Supplementary Materials

Distinct serum immune profiles define the spectrum of acute and chronic pancreatitis from the large, multi-center PROCEED study

Bomi Lee et al.

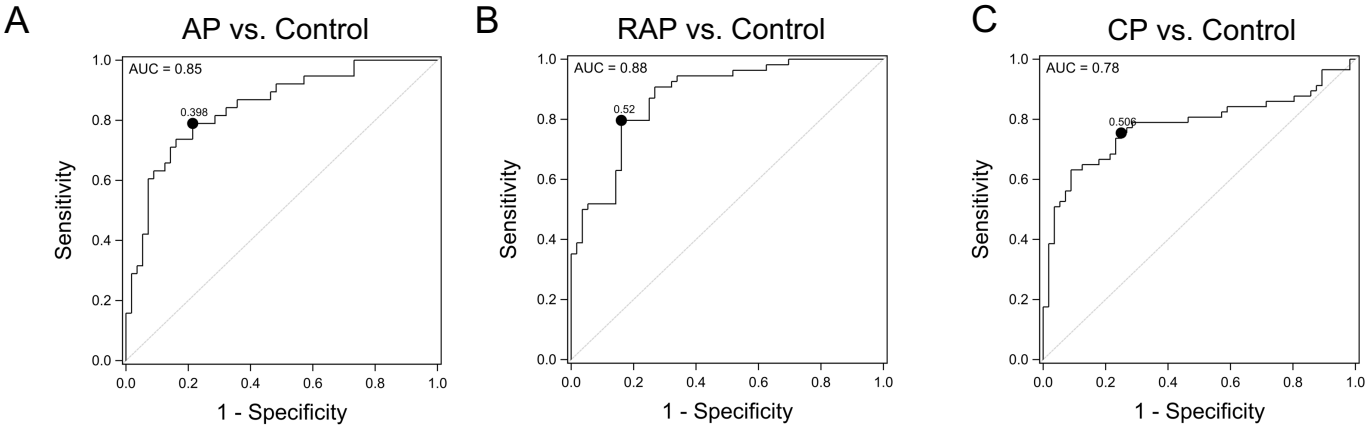
Supplementary Table 1.

	Eligibility criteria for the enrollment of no pancreas disease controls
1	Age ≥18 years and ≤75 years at the time of enrollment
2	No personal history or symptoms of pancreatic disease
3	No upper abdominal symptoms, including a no response to questions on “stomach ache or pain more than six times in the past year”, and “a feeling of wanting to throw up (nausea) in the last year”
4	No family history of pancreatic disorders, celiac disease, cystic fibrosis
5	No history of acute infectious or inflammatory conditions requiring medical treatment or evaluation in the preceding 6 months (per provider clinical judgment)
6	No history of cancer, except for non-melanoma skin cancers
7	No known pregnancy at the time of enrollment
8	No solid organ transplant or history of human immunodeficiency virus (HIV) or Acquired Immunodeficiency Syndrome (AIDS)
9	Not currently incarcerated
10	American Society of Anesthesiology (ASA) class 1-2

Supplementary Figure 1.

Supplemental Figure 1. Serum immune profiling with Olink assay reveals differentially expressed immune markers in pancreatitis and control groups. A. Principal Component Analysis (PCA) plot with raw normalized protein expression (NPX) values of 231 samples. Control, no pancreas disease controls; CAP, chronic abdominal pain; CP, chronic pancreatitis; AP, acute pancreatitis; RAP, recurrent acute pancreatitis. **B.** Heatmap of raw NPX values from 231 serum samples.

Supplementary Figure 2.



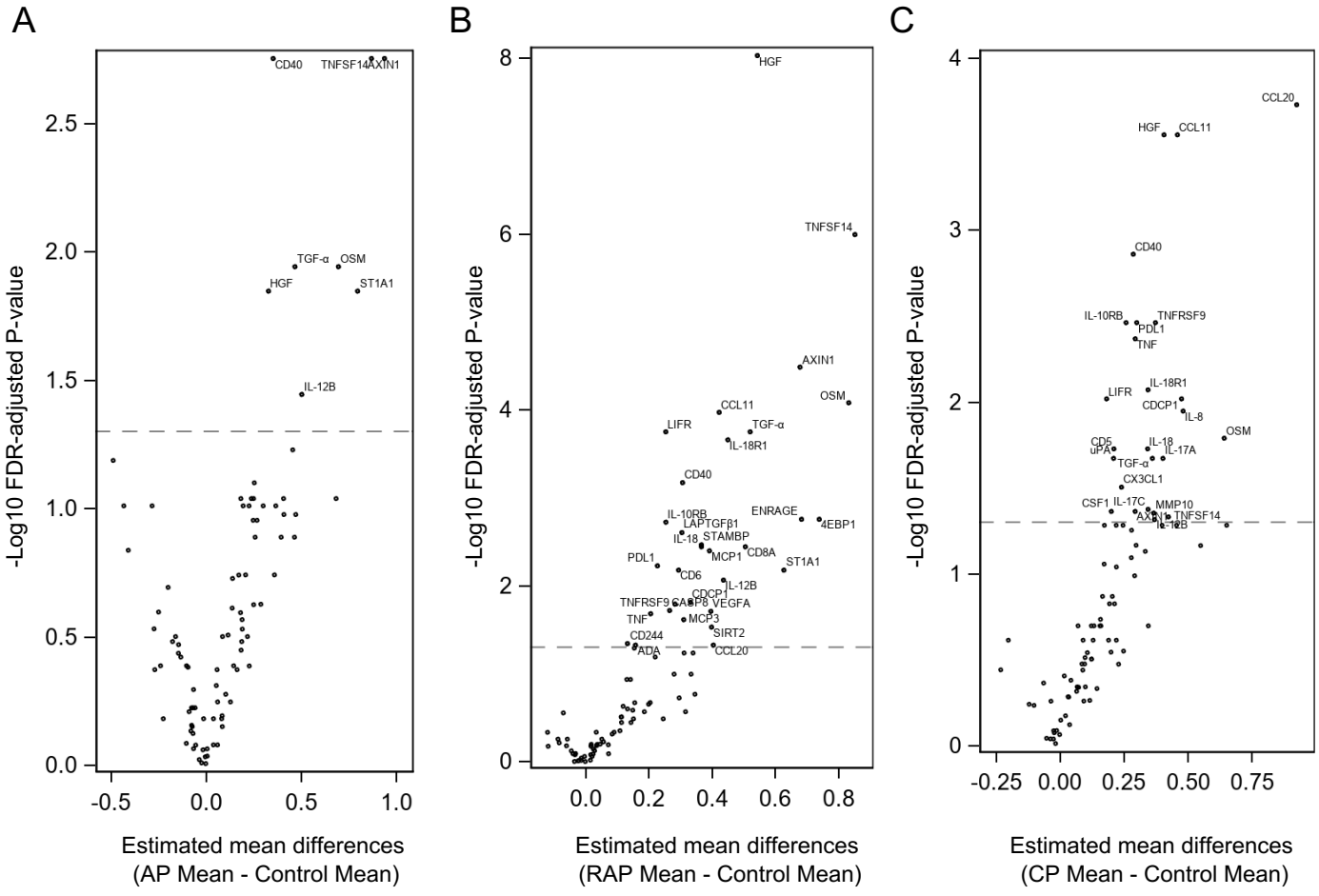
(Intercept)	-1.8549378
CDCP1	1.14E-05
AXIN1	6.99E-05
TGFalpha	7.54E-05
TNFSF14	3.56E-05
ST1A1	1.50E-05
STAMBP	2.30E-05

(Intercept)	0.21130712
MCP3	0.00012146
CDCP1	8.95E-05
AXIN1	8.37E-05
CST5	-5.91E-06
OSM	7.77E-06
CXCL1	-2.75E-05
TSLP	6.70E-05
CCL4	-1.09E-05
SCF	-2.83E-05
TGFalpha	5.55E-05
TNFSF14	1.53E-05
FGF5	-0.0002314
FGF21	5.46E-05
IL24	-5.52E-05
CCL3	-3.65E-05
Flt3L	-1.69E-05
IL20	1.22E-05
DNER	-2.19E-05
ENRAGE	3.45E-05
NRTN	-0.0002371
ST1A1	7.30E-05

(Intercept)	-0.5946459
CDCP1	7.58E-05
IL17A	2.89E-05
SCF	-1.03E-05
FGF21	3.28E-05

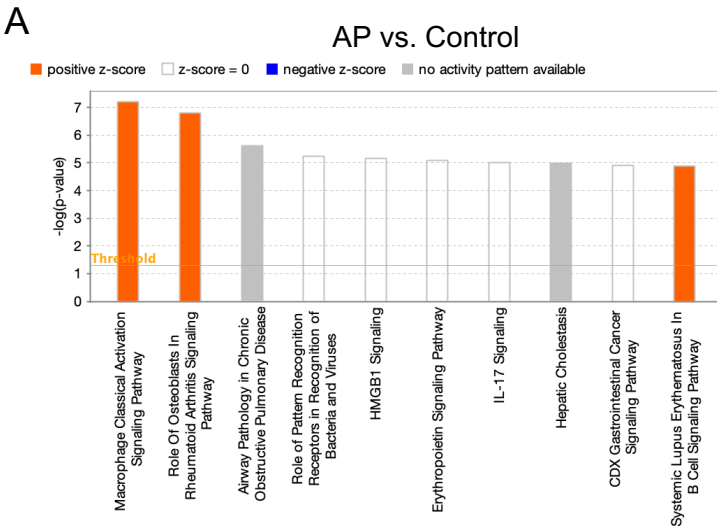
Supplemental Figure 2. Receiver Operator Characteristic (ROC) curves and elastic net estimated regression coefficients of immune markers that discriminate pancreatitis from controls. AP vs. controls (**A**), RAP vs. controls (**B**), and CP vs. controls (**C**). Positive regression coefficients indicate a positive association with the first group listed in the figure title.

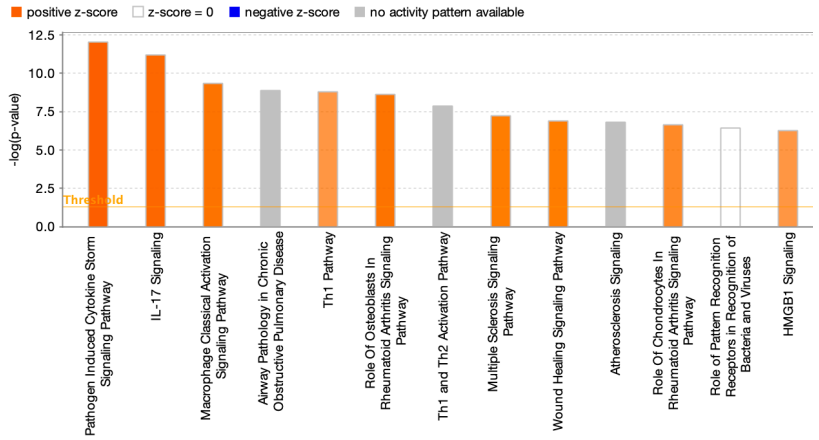
Supplementary Figure 3.

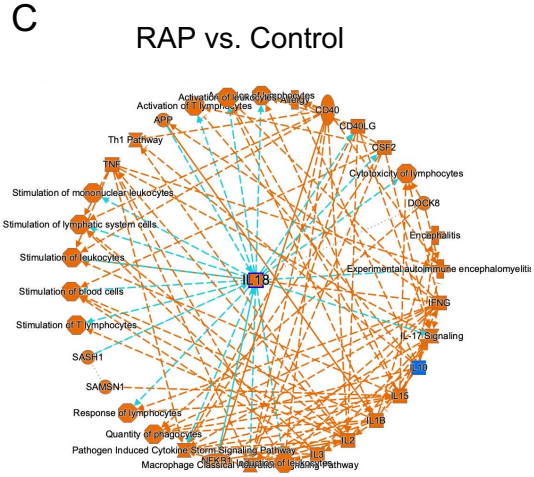


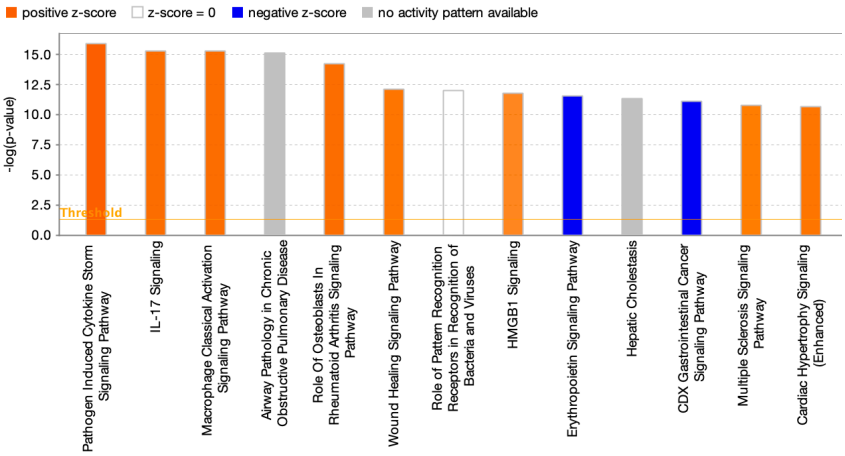
Supplemental Figure 3. Differentially expressed immune markers in each pancreatitis state, AP, RAP, and CP. Volcano plots of differentially expressed immune markers in AP vs. controls (**A**), RAP vs. controls (**B**), and CP vs. controls (**C**). Data are adjusted for the covariates of age, sex, smoking, and drinking status.

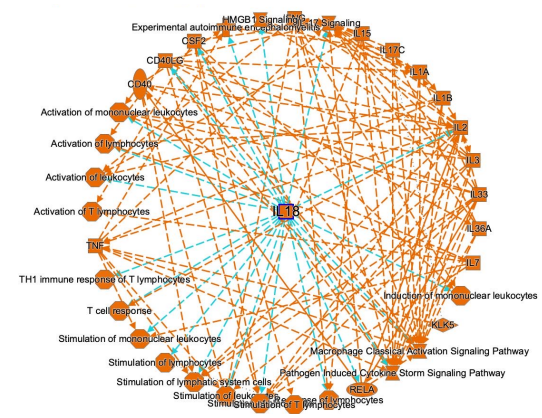
Supplementary Figure 4.





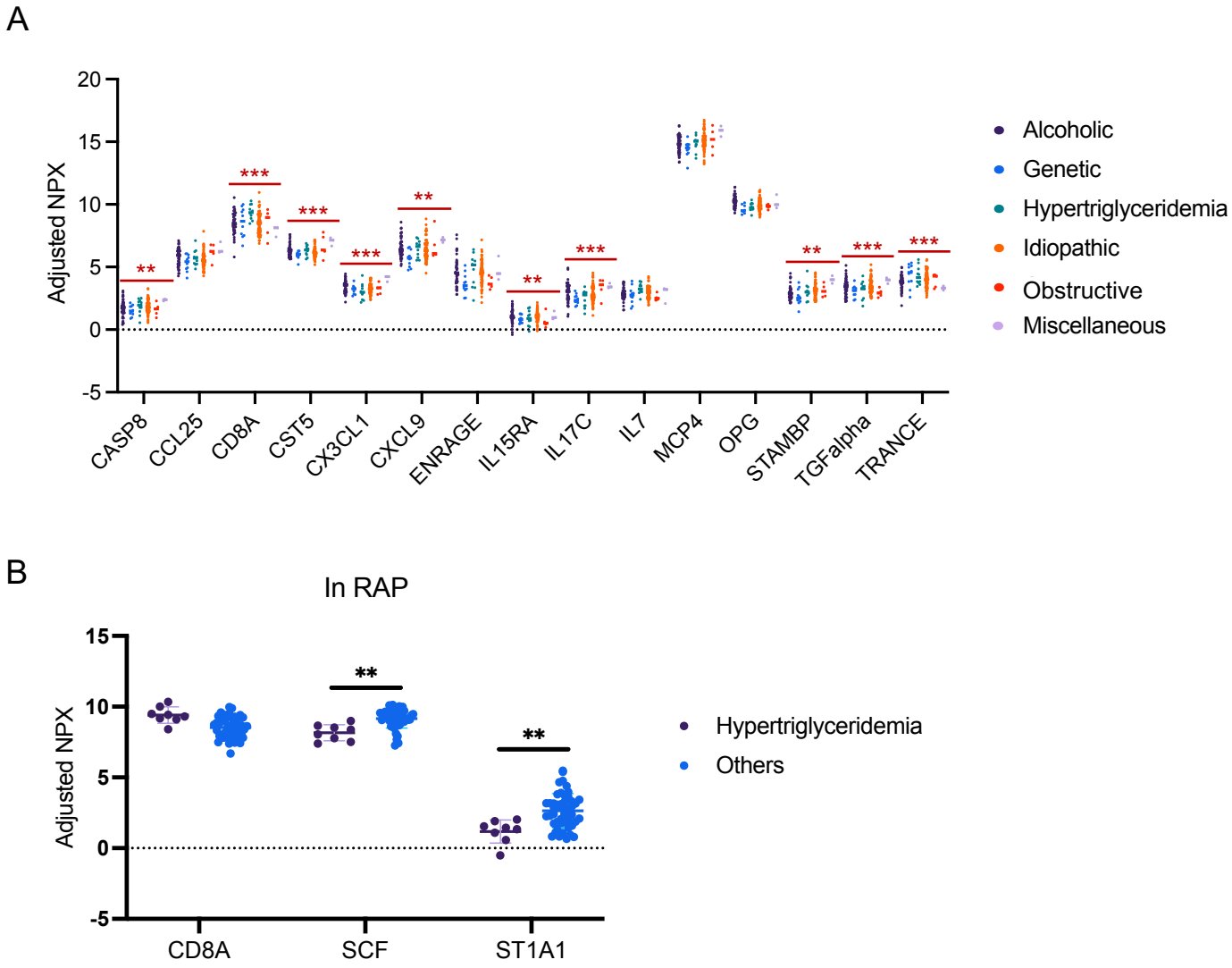






Supplemental Figure 4. Ingenuity Pathway Analysis (IPA) of serum immune marker expressions in each pancreatitis state versus controls demonstrates unique but common proinflammatory signaling pathways. A. Differentially activated canonical pathways in AP vs. control. **B**. Differentially activated canonical pathways in RAP vs. control. **C.** Graphical summary depicting IL-18-centered molecular interactions in RAP vs. control. **D**. Differentially activated canonical pathways in CP vs. control. **E.** Graphical summary depicting IL-18-centered molecular interactions in CP vs. control. IPA was performed with Olink data (Estimated mean differences of NPX values in all pancreatitis vs. controls and FDR-adjusted *p*-values. Data are adjusted for the covariates of age, sex, smoking, and drinking status.).

Supplementary Figure 5.



Supplemental Figure 5. Serum immune markers associated with etiology differences in all pancreatitis. A. Protein expression levels of statistically significant and different serum immune markers in all pancreatitis with different etiologies. **B.** Protein expression levels of statistically significant and different serum immune markers in RAP with hypertriglyceridemia versus those with other etiologies. FDR-adjusted *p*-values of all markers displayed are less than 0.05, ***p*<0.01 and ****p*<0.001.