frontiers

Supplementary Material

Loss of Cadherin-11 in pancreatic ductal adenocarcinoma alters tumor-immune microenvironment

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Supplementary Figures

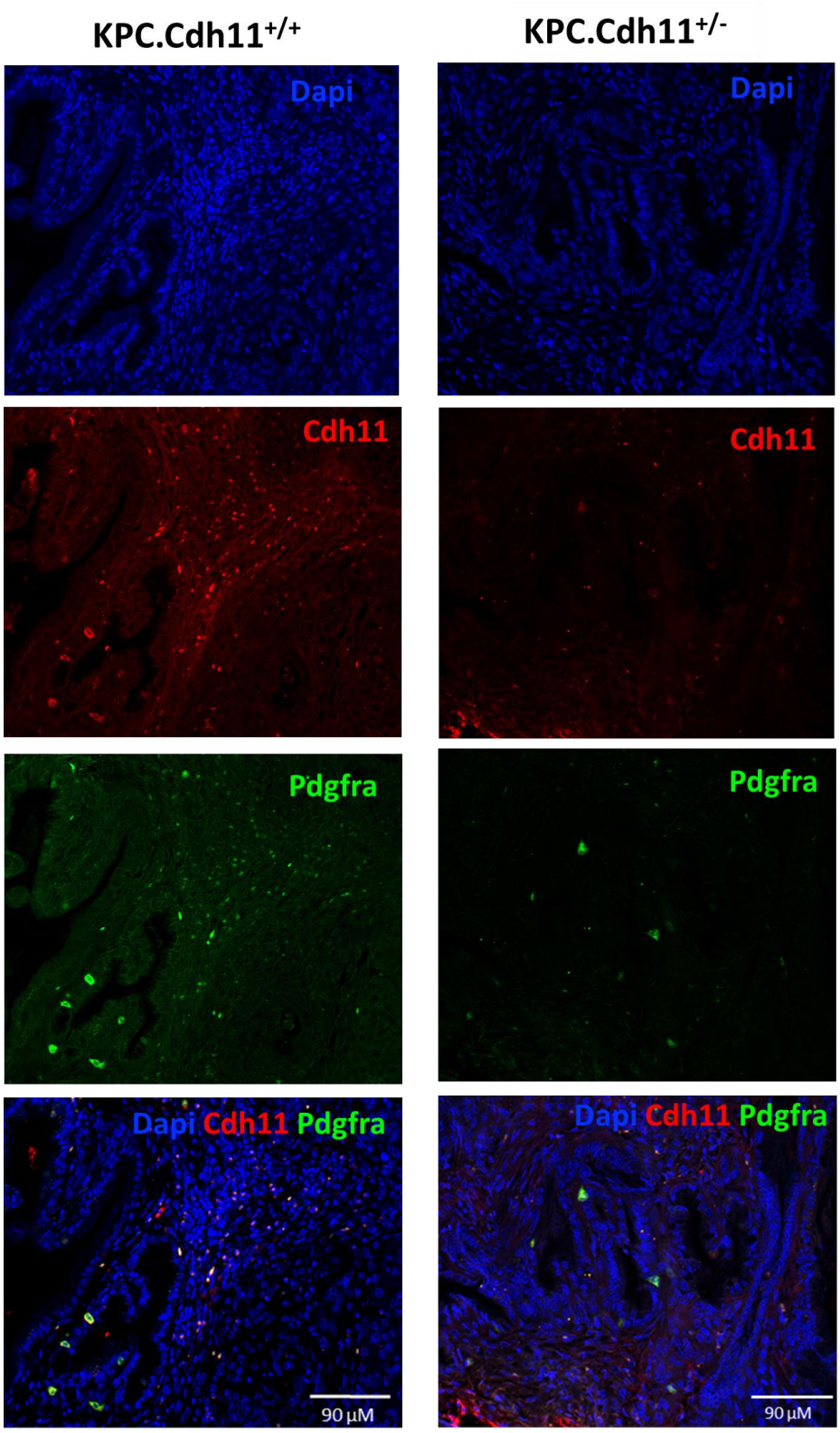

Figure S1: Immunohistochemistry analysis of Cdh11 expression. CAFs from KPC-Cdh11$^{+/+}$ mice co-expressed CAF marker *Pdgfra* and *Cdh11*.

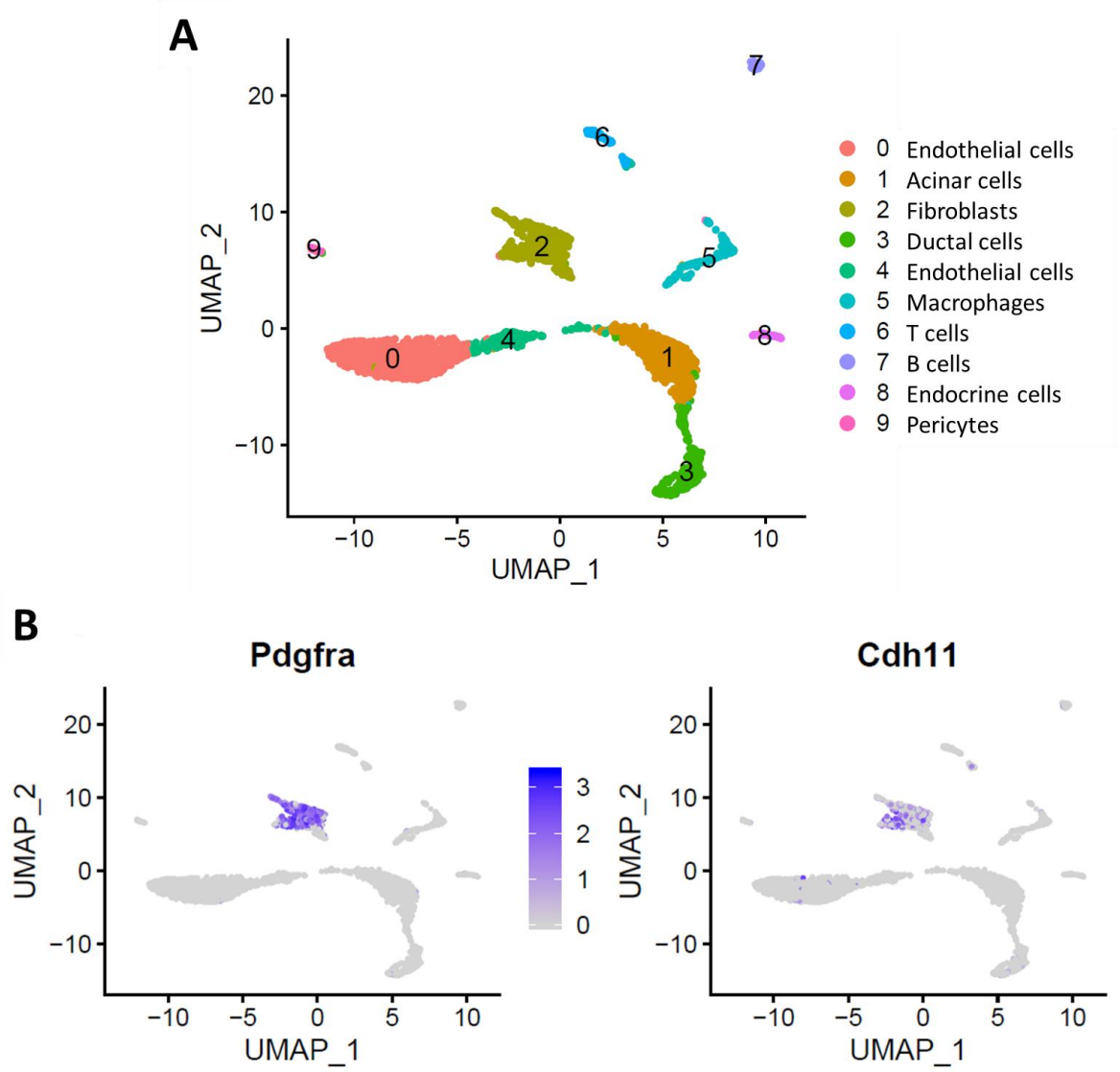

Figure S2: **Cdh11 expression in pancreas from non-tumor bearing mice.** A) UMAP plot showing cell types identified in pancreas from non-tumor bearing wildtype mice. B) *Cdh11* and *Pdgfra* expression in normal fibroblasts from non-tumor bearing mice.

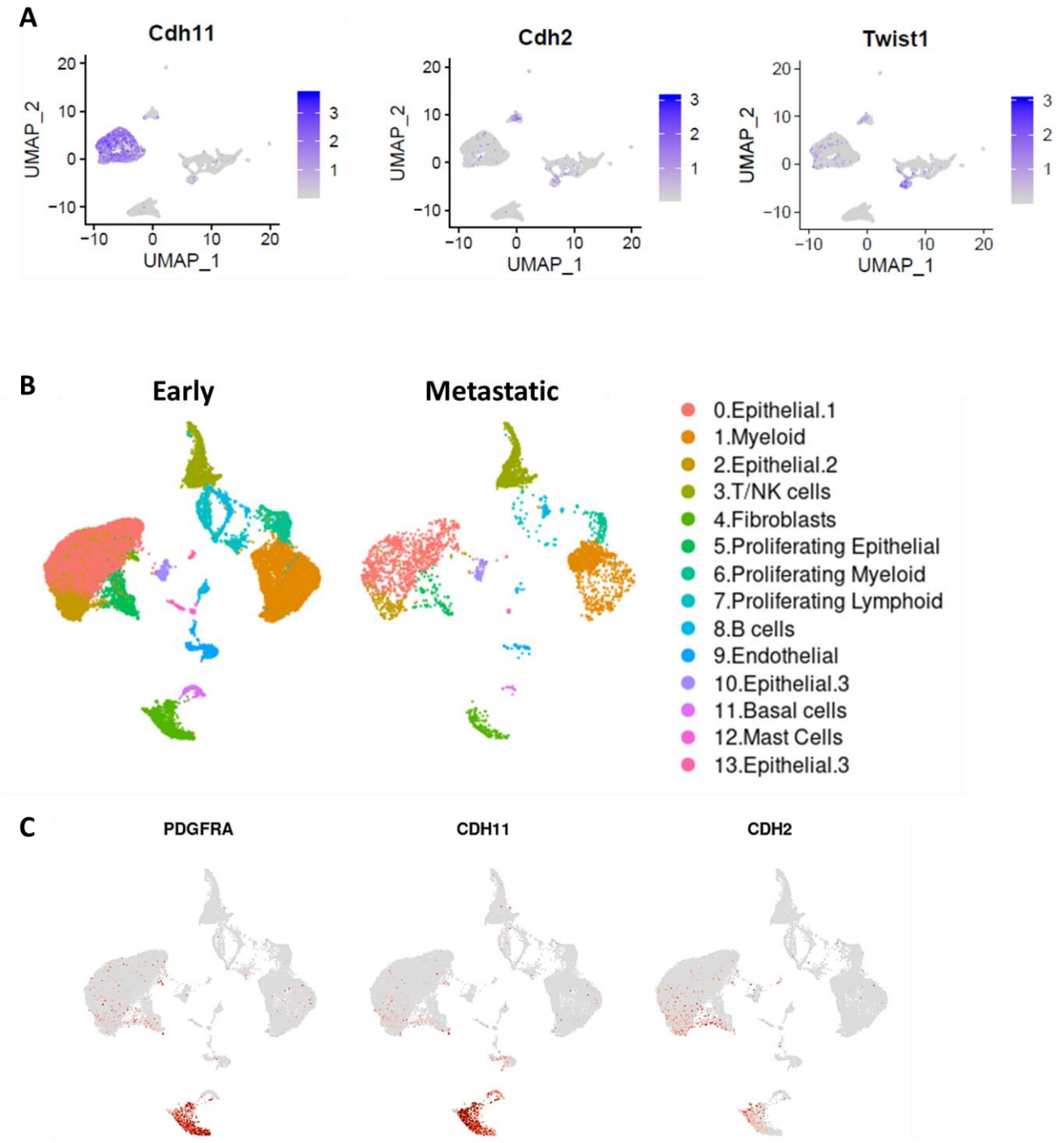

Figure S3. ***Cdh11* expression in EMT cells.** A) EMT cells (red oval) in KPC mice expressed low levels of *Cdh11* along with EMT markers *Cdh2* and *Twist1*. B) UMAP plot of cells from early and metastatic human PDACs. Blue oval shows CAFs and black arrow shows EMT cells expressing *CDH2*. C) *CDH11* expression (red) in CAFs and EMT cells from early and metastatic human PDACs.

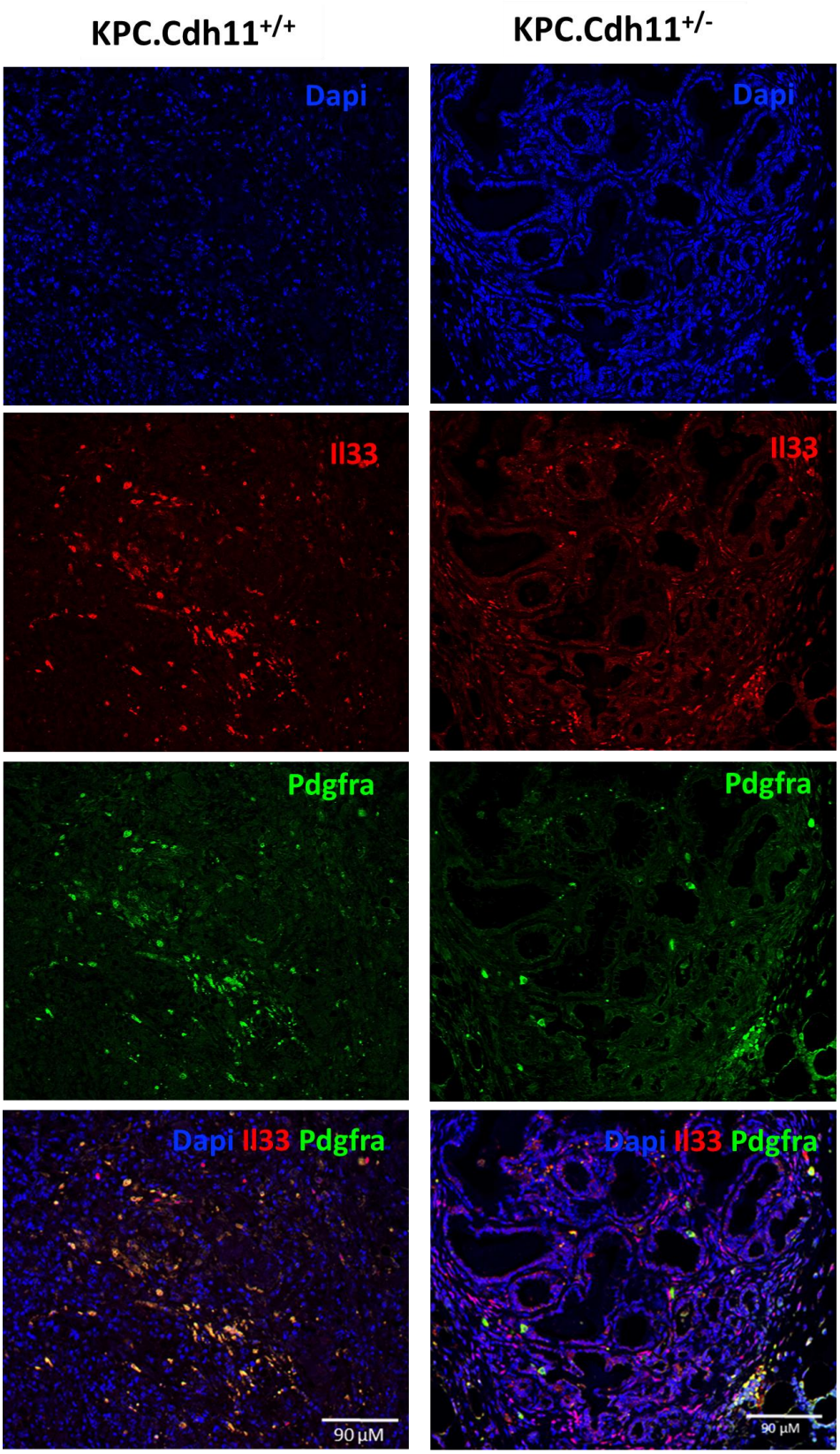

Figure S4. Il33 expression in CAFs. IHC analysis showed an increased number of Il33-expressing CAFs (Pdgfra+ cells) in KPC-Cdh11$^{+/+}$ pancreas compared to KPC-Cdh11$^{+/-}$ pancreas.

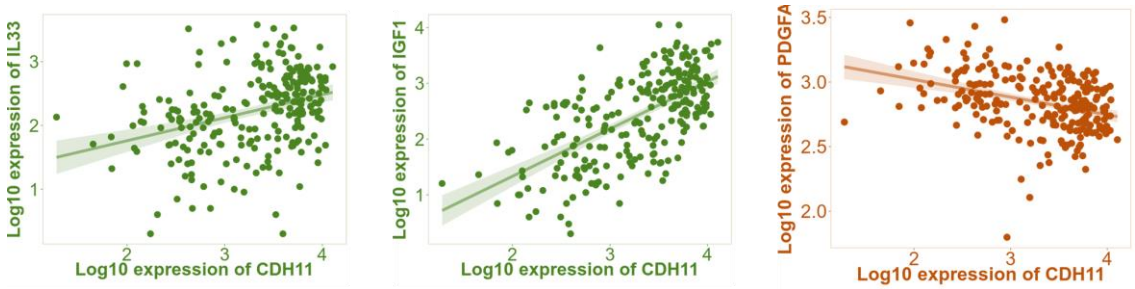

Figure S5. **Correlation between the expression of *Cdh11* and other genes in human PDAC.** Correlations between the genes were determined using TNMplot.

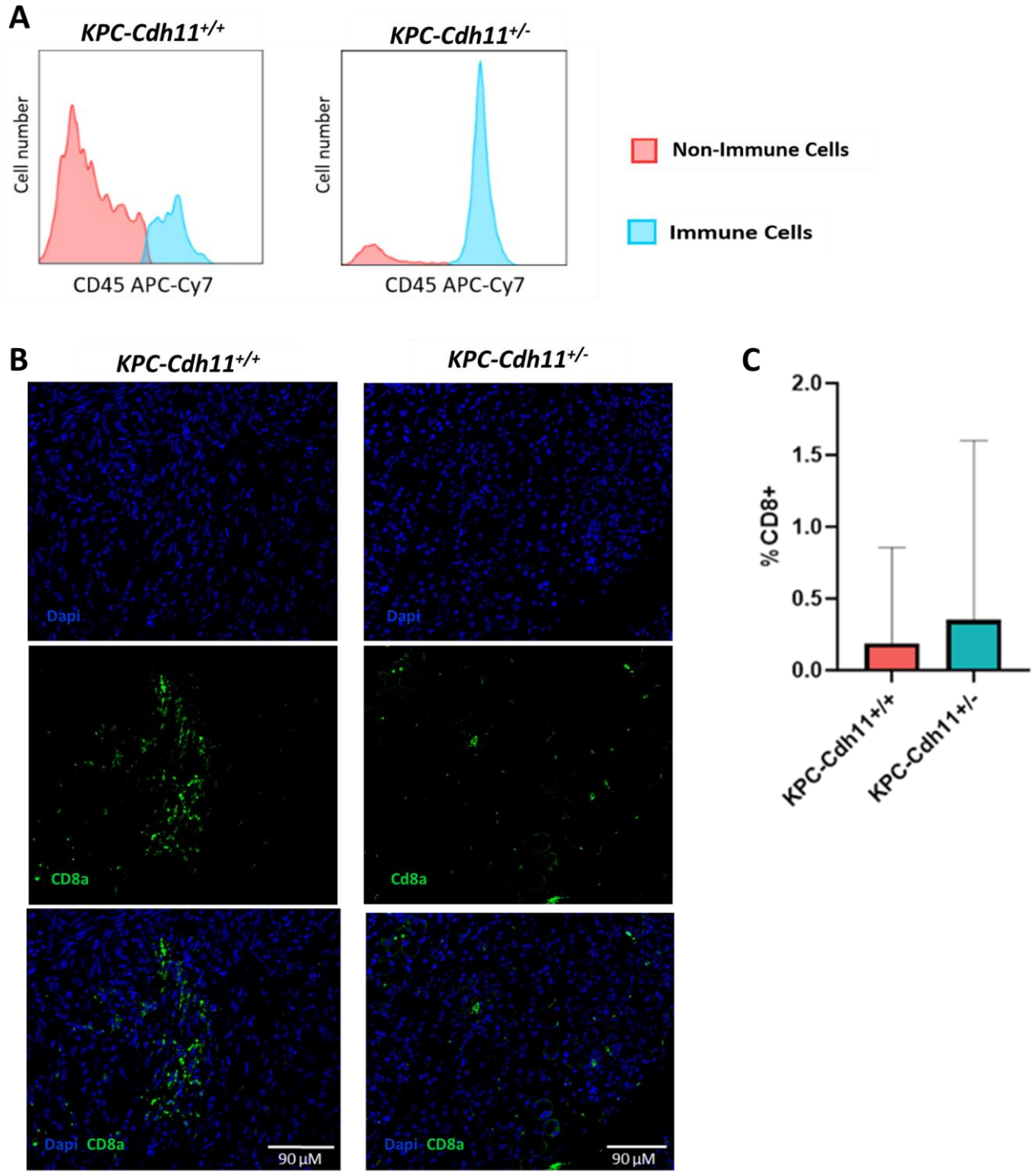

Figure S6. **Immune cells in tumor microenvironment.** A) FACS analysis of cells pooled from five KPC-Cdh11$^{+/+}$ and KPC-Cdh11$^{+/-}$ pancreases showed that Cdh11-deficient tumors have increased immune infiltration. B) IHC images showing CD8a expression in KPC-Cdh11$^{+/+}$ and KPC-Cdh11$^{+/-}$ pancreases. C) Quantification of CD8a staining of KPC-Cdh11$^{+/+}$ and KPC-Cdh11$^{+/-}$ pancreases using Vectra quantitative pathology imaging system.

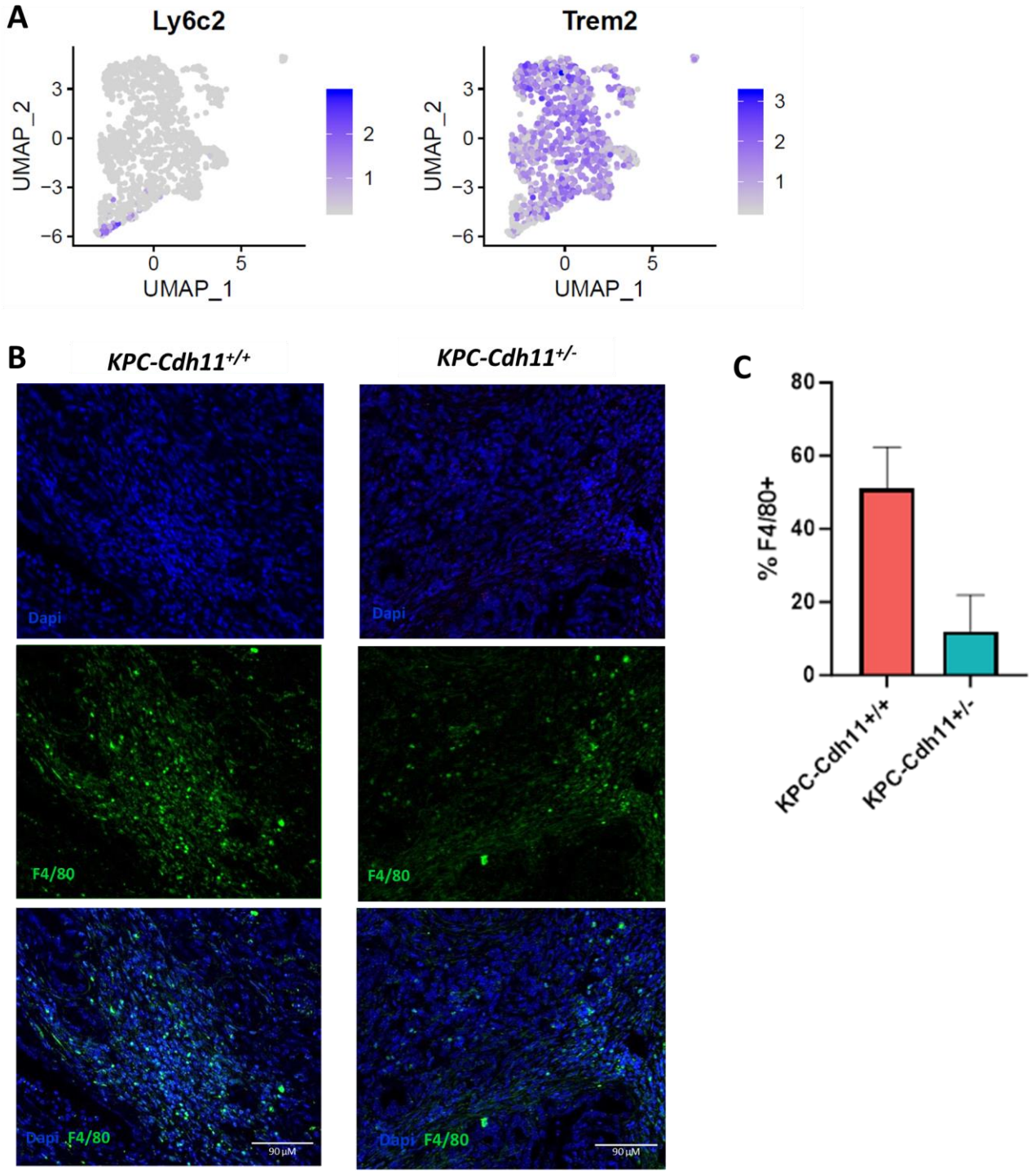

Figure S7. **Macrophages in PDAC tumor microenvironment.** A) *Ly6c2* and *Trem2* expression (blue) in Mono-Mac clusters. B) IHC images showing F4/80 expression in KPC-Cdh11$^{+/+}$ and KPC-Cdh11$^{+/-}$ pancreases. C) Quantification of F4/80^{+} staining of KPC-Cdh11$^{+/+}$ and KPC-Cdh11$^{+/-}$ pancreases.

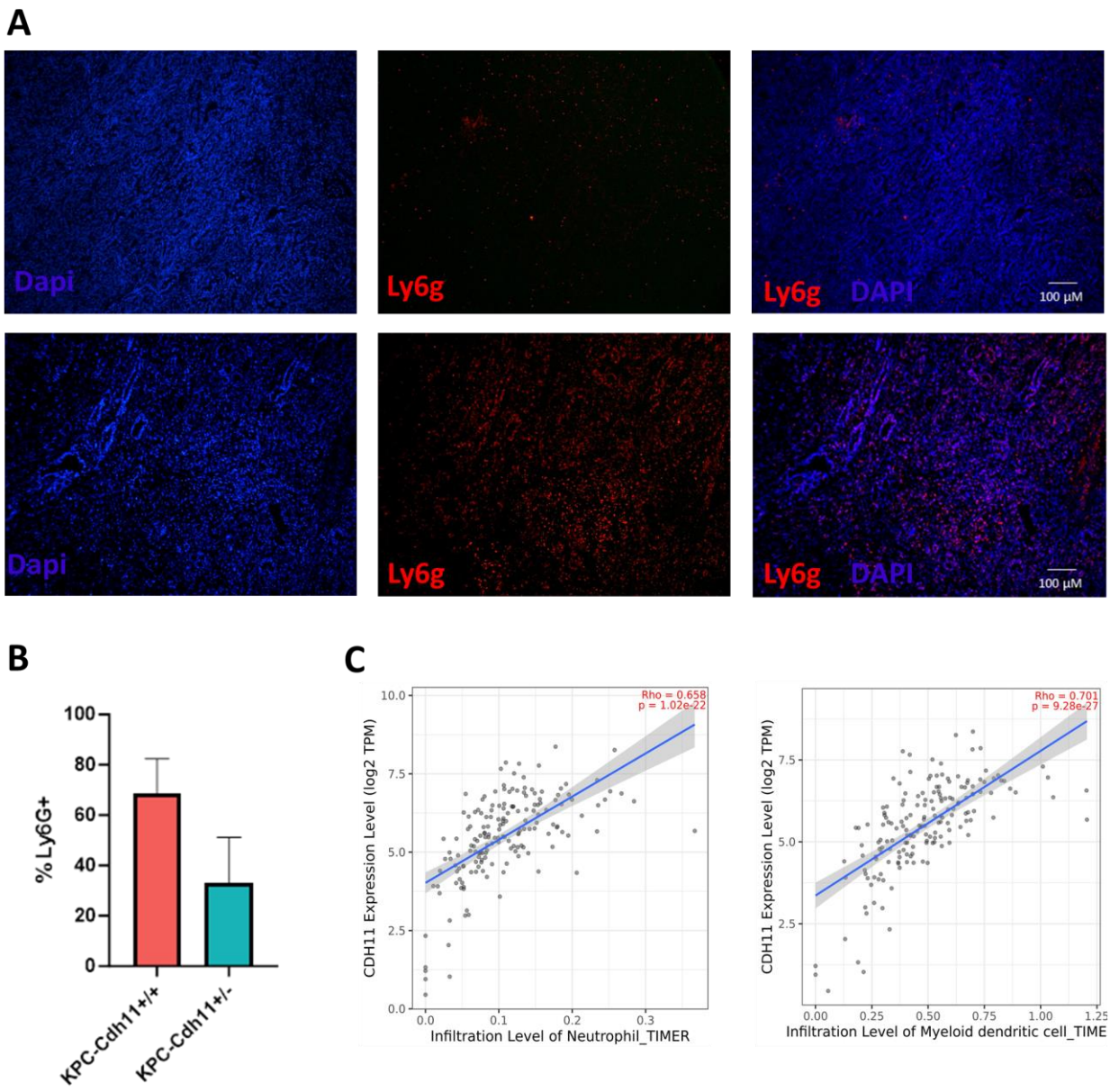

Figure S8. **Neutrophils and other myeloid cells in PDAC tumor microenvironment. A)** IHC images showing Ly6g expression in KPC-Cdh11$^{+/+}$ and KPC-Cdh11$^{+/-}$ pancreases. B) Quantification of Ly6g staining of KPC-Cdh11$^{+/+}$ and KPC-Cdh11$^{+/-}$ pancreases. C) Correlation between Cdh11 expression and neutrophil and myeloid DC infiltration in human PDAC, identified using TIMER.

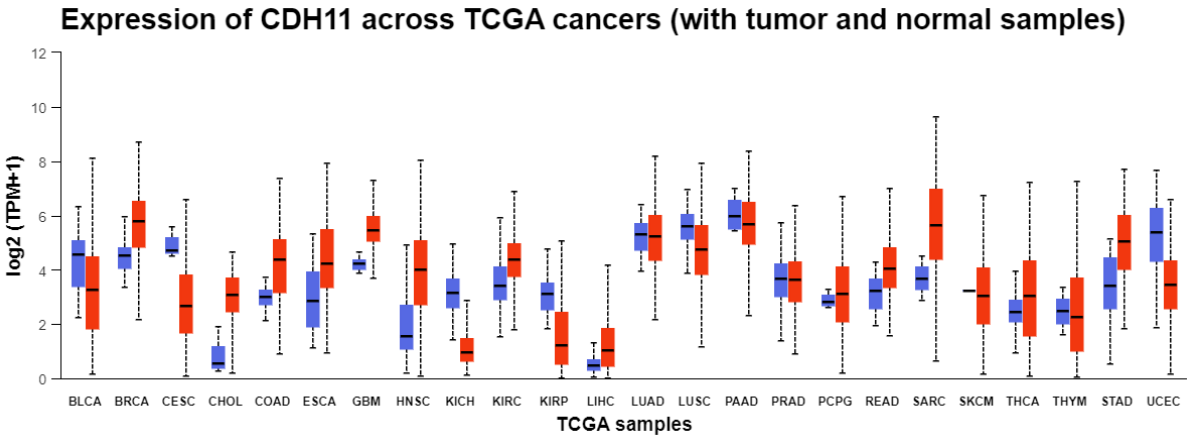

Figure S9. **CDH11 expression across various human tumors.** Data obtained from UALCAN. Blue: normal; red: tumor.