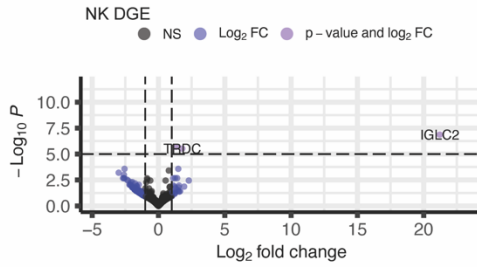


Supplemental Figure 1

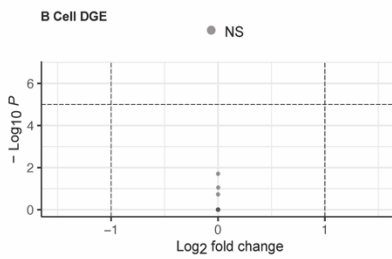
A.

Healthy		Tumor	
Cell Type	Cell Number	Cell Type	Cell Number
Epithelial	7060	Epithelial	9584
CD8	1335	CD8	3813
CD4	1244	CD4	5074
Granulocyte	349	Granulocyte	4859
Acinar	17450	Acinar	1290
Macrophage	5844	Macrophage	9085
Fibroblast	2405	Fibroblast	2434
Endothelial	3911	Endothelial	396
B-Cells	1715	B-Cells	1209
Pericytes	1165	Pericytes	813
Mast	159	Mast	1682
Cycling	639	Cycling	1005
Plasma	90	Plasma	1476
NK	89	NK	1089
Endocrine	529	Endocrine	18
Dendritic	0	Dendritic	127
Neural	35	Neural	43

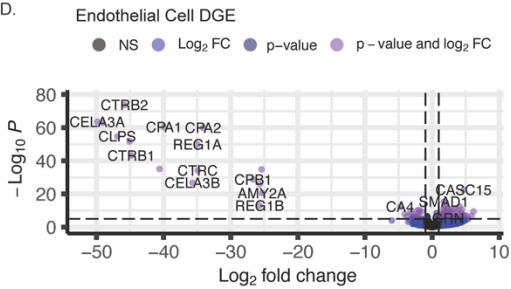
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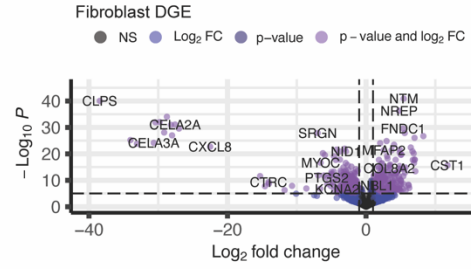
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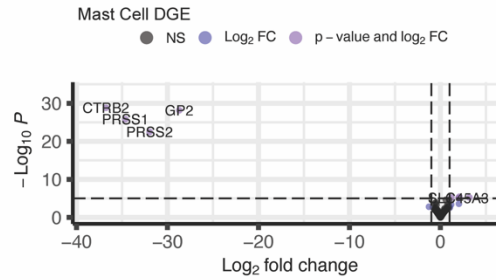
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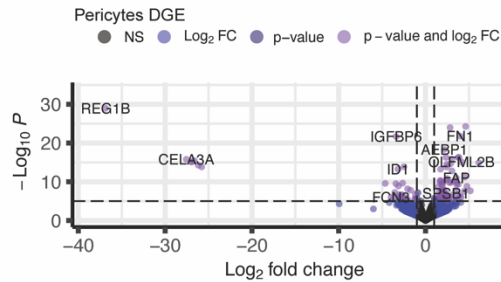
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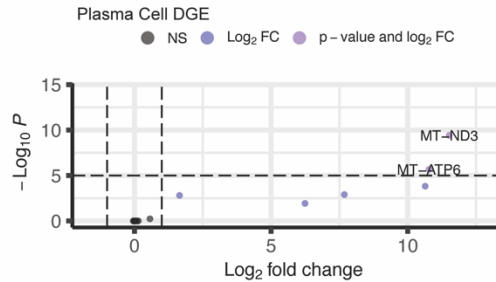
F.



G.

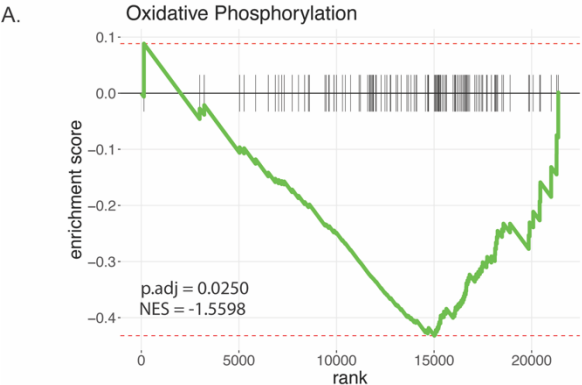


H.



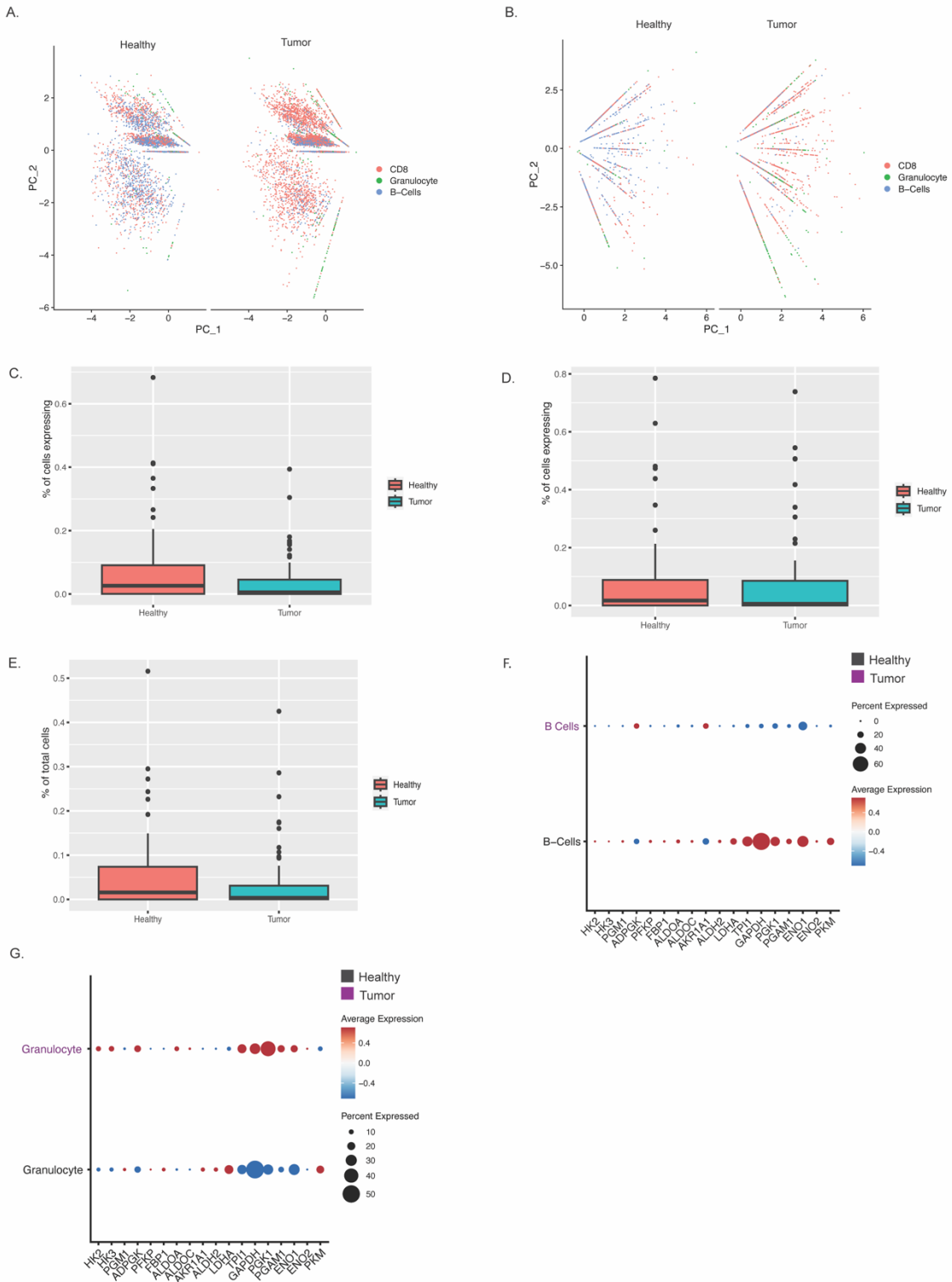
S2: (A) GSEA Enrichment plot of oxidative phosphorylation signature significantly increased in cancer cells, with corresponding NES and adjusted p-value.

Supplemental Figure 2



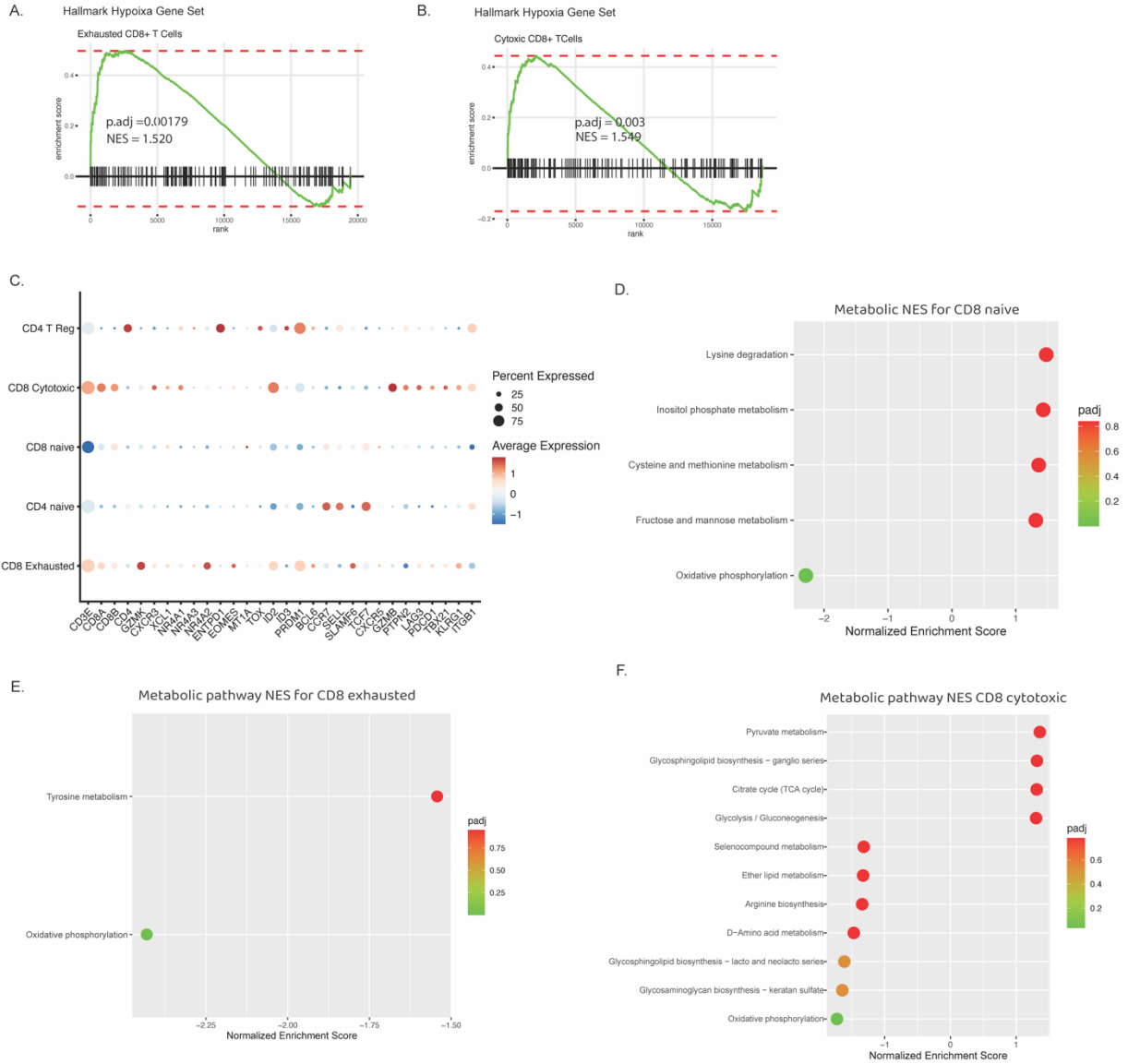
S2: (A) GSEA Enrichment plot of oxidative phosphorylation signature significantly increased in cancer cells, with corresponding NES and adjusted p-value.

Supplemental Figure 3



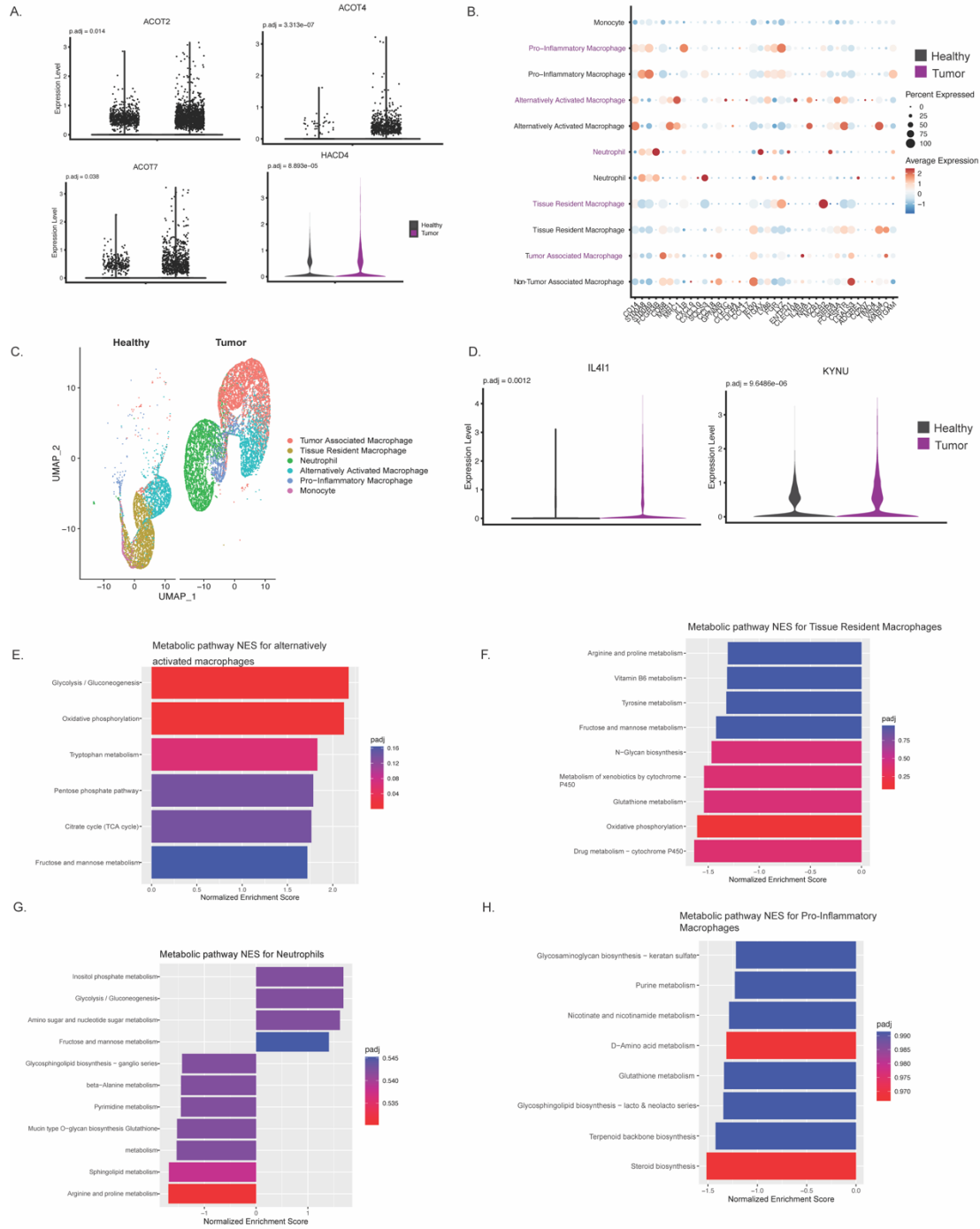
S3: (A) Principal Component Analysis (PCA) visualization based on the average expression and percent of cells expressing genes related to complex IV in B cells, granulocytes, and CD8+ T cells in healthy human and PDA samples. (B) PCA visualization based on the average expression and percent of cells expressing SDH/A/B/C/D in B cells, granulocytes, and CD8+ T cells in healthy human and PDA samples. (C-E) Box plots of reads corresponding to glycolytic genes in healthy and tumor conditions for B cells, CD8+ T cells, and granulocytes. (F-G) Dot Plot visualization of glycolytic genes, displaying average expression and percent expressed in B cells and granulocytes, respectively, in tumor (purple) and healthy pancreas tissue (black).

Supplemental Figure 4



S4: (A-B) GSEA Enrichment plots demonstrating hypoxia is significantly downregulated in exhausted and cytotoxic CD8+ T cells in pancreatic cancer tissue compared to healthy counterpart. **(C)** Dot plot visualization of marker expression utilized to subset T cell populations. **(D-F)** GSEA results for CD8 naive, exhausted, and cytotoxic T cells from PDA samples compared to healthy samples, with corresponding normalized enrichment scores (NES) and adjusted p-values.

Supplemental Figure 5



S5: (A) Violin plots of genes involved in unsaturated fatty acid synthesis, with adjusted p-values for significantly differentially expressed genes. (B) Dot Plot of markers used to identify sub populations of myeloid cells. (C) Uniform Manifold Approximation and Projection (UMAP) of myeloid populations in the healthy and tumor conditions. (D) Violin plots of differentially genes involved in tryptophan metabolism. (E) GSEA results for alternatively activated macrophages. (F) GSEA results for tissue resident macrophages. (G) GSEA analysis for neutrophils. (H) GSEA results for pro-inflammatory macrophages. All GSEA results contain corresponding normalized enrichment scores (NES) and adjusted p-values.

Supplementary Figure Legends

S1: (A) Table with number of cells per population in the healthy and tumor samples. (B-H) Volcano plots of differential gene expression by cell type. Genes that are significantly up- (top-right) and down- regulated (top-left) in tumor versus healthy and the gene symbols are included for representative differentially expressed genes.

S2: (A) GSEA Enrichment plot of oxidative phosphorylation signature significantly increased in cancer cells, with corresponding NES and adjusted p-value.

S3: (A) Principal Component Analysis (PCA) visualization based on the average expression and percent of cells expressing genes related to complex IV in B cells, granulocytes, and CD8+ T cells in healthy human and PDA samples. (B) PCA visualization based on the average expression and percent of cells expressing SDH/A/B/C/D in B cells, granulocytes, and CD8+ T cells in healthy human and PDA samples. (C-E) Box plots of reads corresponding to glycolytic genes in healthy and tumor conditions for B cells, CD8+ T cells, and granulocytes. (F-G) Dot Plot visualization of glycolytic genes, displaying average expression and percent expressed in B cells and granulocytes, respectively, in tumor (purple) and healthy pancreas tissue (black).

S4: (A-B) GSEA Enrichment plots demonstrating hypoxia is significantly downregulated in exhausted and cytotoxic CD8+ T cells in pancreatic cancer tissue compared to healthy counterpart. (C) Dot plot visualization of marker expression utilized to subset T cell populations. (D-F) GSEA results for CD8 naïve, exhausted, and cytotoxic T cells from PDA samples compared to healthy samples, with corresponding normalized enrichment scores (NES) and adjusted p-values.

S5: (A) Violin plots of genes involved in unsaturated fatty acid synthesis, with adjusted p-values for significantly differentially expressed genes. (B) Dot Plot of markers used to identify sub populations of myeloid cells. (C) Uniform Manifold Approximation and Projection (UMAP) of myeloid populations in the healthy and tumor conditions. (D) Violin plots of differentially genes involved in tryptophan metabolism. E, GSEA results for alternatively activated macrophages. (F) GSEA results for tissue resident macrophages. (G) GSEA analysis for neutrophils. (H) GSEA results for pro-inflammatory macrophages. All GSEA results contain corresponding normalized enrichment scores (NES) and adjusted p-values.