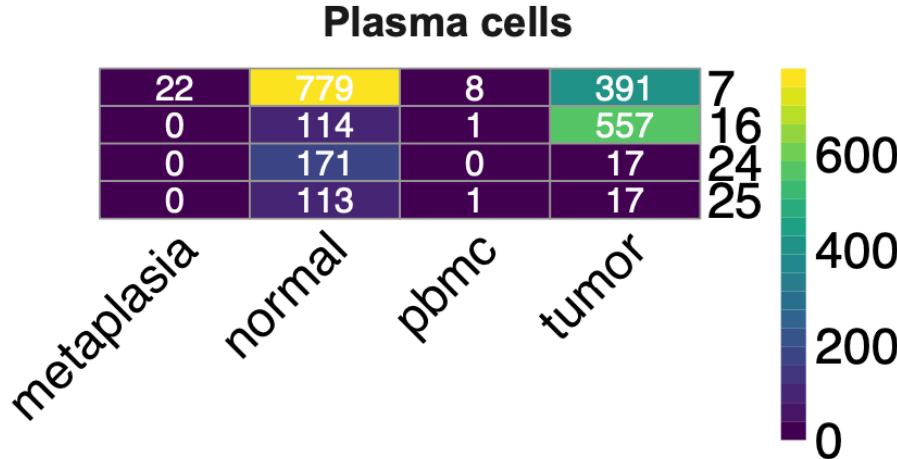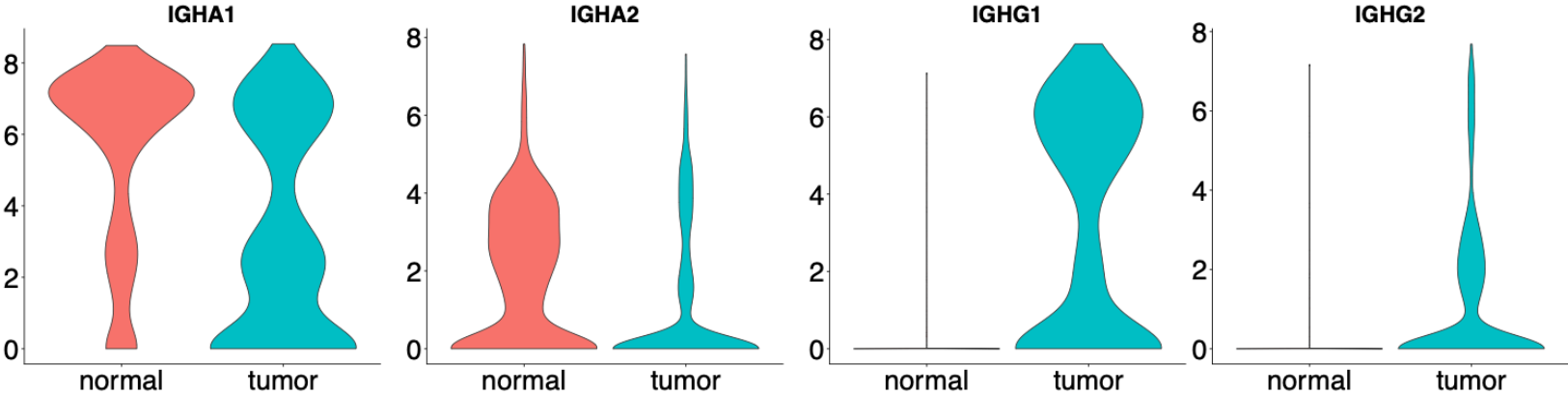
Results

Results

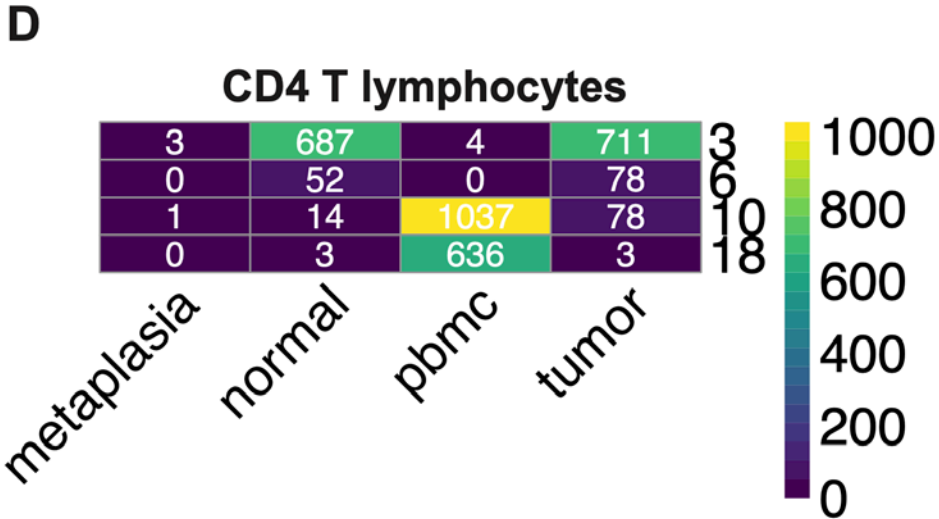# Results

Results

Results

Results

Discussion

- Cellular changes in TME compared to normal stomach mucosa
  - Number of stromal cells and Tregs ↑
  - Unique transcriptional cell states (DCs and exhausted CTLs)
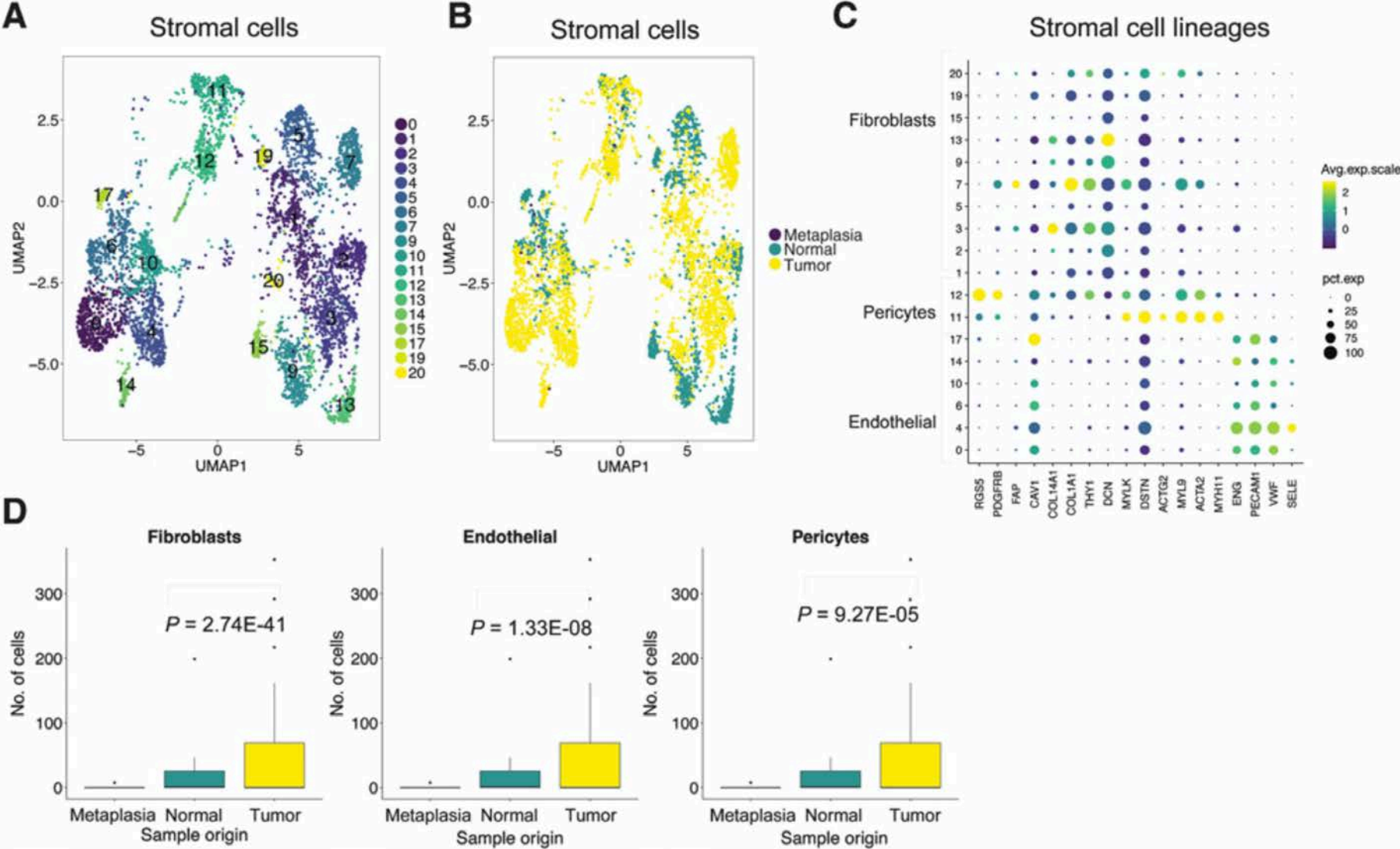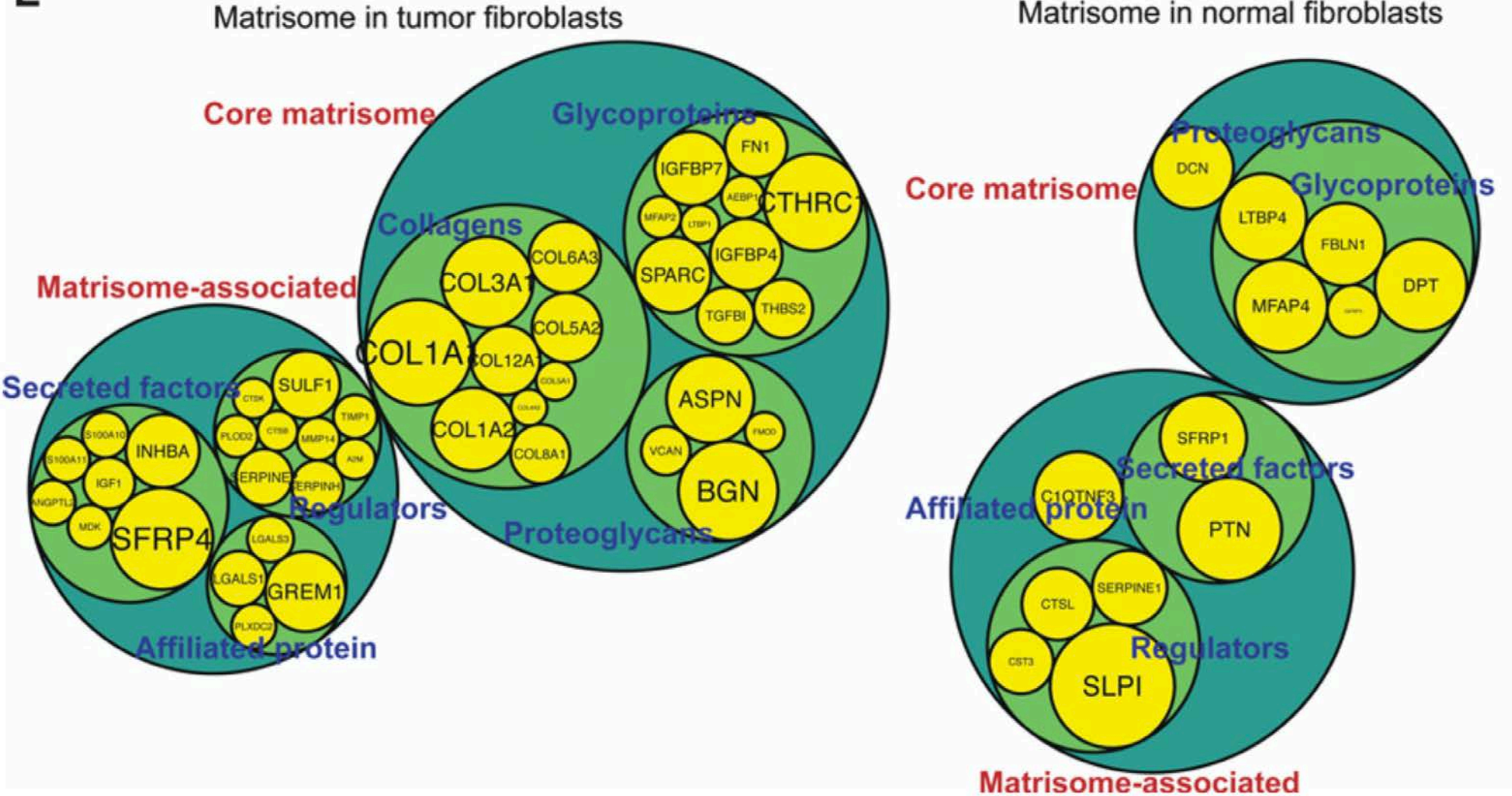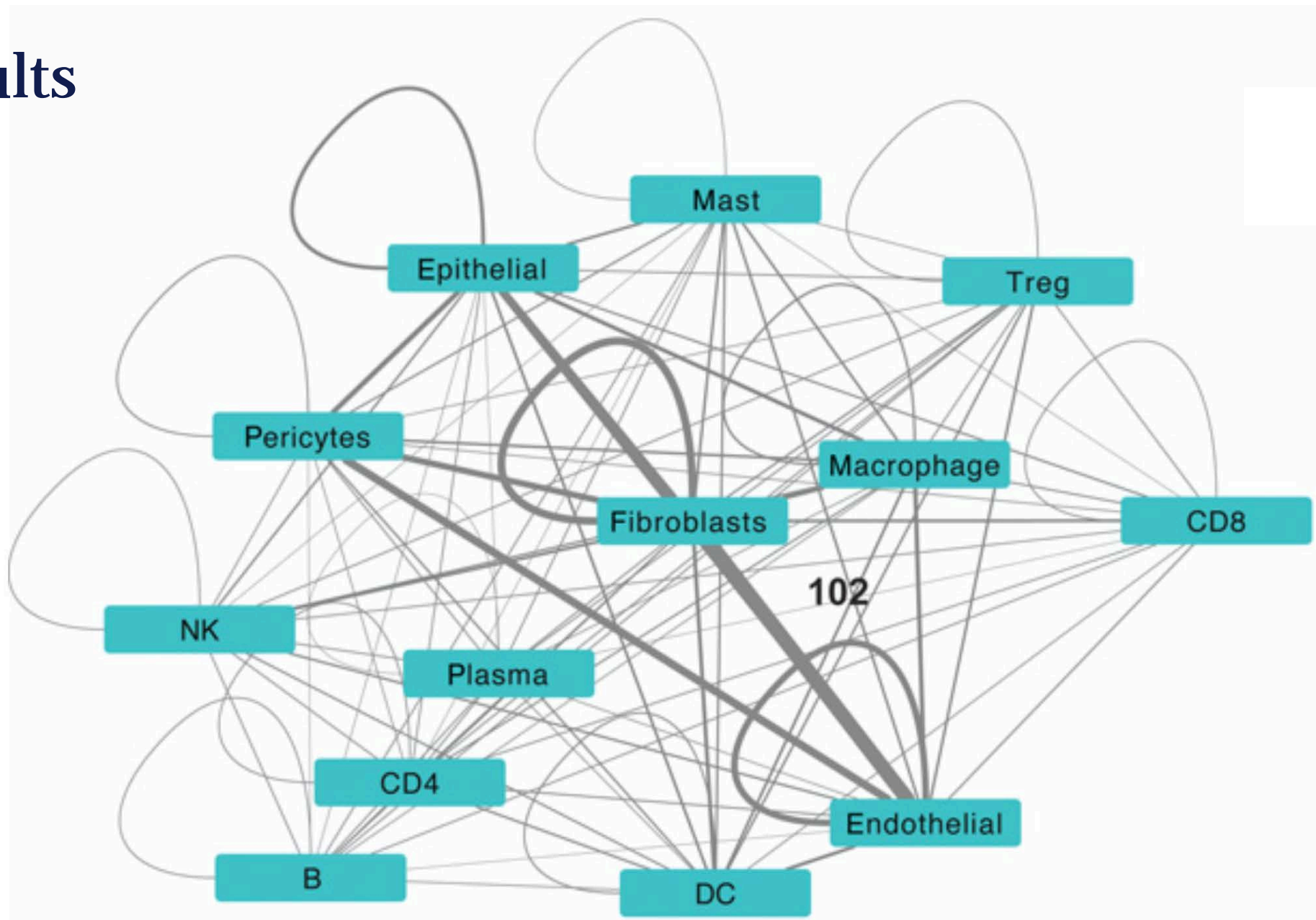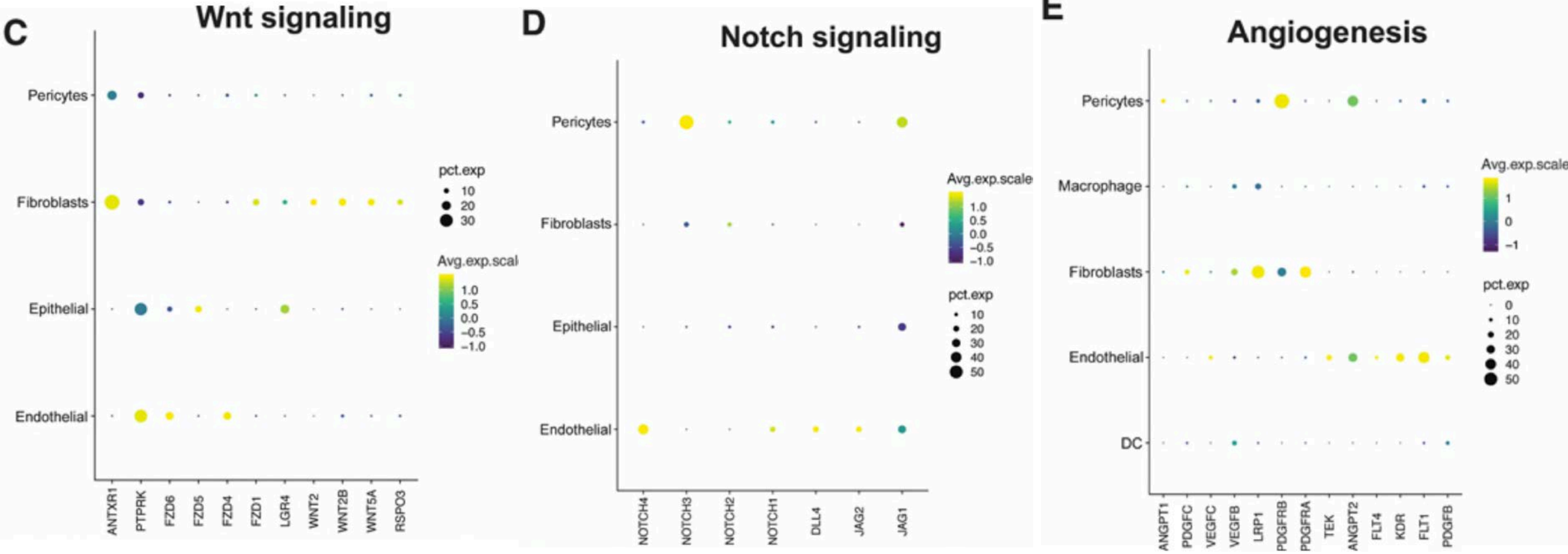 - Heterogenous macrophages gene expression discordant to binary M1/M2 system
  - Specific ECM composition

- Changes in normal, metaplastic and tumorepithelial cells
  - diversity in activation profiles

- Plasma cells in tumor tissue expressed IgGs rather than IgAs
- TEx cells in all patients with neodadjuvant therapy
- Immune cell subtypes did not cluster according MSI/MSS
- Identification of several checkpoint and co-stimulatory molecules