

# Supplemental Table 1

A)

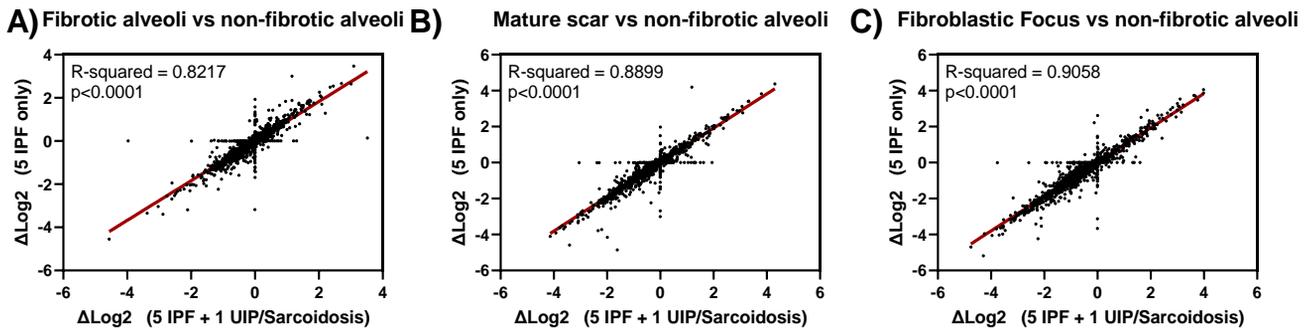
Non-fibrotic	1	2	3	4	5	6
Age	84	77	74	52	75	58
Sex	M	M	F	M	M	F
FEV1 %	79	-	54	89	101	111
FVC %	102	-	62	109	112	124

B)

Fibrotic	1	2	3	4	5	6
Age	64	59	60	52	55	61
Sex	F	M	M	F	M	M
FEV1 %	68	57	61	-	64	59
FVC %	63	49	53	76	64	52
DLCO %	30	33	42	25	44	23
Radiology	Atypical UIP	UIP	NSIP	UIP	UIP	NSIP
Pathology	UIP	UIP with granulomas	UIP	UIP	UIP	UIP
Clinical diagnosis	IPF	Sarcoidosis	IPF	IPF	IPF	IPF
Prednisolone	Y	N	N	N	N	N
Pirfenidone	Y	Y	Y	Y	Y	Y
Nintedanib	N	N	N	N	N	N

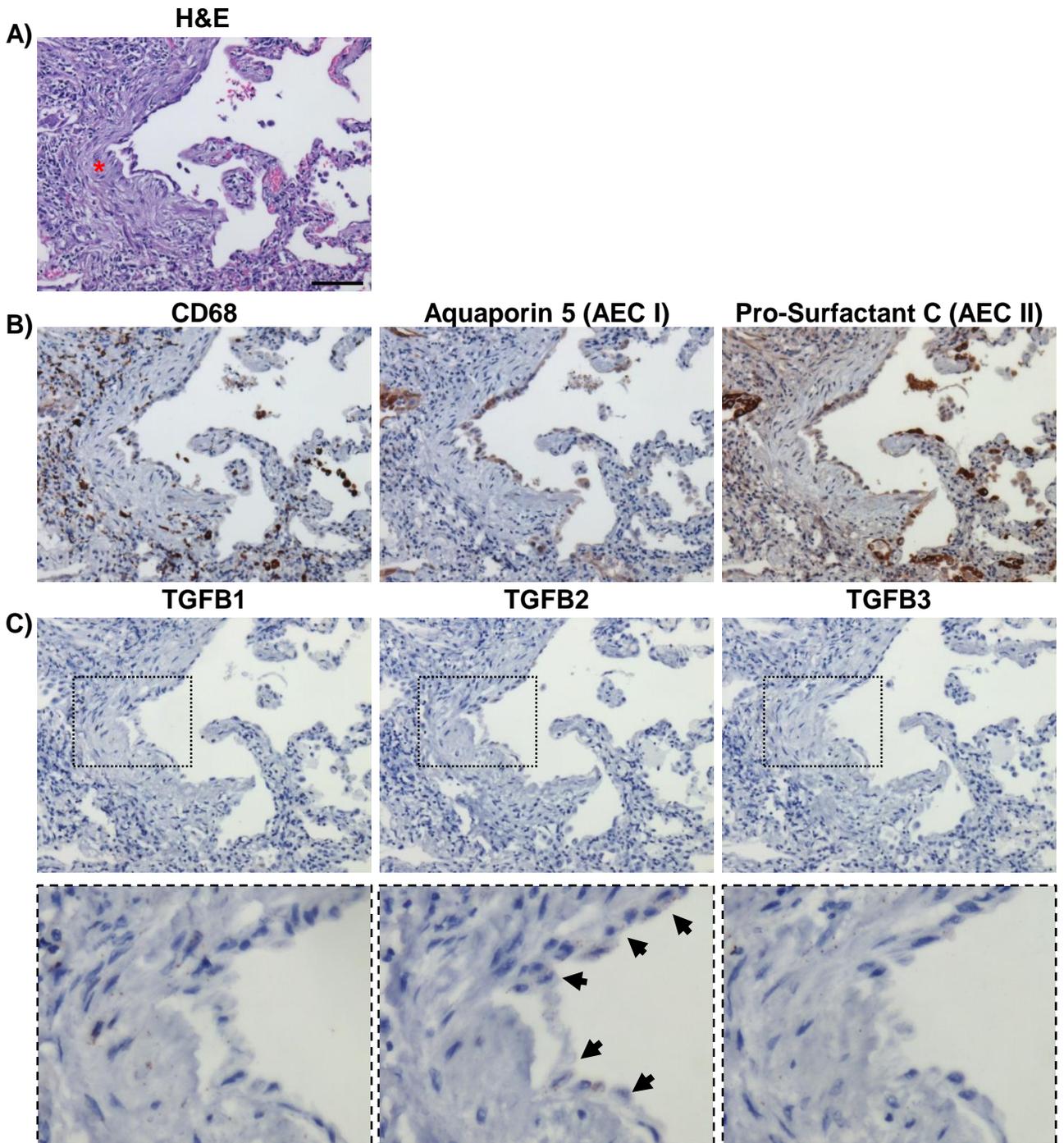
**Supplemental Table 1: Patient Demographics.** Non-fibrotic (A) and fibrotic (B) patient demographics. Lung function for fibrotic patients was taken as the last pulmonary function reading before transplant.

# Supplemental Figure 1



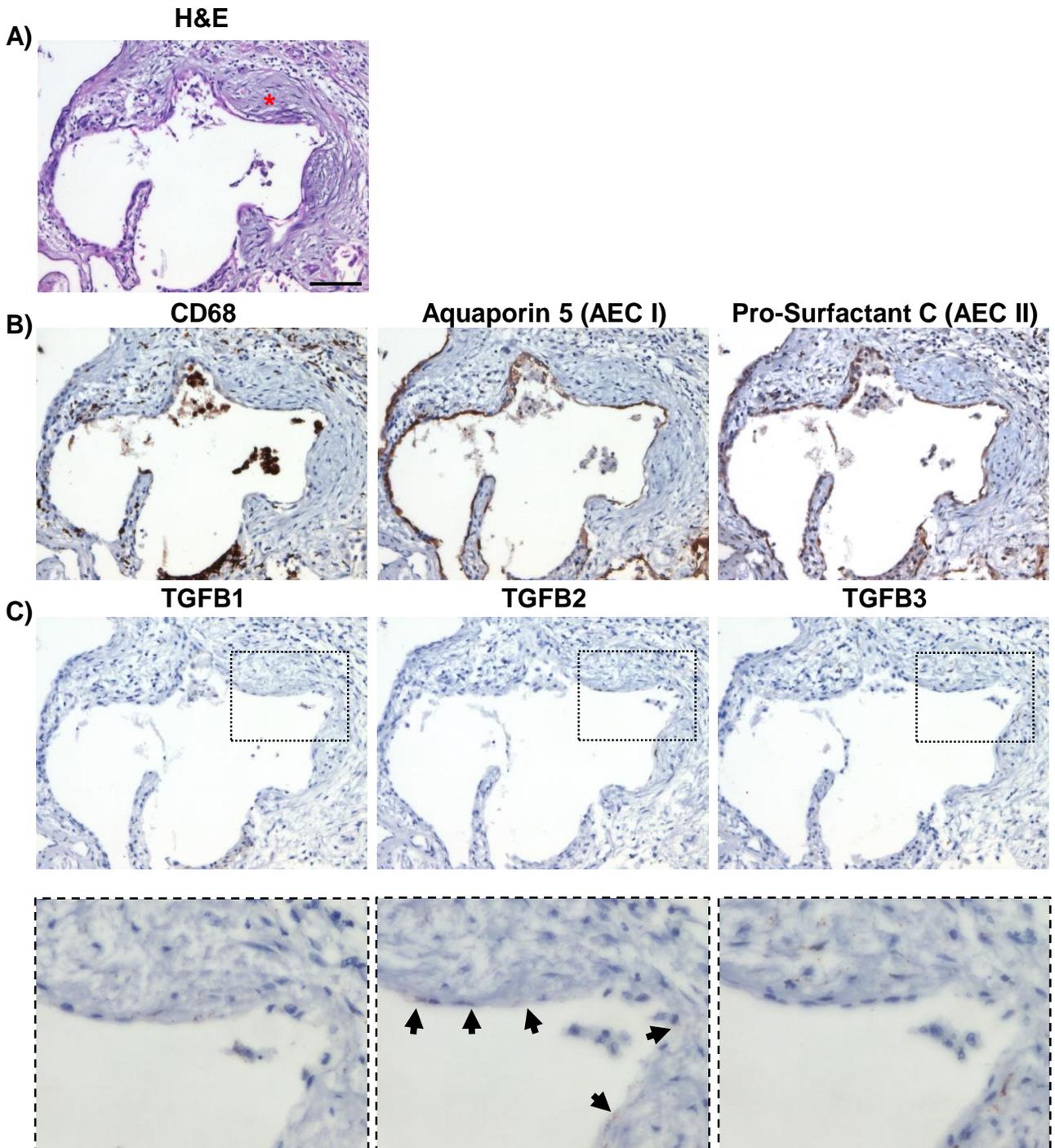
**Supplemental Figure 1: Removal of the UIP/sarcoidosis specimen does not dramatically alter protein expression per region.** A scatter plot showing the correlation of expression when the UIP/Sarcoidosis specimen was kept (X-axis) or removed (Y-axis) when comparing the (A) fibrotic alveoli, (B) mature scar, and (C) fibroblastic focus versus non-fibrotic alveoli control. The linear regression is presented within a 95% confidence interval.

## Supplemental Figure 2



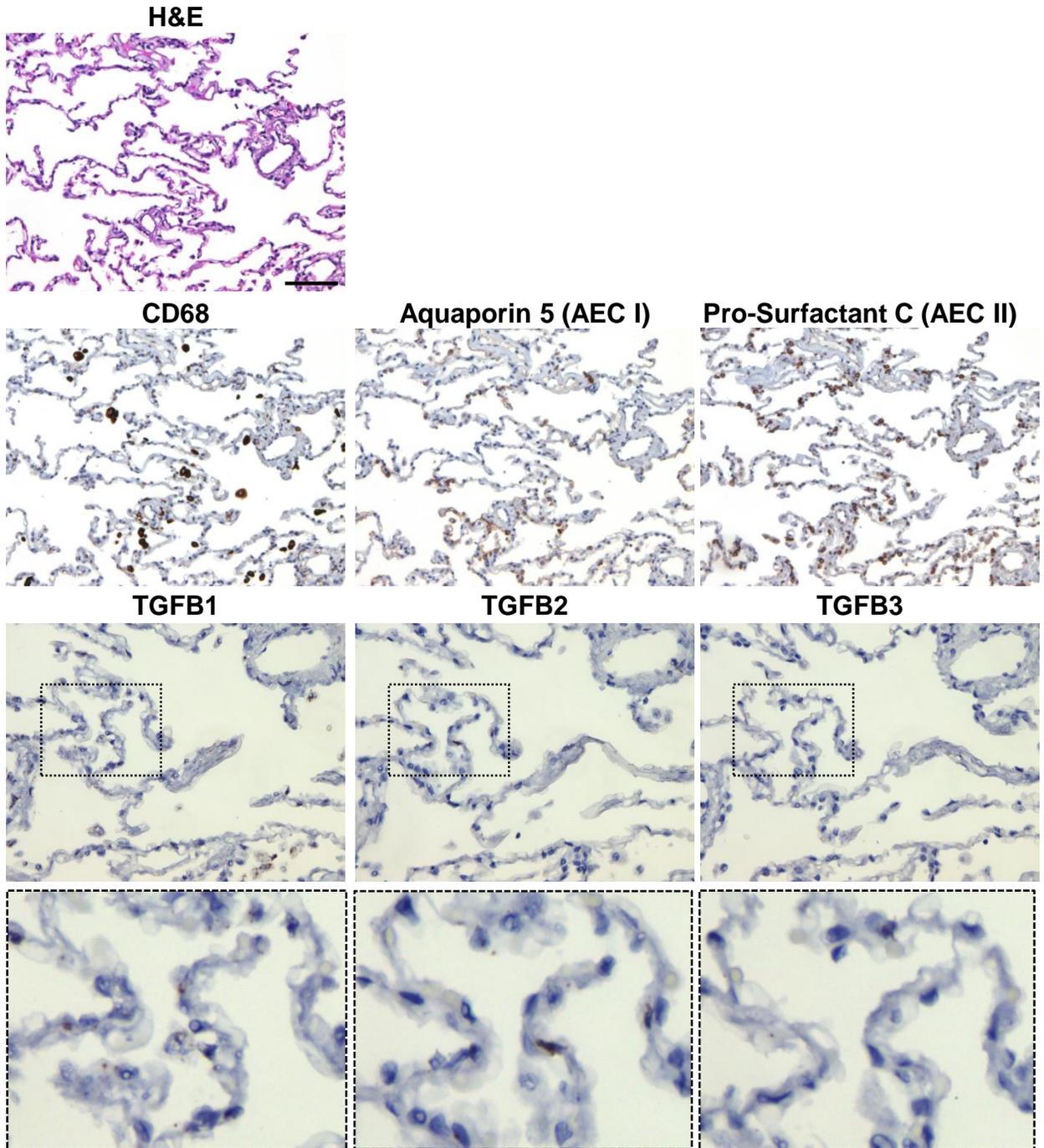
**Supplemental Figure 2: Distribution of type I & II alveolar epithelial cells and TGFβ1-3 in the fibroblastic focus and adjacent alveoli.** Another UIP/IPF specimen was serially sectioned and histologically stained for (A) H&E (red asterisk denotes the fibroblastic focus). (B) Immunostained for macrophages (CD68), type I alveolar epithelial cells (anti-aquaporin 5), & type II alveolar epithelial cells (pro-surfactant C, pSC), (C) RNA in situ hybridization for TGFβ1-3. Scale bar represents 100 microns (N=5 UIP/IPF specimens, this is a second representative image).

## Supplemental Figure 3



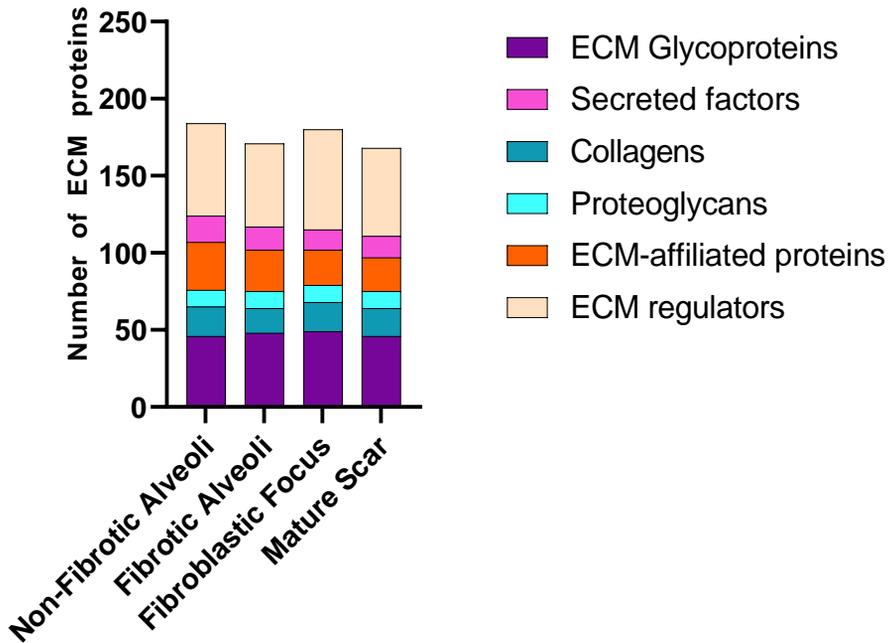
**Supplemental Figure 3: Distribution of type I & II alveolar epithelial cells and TGFβ1-3 in the fibroblastic focus and adjacent alveoli.** Another UIP/IPF specimen was serially sectioned and histologically stained for (A) H&E (red asterisk denotes the fibroblastic focus). (B) Immunostained for macrophages (CD68), type I alveolar epithelial cells (anti-aquaporin 5), & type II alveolar epithelial cells (pro-surfactant C, pSC), (C) RNA in situ hybridization for TGFβ1-3. Scale bar represents 100 microns (N=5 UIP/IPF specimens, this is a third representative image).

## Supplemental Figure 4



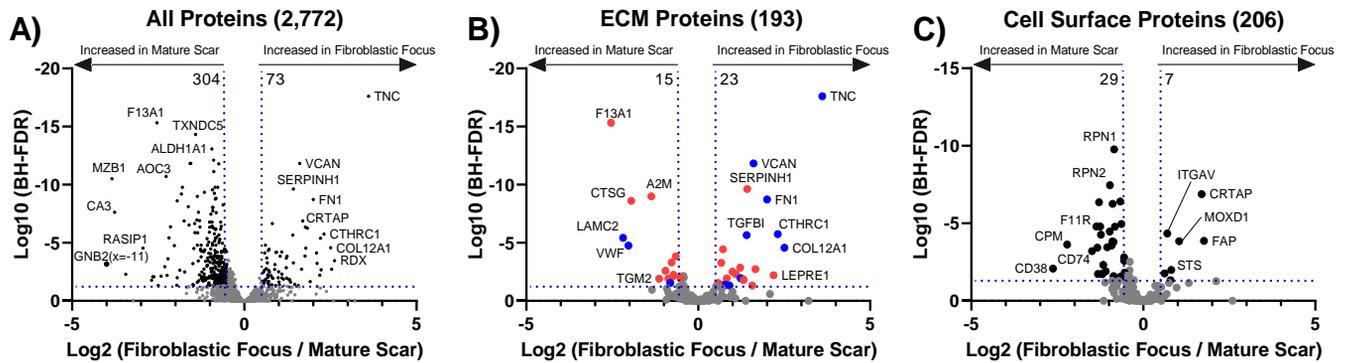
**Supplemental Figure 4: Distribution of type I & II alveolar epithelial cells and TGFβ1-3 in non-fibrotic lung.** A non-fibrotic specimen was serially sectioned and histologically stained for (A) H&E. (B) Immunostained for macrophages (CD68), type I alveolar epithelial cells (anti-aquaporin 5), & type II alveolar epithelial cells (pro-surfactant C, pSC) (C) RNA in situ hybridization for TGFβ1-3. Scale bar represents 100 microns (N = 4 non-fibrotic specimens, representative image shown)

## Supplemental Figure 5



**Supplemental Figure 5: Spatial ECM diversity.** The detected ECM proteins, in each group, were stratified and graphed into 6 ECM categories: ECM glycoproteins, collagens, proteoglycans, ECM-affiliated proteins, ECM regulators, and secreted factors.

# Supplemental Figure 6



## Up-regulated in Fibroblastic Focus

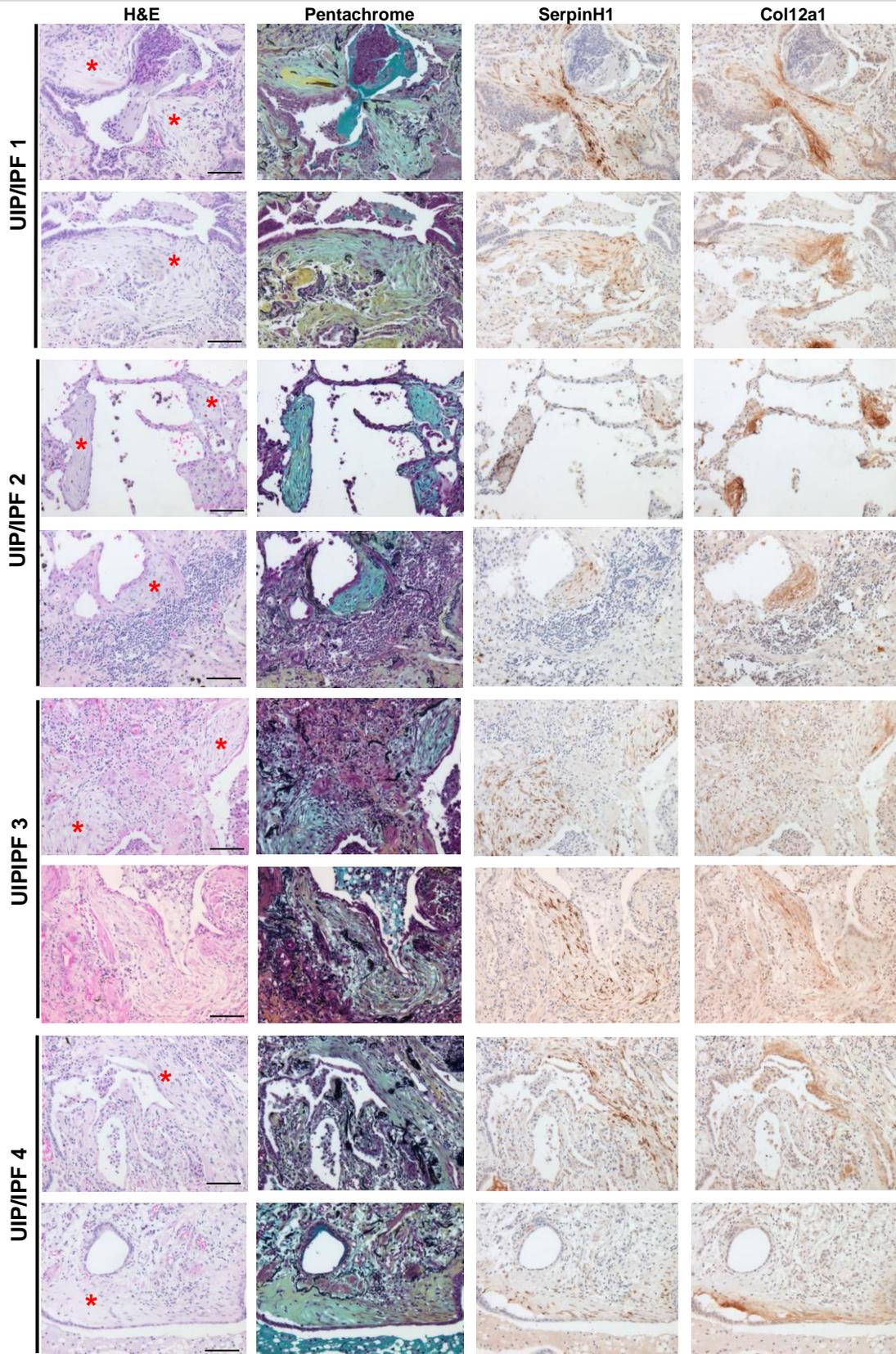
D) Pathway name/reactome pathways identifier (R-HSA)	FDR	Set Size
Extracellular matrix organization/R-HSA-1474244	6.76E-04	12
Collagen biosynthesis and modifying enzymes/R-HSA-1650814	3.89E-03	6
Collagen formation/R-HSA-1474290	1.01E-02	6
Post-translational protein phosphorylation/R-HSA-1474244	1.33E-02	6
Regulation of insulin-like growth factor (IGF) transport and uptake by insulin-like growth factor binding proteins (IGFBPs)/R-HSA-381426	1.76E-02	6

## Down-regulated in Fibroblastic Focus

E) Pathway name/reactome pathways identifier (R-HSA)	FDR	Set Size
TCA cycle and respiratory electron transport/R-HSA-1428517	3.91E-04	27
Pyruvate metabolism and Citric Acid (TCA) cycle/R-HSA-71406	3.91E-04	16
Detoxification of reactive oxygen species/R-HAS-3299685	6.55E-04	13
Maturation of spike protein/R-HSA-9694548	6.55E-04	9
Citric acid cycle (TCA)/R-HSA-71403	8.91E-04	11
Glucogeo genesis/R-HSA-70263	2.96E-03	11

**Supplemental Figure 6. The fibroblastic focus as compared to mature scar tissue. (A-C)** Volcano plots comparing the fibroblastic focus to mature scar showing the negative natural log of the false discovery values (FDR) values plotted against the base 2 log (fold change) for each protein. The data in (A) is for all proteins, whereas (B) was matched against the 'Human Matrisome Project' (<http://matrisomeproject.mit.edu>) and (C) was matched against the 'Cell Surface Protein Atlas' (<http://wlab.ethz.ch/cspa/>). (D) up-regulated or (E) down-regulated Reactome pathways for the fibroblastic focus compared to mature scar.

# Supplemental Figure 7



**Supplemental Figure 7. SerpinH1 and Col12a1 expression in IPF.** 4 UIP/IPF specimens were serially sectioned and stained for H&E, pentachrome, anti-SerpinH1, and anti-Col12a1. We show two additional fibroblastic foci for each specimen (depicted with a red asterisk). Scale bar represents 100 microns.