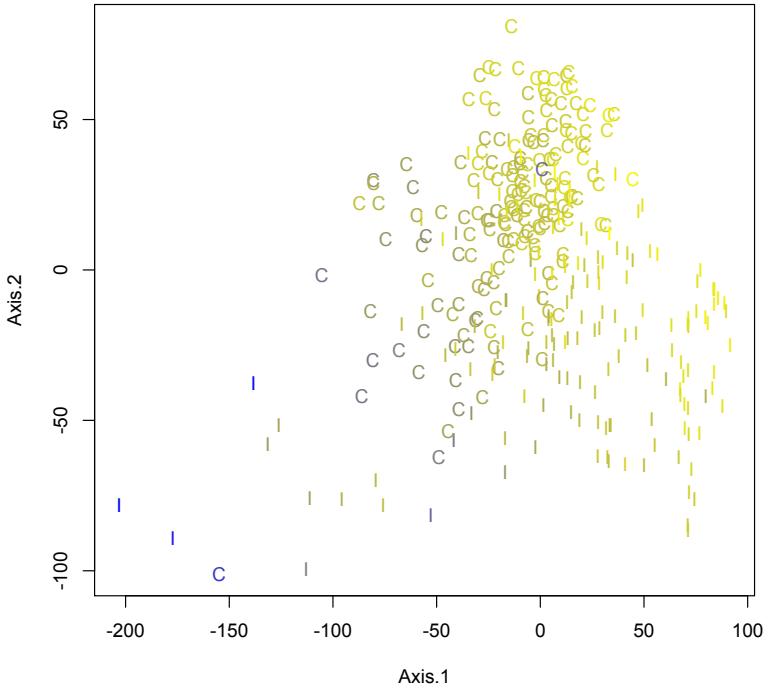
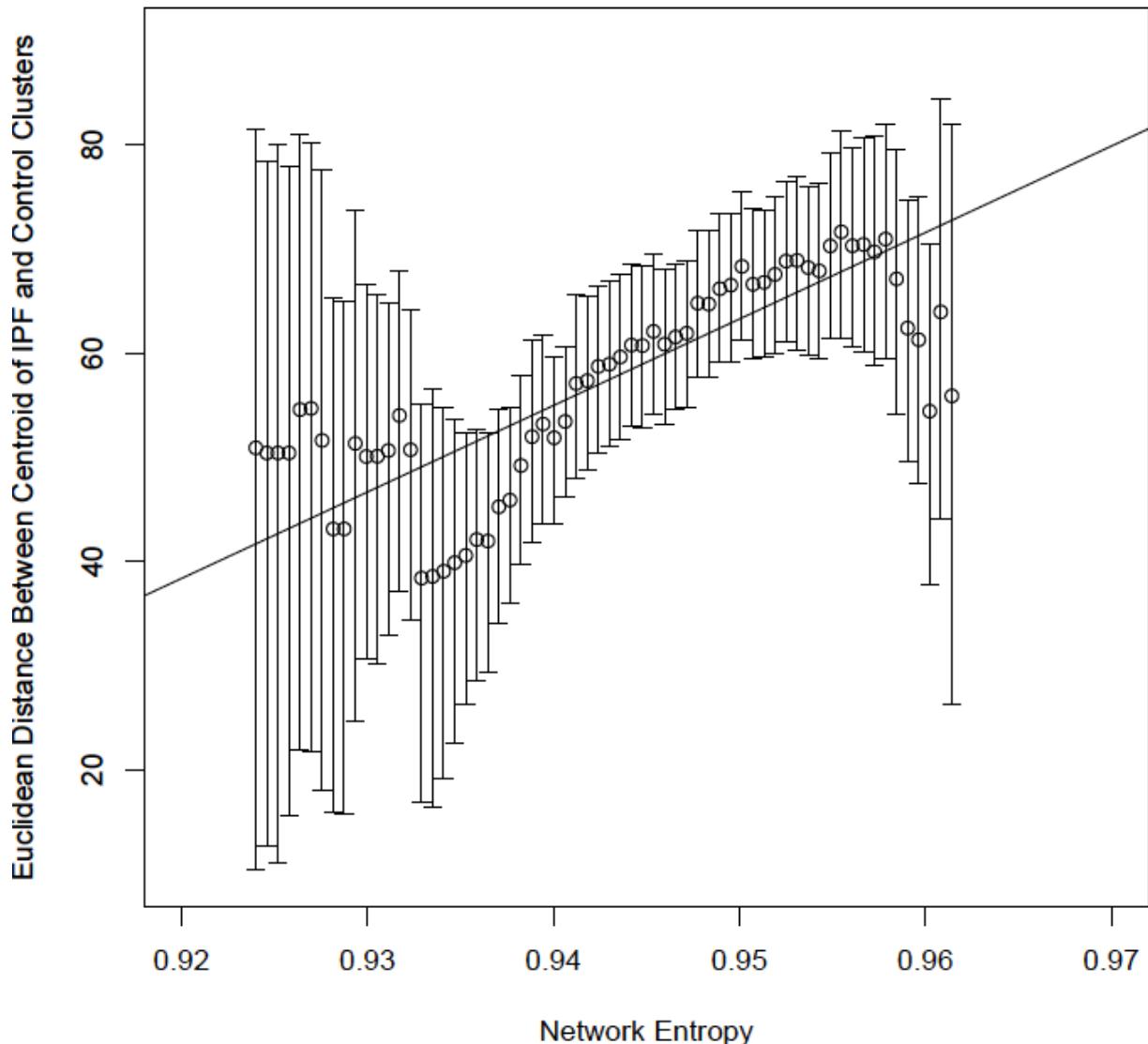


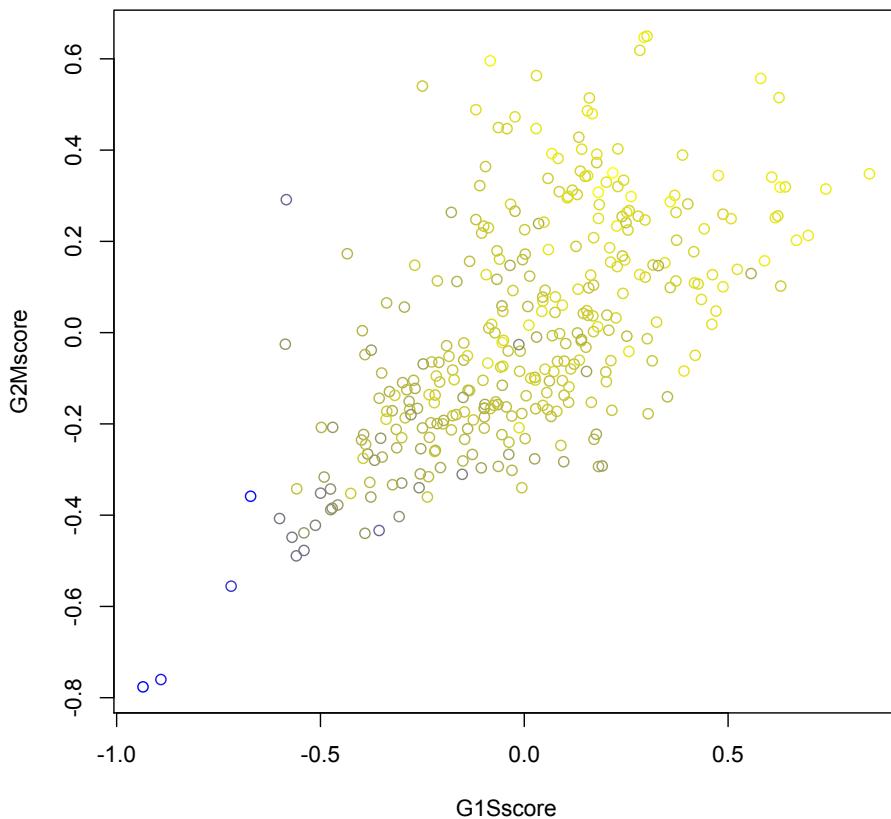
**Supplementary Figure 1. Comparison of Single-cell RNA seq data with bulk RNA seq data from IPF and control SSEA4hi MPCs.** The log2 adjusted TPM value of each detected gene from single cell and bulk RNA sequencing experiments from Control and IPF derived SSEA4hi MPCs is shown. An agreement between the bulk and single cell sequencing data is shown with Spearman rank correlations for IPF ( $r=0.72$ ,  $p<2.2\times 10^{-16}$ ) and Control ( $r=0.74$ ,  $p<2.2\times 10^{-16}$ ). A tail can be seen where lower average expression in single cell sequencing compared to bulk RNA sequencing is found for the low abundance transcripts. This likely reflects the expected lower capture efficiency of the low abundance transcripts in single cell sequencing experiments compared to bulk RNA sequencing experiments.



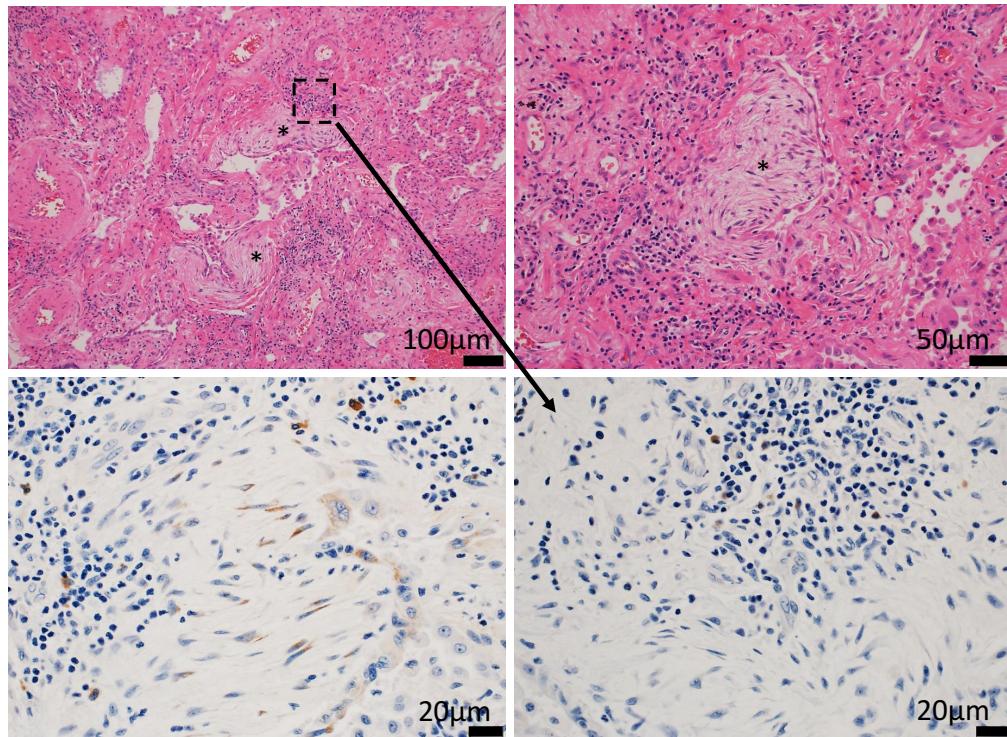
**Supplementary Figure 2. PCA analysis of drop-out rate corrected data.** We corrected for drop-out rate using the Clustering through Imputation and Dimensional Reduction (CIDR) algorithm. The top 10,000 most variable detected genes were included in this analysis. Plotted are the first 2 components from the PCA analysis on the imputed data. Each data point represents a cell (I=IPF, C=Control). Points are colored to indicate the network entropy of each cell (blue= lowest network entropy, yellow = highest network entropy).



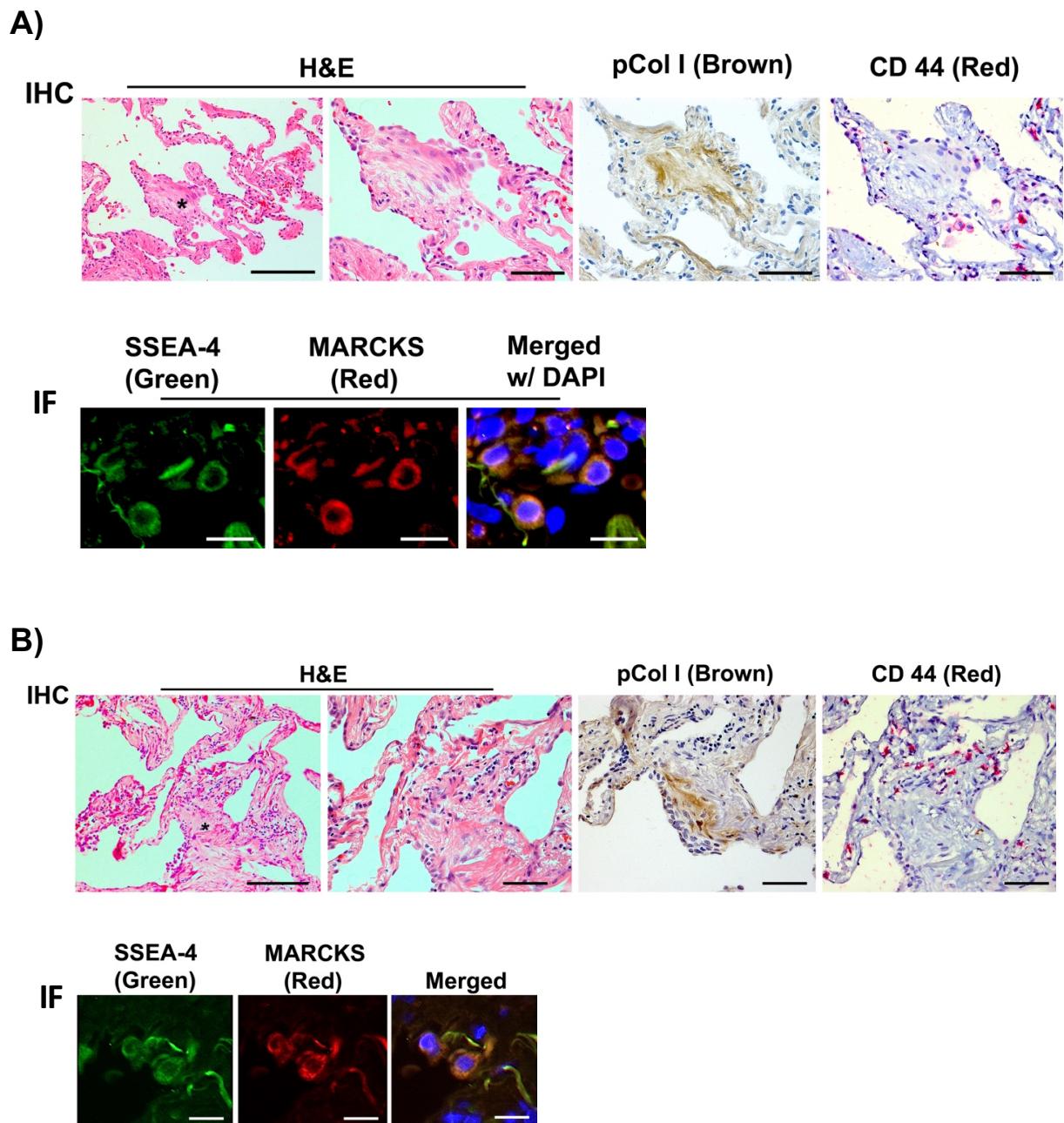
**Supplementary Figure 3. Distance Between IPF and Control Cell Clusters Increases with Increasing Network Entropy.** Euclidean distances between the centroids of the IPF and Control cell clusters were calculated across the network entropy spectrum. Cells were analyzed in a sliding boxcar fashion, with the width of the boxcar including approximately 25% of the observed network entropy range, and with steps of 1/100<sup>th</sup> of the observed network entropy range. Error bars represent the 95% confidence interval, calculated using a bootstrap approach. The line shown represents the weighted linear fit. It has a positive slope that is non-zero with a p-value <2.2x10<sup>-16</sup>.



**Supplementary Figure 4. Cell cycle phase score is not correlated with network entropy.**  
Cell-cycle phase scores for G1/S and G2/M phase were calculated, and plotted for each cell. Overlayed on this plot are network entropy scores (blue= low entropy, yellow= high entropy)  
There is no cell cycle phase bias based on network entropy.



**Supplementary Figure 5. IHC staining of additional fibroblastic foci identifies SSEA4 positive cells in the perimeter region.** Low and high magnification views of H&E staining of two different fibroblastic foci are shown in upper left and right panels demonstrating a myofibroblast dense core region (asterisks) and adjacent highly cellular perimeter region. Procollagen-1 staining (brown) of a separate focus (lower left panel) demonstrates sharp demarcation of the fibroblastic focus core region with procollagen positive myofibroblasts. Higher magnification view of dashed region of panel upper left panel with SSEA4 staining (brown) is shown in lower right hand panel, demonstrating SSEA4 positive cells within the highly cellular perimeter region of the fibroblastic focus.



**Supplementary Figure 6 Identification of highly entropic MPCs in the active front region of the fibroblastic focus in IPF lung tissue.** Idiopathic Pulmonary Fibrosis (IPF) specimens from two additional patients (A and B) were serially sectioned at 4  $\mu$ m and processed for histology, immunohistochemistry (IHC) and immunofluorescence (IF). Upper panel: Representative images for Hematoxylin and Eosin (H&E) staining (scale bar 400 $\mu$ m and 100 $\mu$ m) with asterisk labeling afibroblastic focus; Immunostaining for anti-procollagen type I (brown, scale bar 100 $\mu$ m); anti-CD44 (red, scale bar 100 $\mu$ m, dashed outline box, scale bar 50 $\mu$ m). Lower panel: Immunostaining for anti-SSEA-4 (green), MARCKS (red), DAPI (blue, scale bar 20 $\mu$ m).

**Supplementary Table 1. Characteristics of Single Cell Sequencing.**

	Control 1	Control 2	Control 3	IPF 1	IPF 2	IPF 3
<b>Average Number of Reads Total</b>	<b>389307</b>	<b>417136</b>	<b>440502</b>	<b>447879</b>	<b>443101</b>	<b>570528</b>
std dev of reads total	103539	92940	317377	186643	124654	279437
<b>Average Number of Reads Mapped</b>	<b>340746</b>	<b>350811</b>	<b>334393</b>	<b>393681</b>	<b>383030</b>	<b>388627</b>
stdev Number of Reads Mapped	92926	81460	232929	174808	108741	87579
<b>Average Percent Reads Mapped</b>	<b>93</b>	<b>90</b>	<b>90</b>	<b>93</b>	<b>92</b>	<b>93</b>
<b>Average # Genes Detected</b>	<b>4672</b>	<b>4796</b>	<b>3789</b>	<b>4853</b>	<b>4444</b>	<b>4796</b>
stdev # genes detected	630	653	695	680	696	630

**Supplementary Table 2. Gene Ontology Terms Enriched in IPF-Specific Nodes**

GO term	Description	P-value	FDR q-value
GO:0045787	positive regulation of cell cycle	2.94E-07	1.84E-03
GO:0051726	regulation of cell cycle	3.28E-07	1.03E-03
GO:0022402	cell cycle process	3.71E-07	7.77E-04
GO:0007346	regulation of mitotic cell cycle	4.49E-07	7.05E-04
GO:0010564	regulation of cell cycle process	5.47E-07	6.87E-04
GO:1903047	mitotic cell cycle process	1.17E-06	1.22E-03
GO:0090068	positive regulation of cell cycle process	4.21E-06	3.78E-03
GO:0045786	negative regulation of cell cycle	8.28E-06	6.50E-03
GO:0010948	negative regulation of cell cycle process	2.70E-05	1.88E-02
GO:1901990	regulation of mitotic cell cycle phase transition	2.76E-05	1.73E-02
GO:1901987	regulation of cell cycle phase transition	2.76E-05	1.58E-02
GO:0045930	negative regulation of mitotic cell cycle	4.96E-05	2.59E-02
GO:1902806	regulation of cell cycle G1/S phase transition	7.54E-05	3.64E-02
GO:2000045	regulation of G1/S transition of mitotic cell cycle	7.54E-05	3.38E-02
GO:1902807	negative regulation of cell cycle G1/S phase transition	8.47E-05	3.55E-02
GO:2000134	negative regulation of G1/S transition of mitotic cell cycle	8.47E-05	3.32E-02
GO:0043408	regulation of MAPK cascade	8.72E-05	3.22E-02
GO:0045931	positive regulation of mitotic cell cycle	1.13E-04	3.94E-02
GO:0007088	regulation of mitotic nuclear division	1.20E-04	3.95E-02