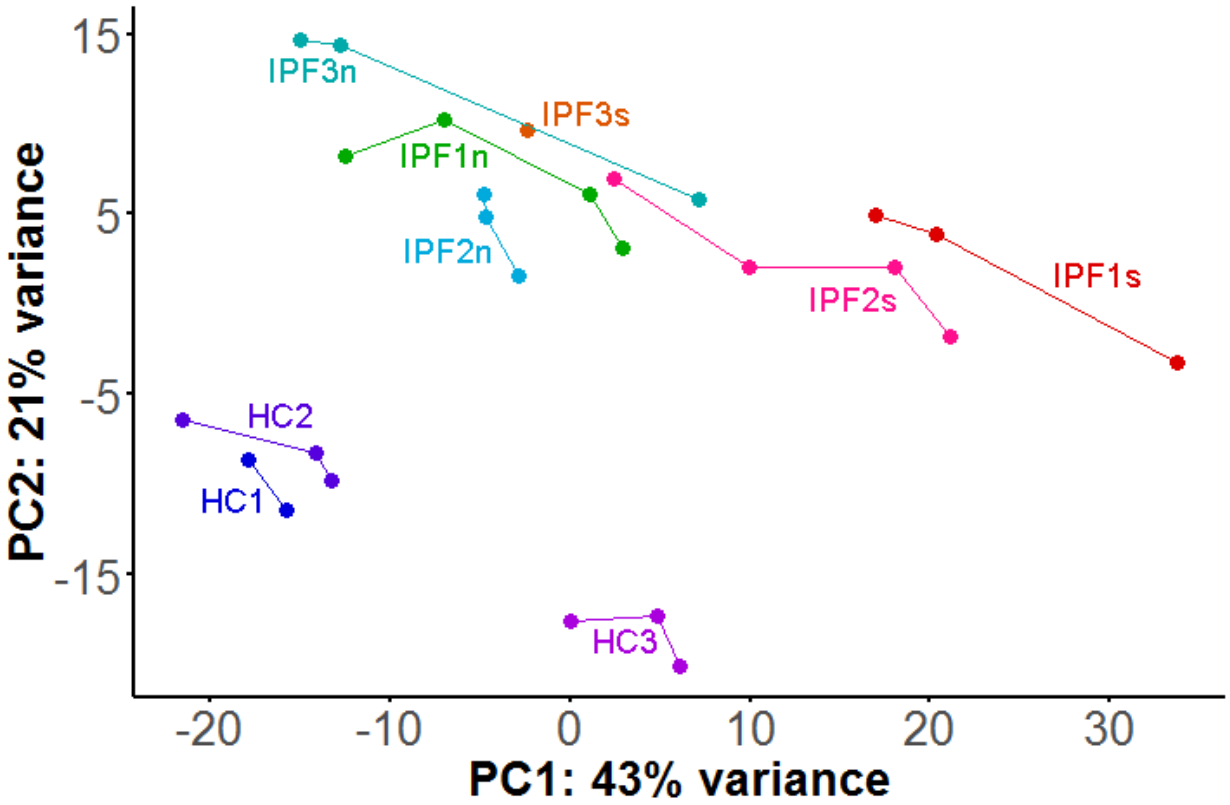
Supplementary Table 1. Characteristics of IPF Patients and Healthy Controls

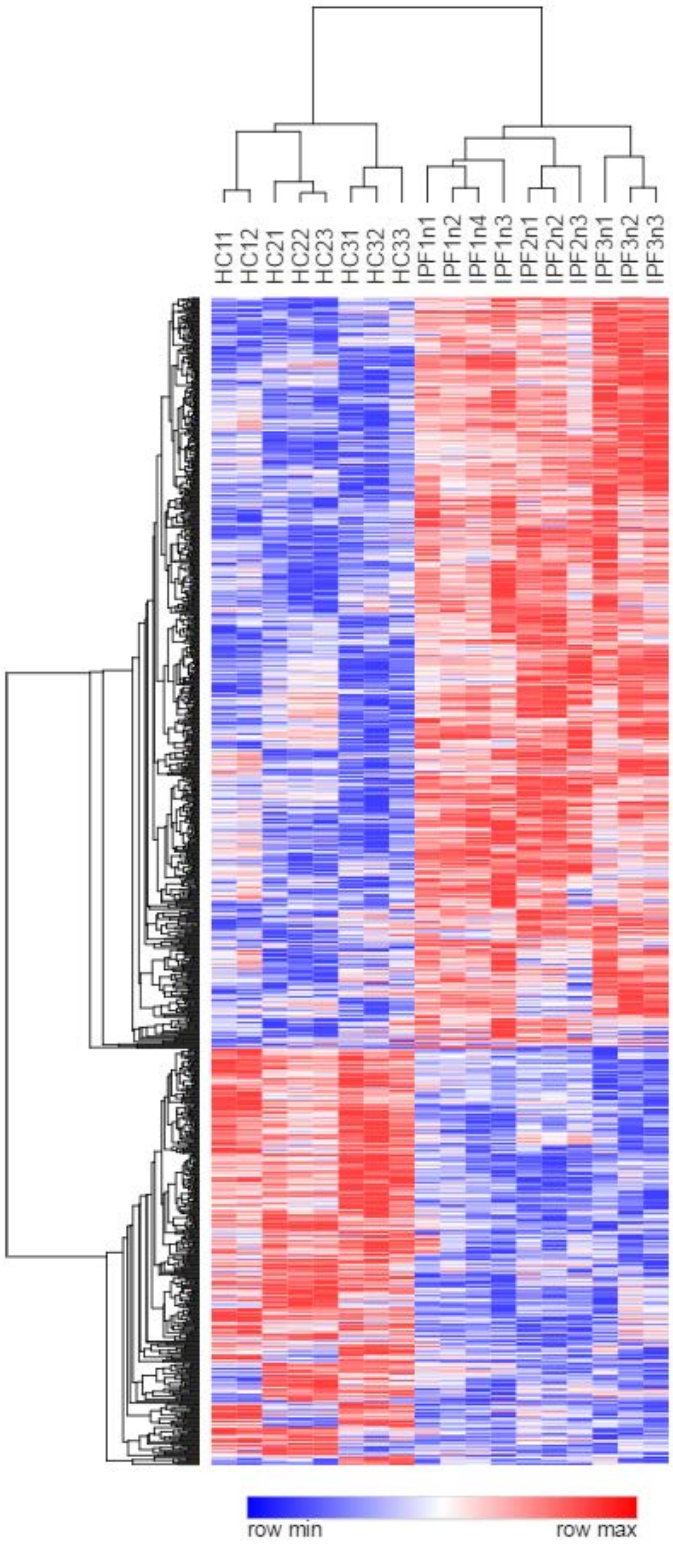
	IPF 1	IPF 2	IPF 3	HC 1	HC 2	HC 3
Age (yrs)	70	74	68	29	37	21
Gender	Male	Male	Male	Male	Male	Male
Race	Caucasian	Caucasian	Caucasian	Caucasian	Caucasian	Caucasian
Ever-smoker (y/n)	No	No	Yes	No	Yes	No
Pack/yrs, *n*	--	--	20	--	25	--
Prednisone (y/n)	Yes	Yes	Yes			
Pirfenidone (y/n)	Yes	No	Yes			
Nintedanib (y/n)	No	No	No			
FVC, liters *(%pred)*	1.5 (39)	2.7 (58)	1.1 (32)			
FEV_1 / FVC	80	83	94			
DLCO, mL/mmHg/min *(%pred)*	7.8 (31)	10.7 (40)	--			
RHC, *mm Hg* (S/D/mean)	38 / 5 / 16	38 / 19 / 26	29 / 10 / 16			
Chest CT	Consist UIP	Poss UIP	Consist UIP			
Histology, explant	UIP	UIP	UIP			
Tissue samples analyzed	IPF1n1 IPF1n2 IPF1n3 IPF1n4 IPF1s1 IPF1s2 IPF1s3	IPF2n1 IPF2n2 IPF2n3 IPF2s1 IPF2s2 IPF2s3 IPF2s4	IPF3n1 IPF3n2 IPF3n3 IPF3s1	HC11 HC12	HC21 HC22 HC23	HC31 HC32 HC33

Definition of abbreviations: IPF = idiopathic pulmonary fibrosis, HC = healthy controls, FEV_1 = forced expiratory volume in one second, FVC = forced vital capacity, DLCO = diffusing capacity for carbon monoxide, RHC = right heart catheterization pulmonary artery pressures (systolic / diastolic / mean), CT = computed tomography, UIP = usual interstitial pneumonia, Poss = possible, Consist = consistent with

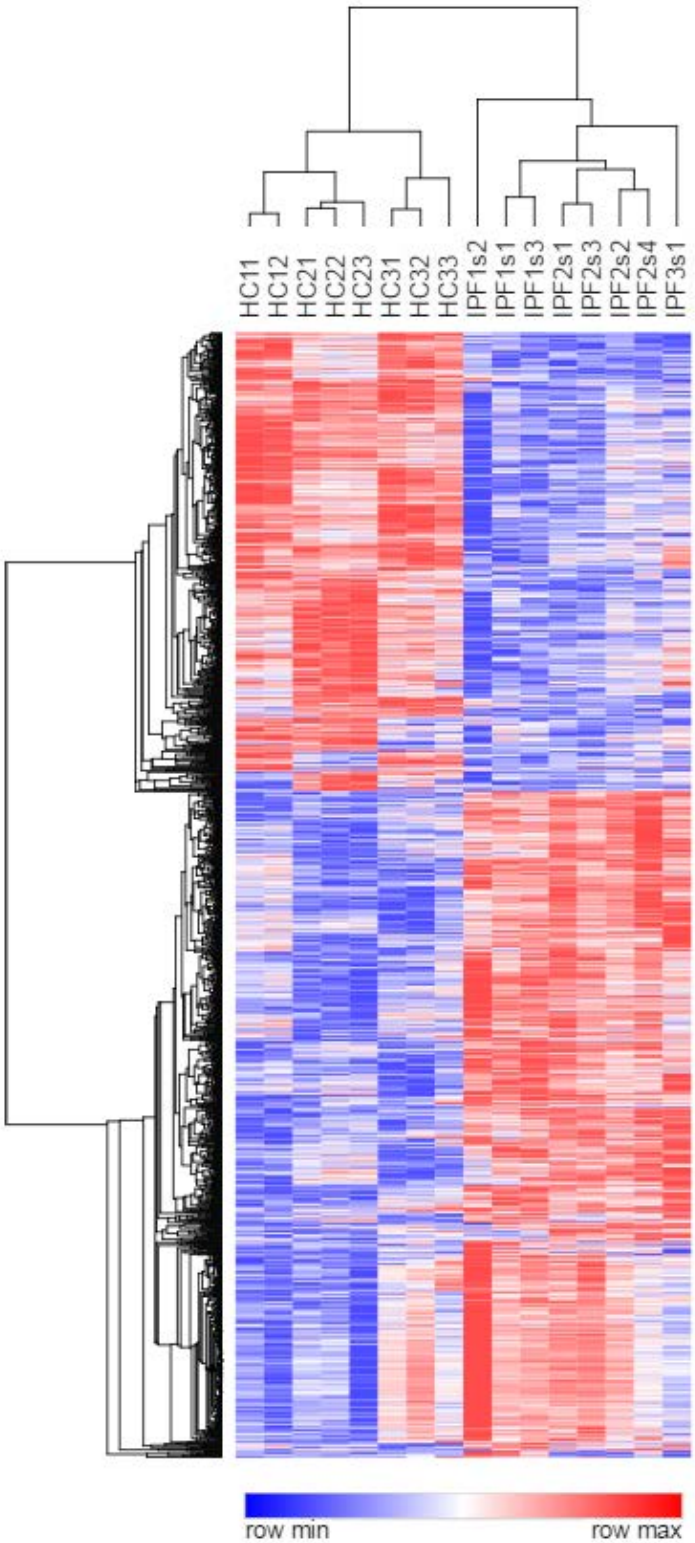
Recorded values for FVC, FEV1/FVC, DLCO, RHC, and Chest CT were those performed closest to the date of lung transplantation.



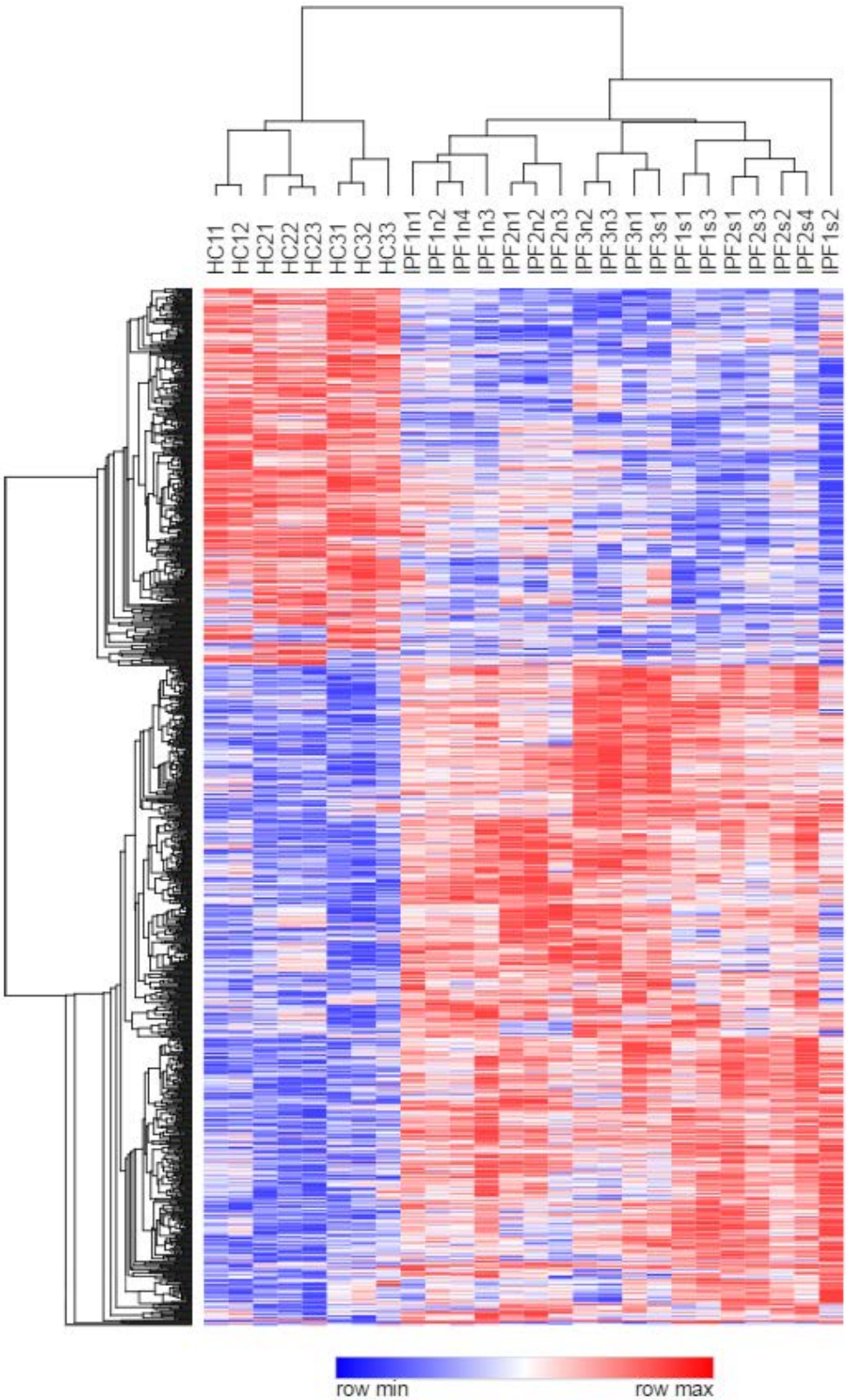
Supplementary Figure 1. Principal component analysis of the RNASeq transcriptome dataset identical to that shown in Figure 2A but with indication of origin of tissue samples by donor. Dots represent tissue samples and the lines connect tissue samples in the same group (HC, IPFn, IPFs) derived from the same donor.



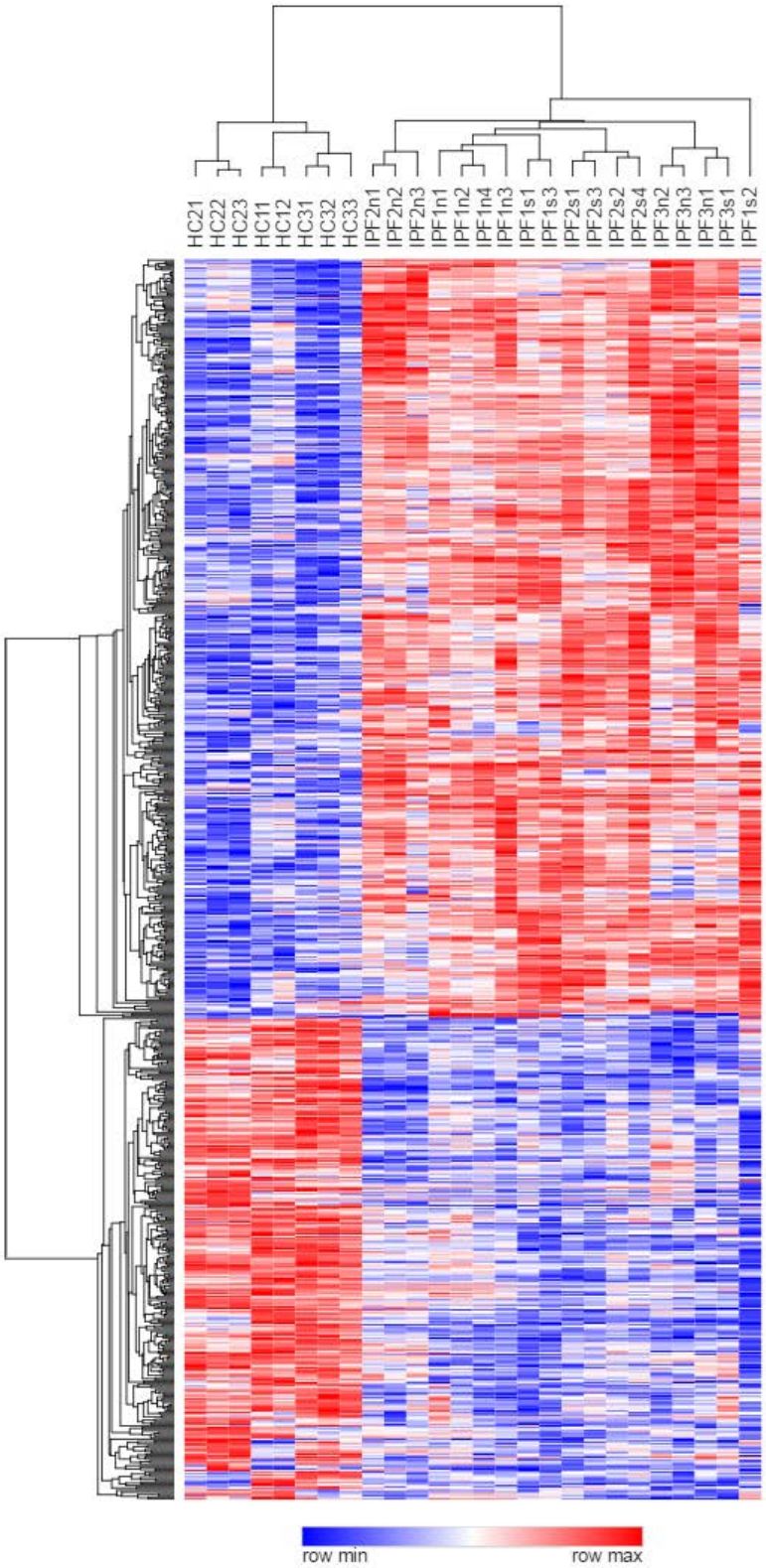
Supplementary Figure 2. Heatmap of differentially expressed genes between HC and IPFn tissues. Unsupervised clustering of tissue samples was performed using Spearman rank correlation with average linkage based on log2-transformed normalized counts of 1,110 differentially expressed genes (713 elevated and 397 decreased in the IPFn group vs HC). The genes were clustered using identical procedure.



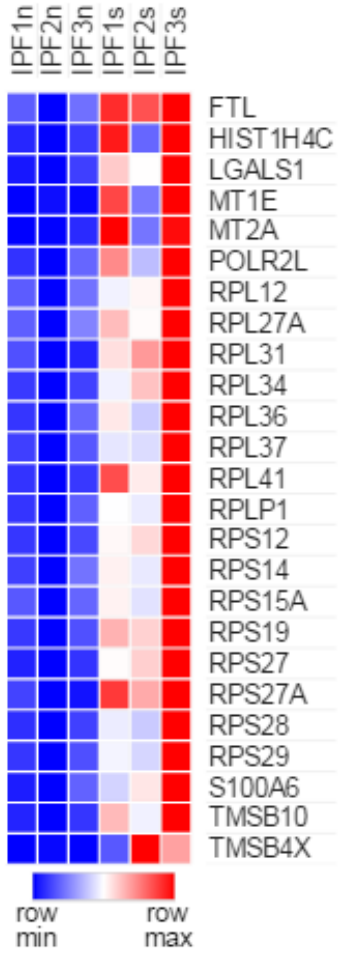
Supplementary Figure 3. Heatmap of differentially expressed genes between HC and IPFs tissues. Unsupervised clustering of tissue samples was performed using Spearman rank correlation with average linkage based on log2-transformed normalized counts of 1,554 differentially expressed genes (920 elevated and 634 decreased in the IPFs group vs HC). The genes were clustered using identical procedure.



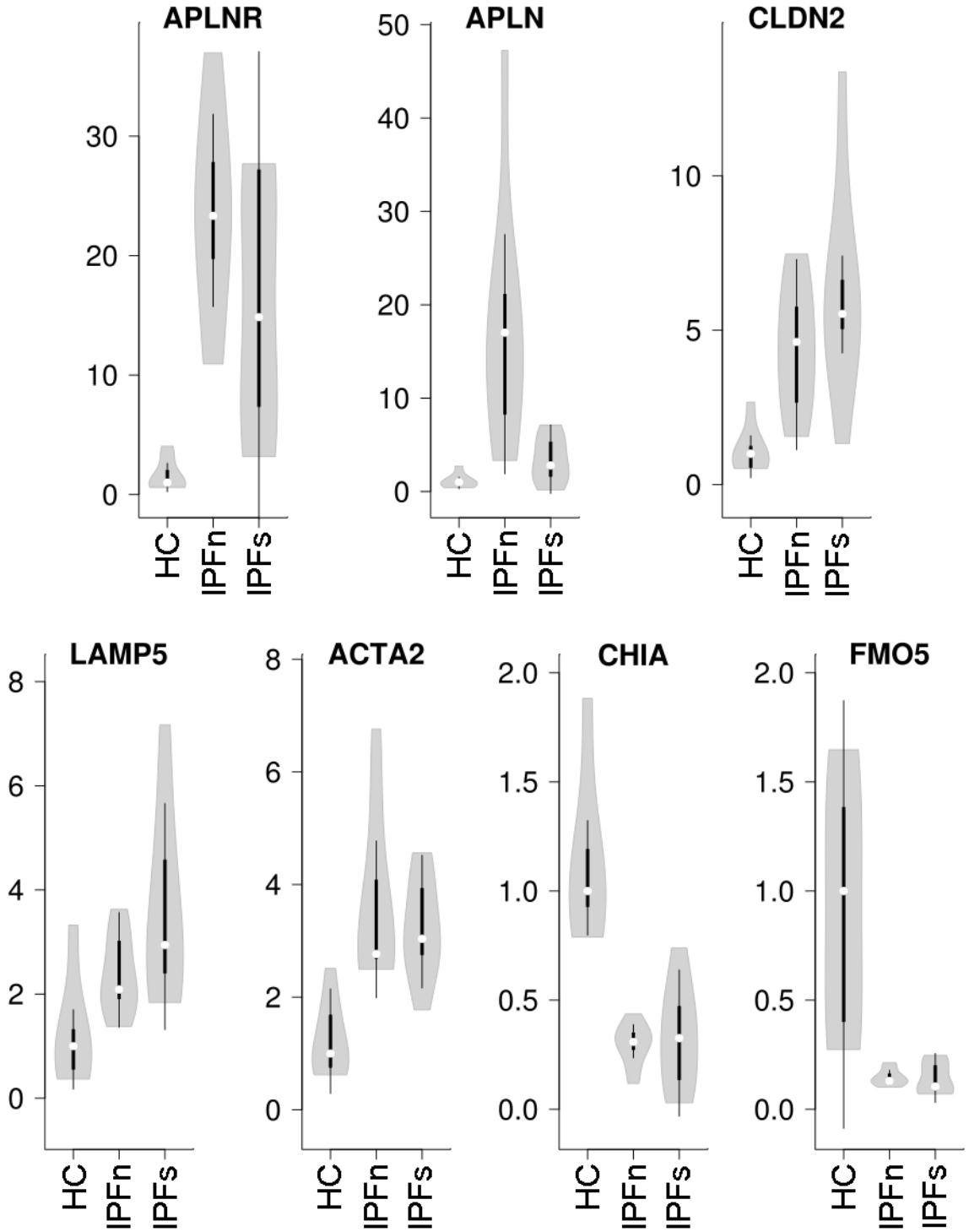
Supplementary Figure 4. Heatmap of differentially expressed genes between HC and IPF (combined IPFn and IPFs) tissues. Unsupervised clustering of tissue samples was performed using Spearman rank correlation with average linkage based on log2-transformed normalized counts of 1,119 differentially expressed genes (710 elevated and 409 decreased in the IPF combined group vs HC). The genes were clustered using identical procedure.



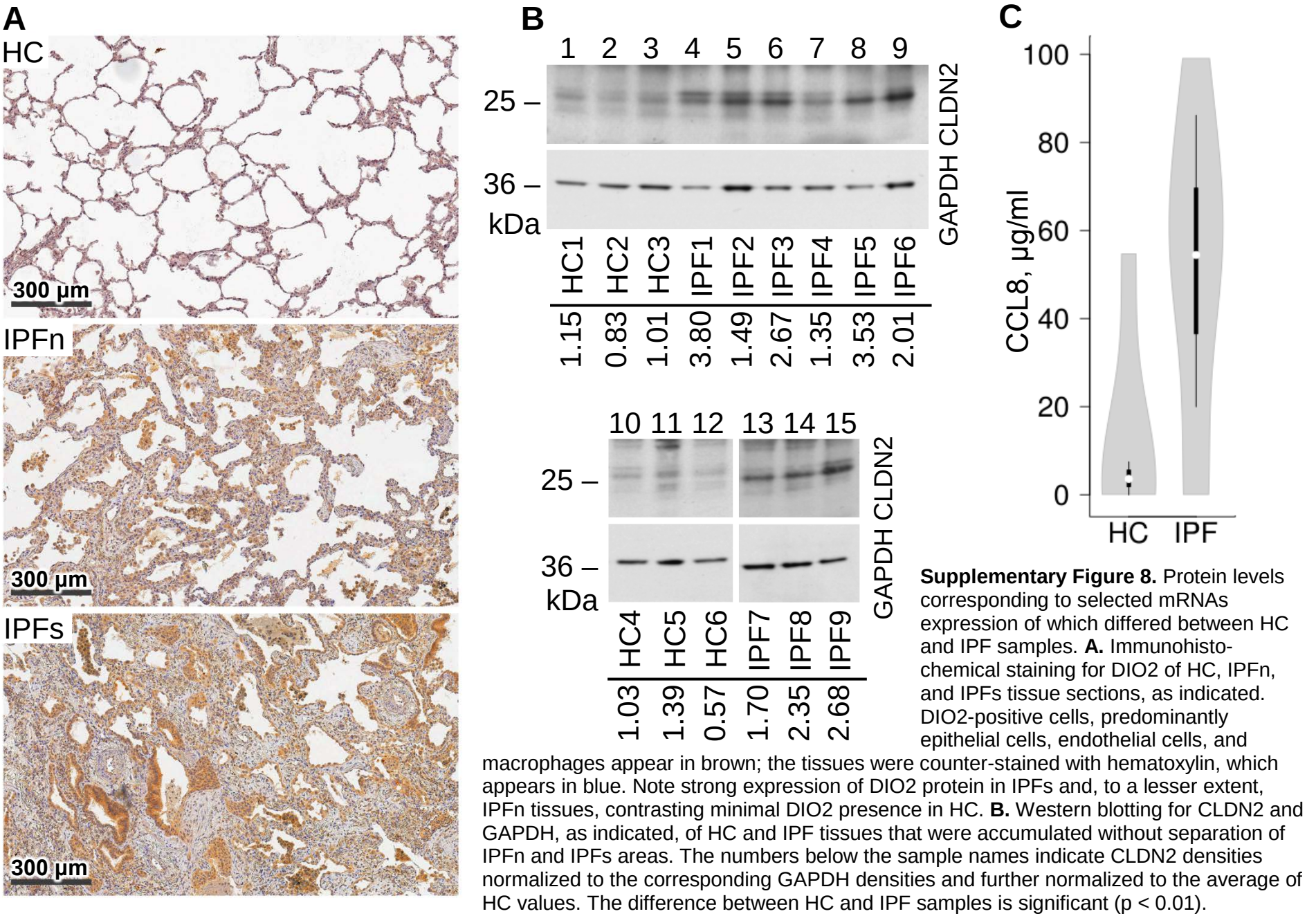
Supplementary Figure 5. Expression heatmap of genes with similarly elevated or similarly reduced levels in IPFn and IPFs tissues each compared to HC (IPF overlap group). Unsupervised clustering of tissue samples was performed using Spearman rank correlation with average linkage based on log2-transformed normalized counts of 458 genes with elevated and 291 genes with decreased expression in IPF overlap vs HC. The genes were clustered using identical procedure.



Supplementary Figure 6. Heatmap of genes that were differentially expressed in primary pulmonary fibroblast cultures from IPFn and IPFs tissues.



Supplementary Figure 7. Confirmation of selected RNASeq findings by RT-qPCR similar to Figure 6, but with data for each target normalized to GAPDH.



Supplementary Figure 8. Protein levels corresponding to selected mRNAs expression of which differed between HC and IPF samples. **A.** Immunohisto-chemical staining for DIO2 of HC, IPFn, and IPFs tissue sections, as indicated. DIO2-positive cells, predominantly epithelial cells, endothelial cells, and macrophages appear in brown; the tissues were counter-stained with hematoxylin, which appears in blue. Note strong expression of DIO2 protein in IPFs and, to a lesser extent, IPFn tissues, contrasting minimal DIO2 presence in HC. **B.** Western blotting for CLDN2 and GAPDH, as indicated, of HC and IPF tissues that were accumulated without separation of IPFn and IPFs areas. The numbers below the sample names indicate CLDN2 densities normalized to the corresponding GAPDH densities and further normalized to the average of HC values. The difference between HC and IPF samples is significant ($p < 0.01$). **C.** Violin plot of ELISA for CCL8 of lung homogenates from 5 HC and 12 IPF donors. The tissues were collected without separation of IPFn and IPFs areas. The difference between HC and IPF samples is significant ($p < 0.05$).

Legends to Supplementary Datasets (included as separate Excel files)

Supplementary Dataset 1. Differentially expressed genes across the three tested groups of samples (HC, IPFn, IPFs) revealed by the DESeq2 likelihood ratio test (LRT). Log2-transformed normalized counts are arranged in rows (differentially expressed genes) and columns (tissue samples) to match those in the corresponding heat map in Figure 2B.

Supplementary Dataset 2. Differentially expressed genes between HC and IPFn groups. Log2-transformed normalized counts are arranged in rows (differentially expressed genes) and columns (tissue samples) to match those in the corresponding heat map in Supplementary Figure 2.

Supplementary Dataset 3. Differentially expressed genes between HC and IPFs groups. Log2-transformed normalized counts are arranged in rows (differentially expressed genes) and columns (tissue samples) to match those in the corresponding heat map in Supplementary Figure 3.

Supplementary Dataset 4. Differentially expressed genes between HC and IPF (combined IPFn and IPFs) groups. Log2-transformed normalized counts are arranged in rows (differentially expressed genes) and columns (tissue samples) to match those in the corresponding heat map in Supplementary Figure 4.

Supplementary Dataset 5. Differentially expressed genes between IPFn and IPFs groups. Log2-transformed normalized counts are arranged in rows (differentially expressed genes) and columns (tissue samples) to match those in the corresponding heat map in Figure 4A.

Supplementary Dataset 6. Differentially expressed genes similarly elevated or similarly reduced in IPFn and IPFs groups of tissues, each compared with the HC group. Log2-transformed normalized counts are arranged in rows (differentially expressed genes) and columns (tissue samples) to match those in the corresponding heat map in Supplementary Figure 5.

Supplementary Dataset 7. Genes with the most prominent expression level differences, based on magnitude or statistical significance. Log2-fold values are color-coded by columns using the blue–white–red palette to denote the distribution of values as minimal–median–maximal, respectively. Blank cells indicate expression levels that were too low for a reliable pair-wise comparison. Cells with –log10padj > 1.30103 corresponding to padj > 0.05 are shaded in gray.