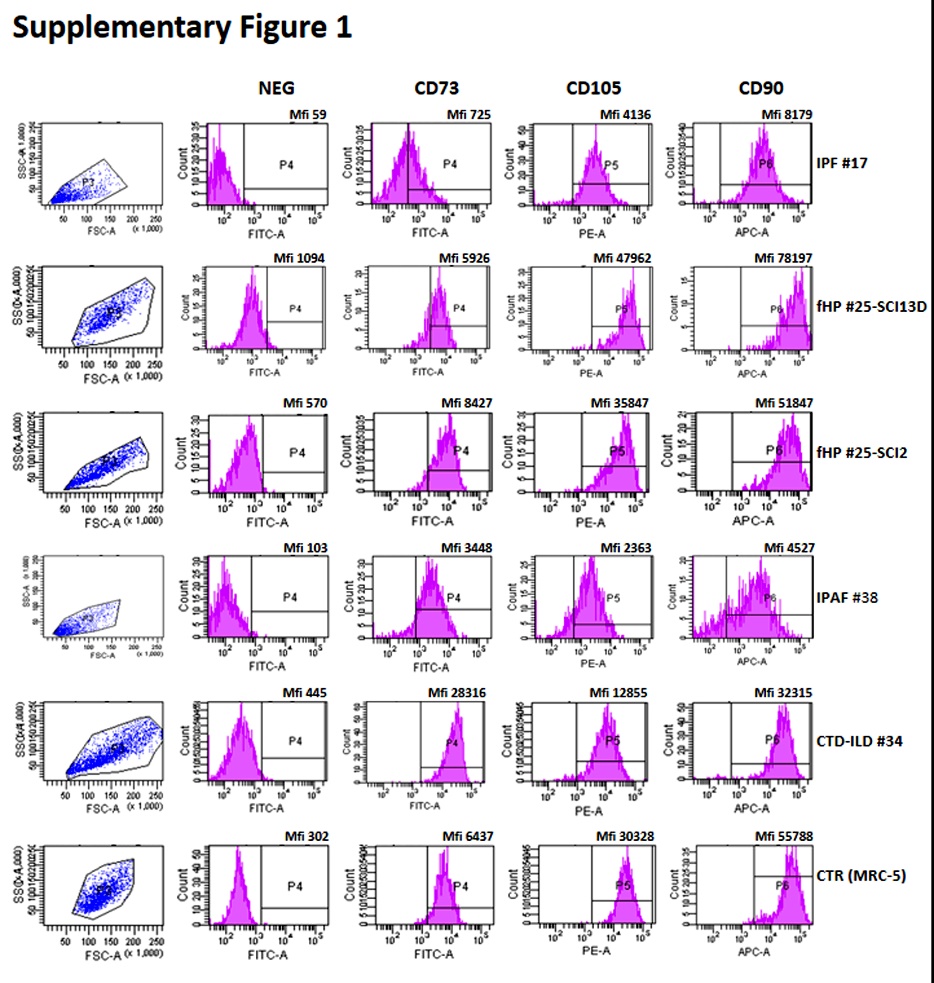
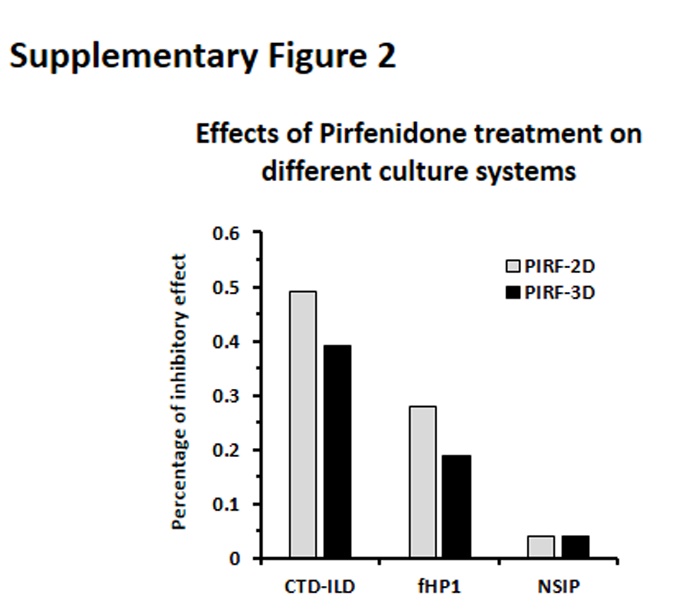
****

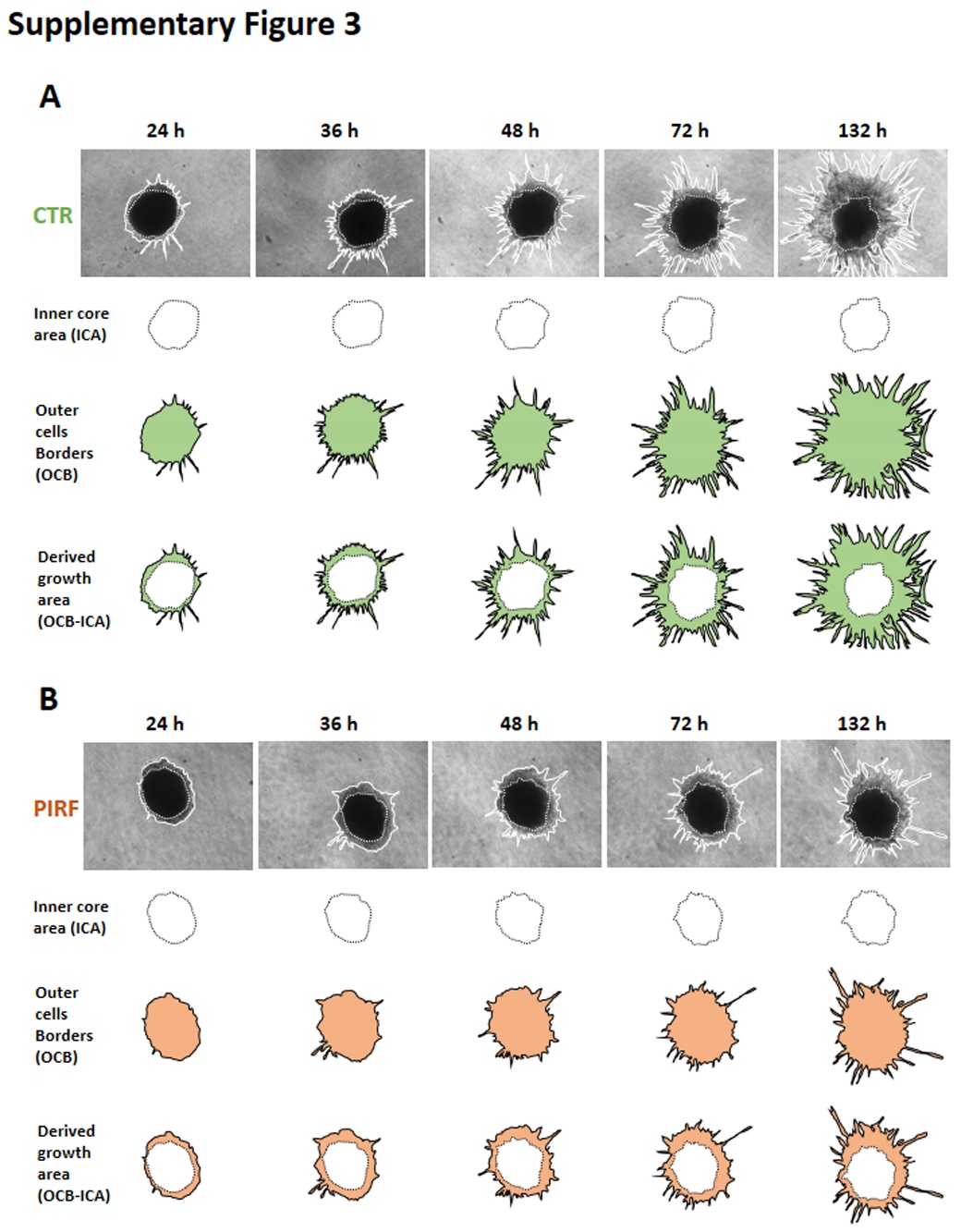
**SUPPLEMENTARY FIGURE 1: Characterization of typical mesenchymal markers in fibroblasts derived from ILD patients versus the MRC5 cell line used as control by cytofluorographic analysis.**

Typical mesenchymal markers (CD73, CD105; CD90) were all homogeneously expressed in all ILD types assessed.

******

**SUPPLEMENTARY FIGURE 2: Analysis of the inhibitory effect of Pirfenidone in 2D or 3D models of fibroblast growth.**

The trend of inhibition of proliferation exerted by Pirfenidone resulted similar when fibroblasts from the same patients were assessed in 2D or in 3D. Patients: CTD-ILD (#34), fHP1 (#25), NSIP (#41).



**SUPPLEMENTARY FIGURE 3: Evaluation of the invasion area**

The images display the different steps adopted to evaluate the area of cell invasion. Original images of the same spheroid at different time points (24-132 hrs) are depicted. Each image is superimposed with the visible boundaries of the inner spheroid core (dotted white lines; inner core area: ICA) and with the outer boundary of the migrated cells (continuous white line; outer cell borders: OCB). Each area is then assessed independently and the resulting values, expressed in pixels, subtracted from each other (OCB-ICA) to obtain the resulting growth area. Panels **A** and **B** refer to one representative analysis performed onto a control (CTR) and a Pirfenidone-treated (PIRF) spheroid, respectively.

**Supplementary Table 1**

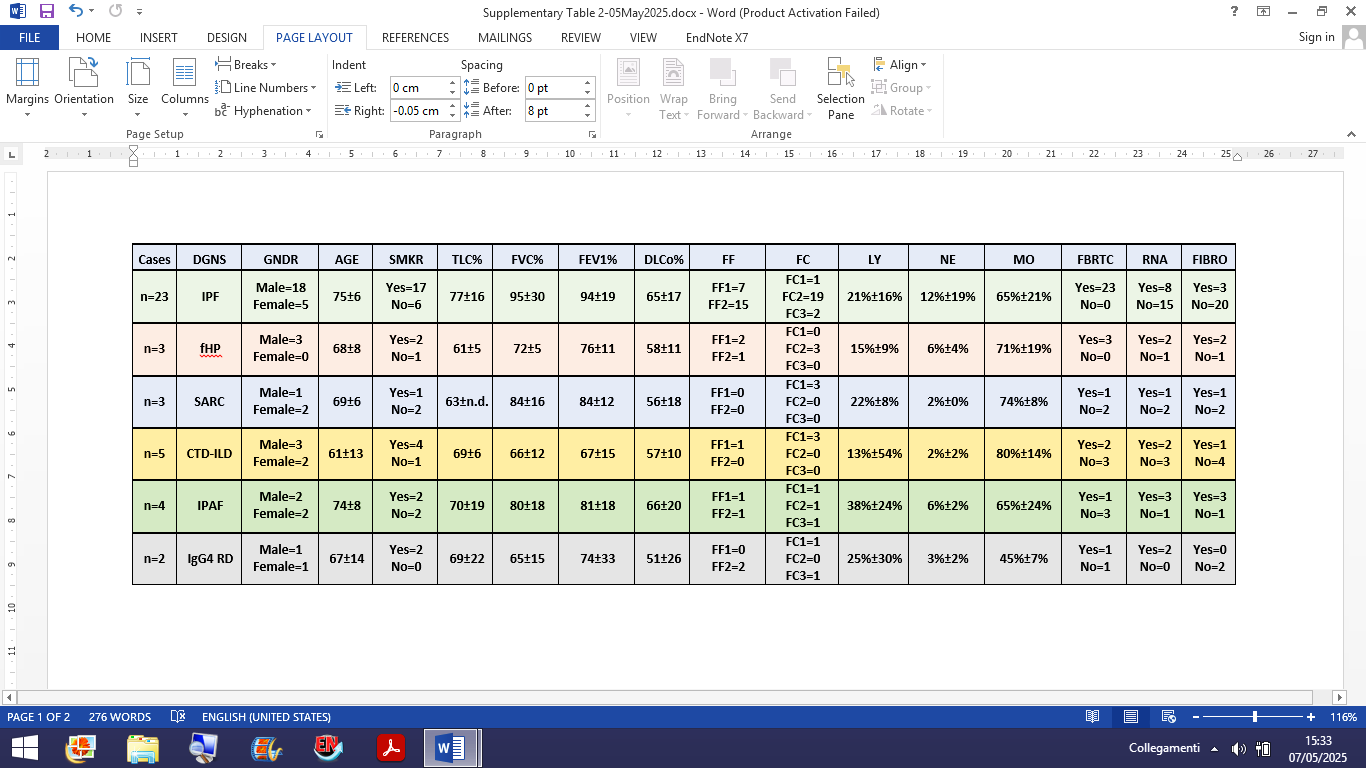
**Main clinical and histological data of each ILD patient**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **CASE** | **DIAGNOSIS** | **GENDER** | **AGE** | **SMOKER** | **TLC%** | **FVC%** | **FEV1%** | **DLCo%** | **FF** | **FC** | **LY** | **NE** | **MO** | **FIBROTIC** | **RNA** | **FIBRO** |
| 1 | IPF | MALE | 74 | Yes | 71 | 87 | 86 | 36 | 2 | 2 | 62% | 1% | 37% | Yes | Yes | No |
| 2 | IPF | FEMALE | 64 | Yes | 59 | 76 | 78 | 43 | 2 | 2 | 29% | 7% | 63% | Yes | Yes | No |
| 3 | IPF | MALE | 76 | No | 60 | 76 | 88 | 81 | 1 | 2 | 18% | 50% | 32% | Yes | No | No |
| 4 | IPF | MALE | 81 | Yes | 87 | 97 | 107 | 76 | 2 | 2 | 13% | 3% | 84% | Yes | No | No |
| 5 | IPF | FEMALE | 80 | Yes | 68 | 101 | 116 | nd | 2 | 2 | 6% | 1% | 90% | Yes | Yes | No |
| 6 | IPF | MALE | 79 | Yes | 84 | 196 | 113 | 78 | 1 | 2 | 5% | 61% | 34% | Yes | Yes | No |
| 7 | IPF | MALE | 75 | Yes | 82 | 86 | 91 | 63 | 2 | 2 | 27% | 3% | 70% | Yes | No | No |
| 8 | IPF | MALE | 83 | No | 113 | 74 | 88 | 73 | 1 | 2 | 13% | 10% | 69% | Yes | No | No |
| 9 | IPF | MALE | 75 | Yes | 110 | 136 | 123 | 89 | 1 | 2 | 52% | 1% | 47% | Yes | No | No |
| 10 | IPF | MALE | 83 | Yes | 78 | 101 | 110 | 70 | 2 | 2 | 2% | 74% | 24% | Yes | No | No |
| 11 | IPF | MALE | 85 | Yes | 89 | 103 | 109 | 85 | 1 | 1 | 4% | 2% | 94% | Yes | No | No |
| 12 | IPF | FEMALE | 76 | Yes | 69 | 112 | 110 | 63 | 1 | 2 | 2% | 1% | 97% | Yes | No | No |
| 13 | IPF | MALE | 78 | Yes | 72 | 109 | 96 | 52 | 2 | 2 | 24% | 7% | 69% | Yes | No | No |
| 14 | IPF | MALE | 74 | No | 55 | 39 | 51 | 32 | 2 | 2 | 14% | 2% | 84% | Yes | No | No |
| 15 | IPF | MALE | 57 | Yes | 66 | 73 | 81 | 84 | 2 | 3 | 20% | 7% | 73% | Yes | No | No |
| 16 | IPF | MALE | 77 | Yes | 74 | 99 | 106 | 74 | 2 | 2 | 8% | 1% | 91% | Yes | No | No |
| 17 | IPF | FEMALE | 73 | Yes | nd | 75 | 66 | 38 | 2 | 3 | 5% | 8% | 87% | Yes | Yes | Yes |
| 18 | IPF | MALE | 74 | No | 86 | 104 | 111 | 77 | 1 | 2 | 35% | 3% | 54% | Yes | Yes | Yes |
| 19 | IPF | MALE | 79 | Yes | 96 | 126 | 116 | 79 | nd | nd | 17% | 17% | 66% | Yes | No | No |
| 20 | IPF | MALE | 71 | Yes | 90 | 108 | 107 | 71 | 2 | 2 | 24% | 12% | 62% | Yes | No | No |
| 21 | IPF | MALE | 78 | Yes | 62 | 65 | 68 | 58 | 2 | 2 | 40% | 3% | 48% | Yes | No | No |
| 22 | IPF | MALE | 78 | No | 55 | 70 | 75 | 46 | 2 | 2 | 47% | 1% | 52% | Yes | Yes | No |
| 23 | IPF | FEMALE | 77 | No | 72 | 85 | 86 | 78 | 2 | 2 | 13% | 8% | 79% | Yes | Yes | Yes |
| 24 | fHP | MALE | 75 | Yes | 63 | 78 | 86 | 72 | 1 | 2 | 20% | 8% | 67% | Yes | No | No |
| 25 | fHP | MALE | 59 | Yes | 65 | 71 | 64 | 49 | 1 | 2 | 21% | 10% | 54% | Yes | Yes | Yes |
| 26 | fHP | MALE | 71 | No | 55 | 68 | 78 | 55 | 2 | 2 | 5% | 1% | 93% | Yes | Yes | Yes |
| 27 | SARCOIDOSIS | MALE | 76 | Yes | nd | 73 | 75 | 51 | 0 | 1 | 21% | 2% | 74% | Yes | No | No |
| 28 | SARCOIDOSIS | FEMALE | 69 | No | 63 | 103 | 99 | 42 | 0 | 1 | 32% | 2% | 66% | No | No | No |
| 29 | SARCOIDOSIS | FEMALE | 64 | No | nd | 77 | 79 | 77 | 0 | 1 | 15% | 2% | 83% | No | Yes | Yes |
| 30 | CTD-ILD | FEMALE | 79 | Yes | 66 | 85 | 91 | 67 | 0 | 1 | 8% | 1% | 91% | Yes | No | No |
| 31 | CTD-ILD | MALE | 48 | Yes | 65 | 49 | 49 | 51 | 0 | 0 | 6% | 1% | 92% | No | No | No |
| 32 | CTD-ILD | MALE | 69 | Yes | nd | 66 | 67 | 70 | 0 | 1 | 14% | 1% | 85% | No | Yes | No |
| 33 | CTD ILD | MALE | 64 | Yes | 76 | 63 | 65 | 53 | 1 | 1 | 1% | 7% | 77% | No | No | No |
| 34 | CTD-ILD | FEMAE | 48 | No | nd | 67 | 67 | 45 | 0 | 0 | 40% | 3% | 57% | Yes | Yes | Yes |
| 35 | IPAF | MALE | 82 | No | 57 | 73 | 87 | 52 | 2 | 3 | 12% | 4% | 80% | Yes | Yes | Yes |
| 36 | IPAF | FEMALE | 73 | Yes | 83 | 99 | 101 | 96 | 1 | 2 | 21% | 6% | 73% | No | Yes | Yes |
| 37 | IPAF | FEMALE | 80 | No | 51 | 58 | 57 | 59 | 0 | 1 | 14% | 9% | 77% | No | No | No |
| 38 | IPAF | MALE | 64 | Yes | 91 | 90 | 82 | 58 | 0 | 0 | 64% | 6% | 29% | No | Yes | Yes |
| 39 | NSIP | MALE | 61 | Yes | 45 | 43 | 43 | 21 | nd | nd | 2% | 7% | 91% | Yes | Yes | No |
| 40 | NSIP | MALE | 51 | No | nd | 52 | 55 | 55 | 1 | 3 | 27% | 2% | 71% | Yes | No | No |
| 41 | NSIP | FEMALE | 77 | No | 72 | 87 | 92 | 51 | 0 | 1 | 78% | 7% | 15% | No | Yes\* | Yes |
| 42 | IgG4 RD | MALE | 78 | Yes | 85 | 76 | 98 | 70 | 2 | 3 | 3% | 1% | 40% | Yes | Yes | No |
| 43 | IgG4 RD | FEMALE | 57 | Yes | 53 | 54 | 50 | 32 | 2 | 1 | 46% | 4% | 50% | No | Yes | No |

TLC: total lung capacity; FVC: forced vital capacity; FEV: forced expiratory volume; DLCo: diffusing lung capacity for carbon monoxide; FF: fibroblastic foci; FC: collagen fibrosis; LY: lymphocytes; NE: neutrophils; MO: monocytes; FIBROTIC: progressive fibrosis; IPF: interstitial pulmonary fibrosis; fHP: fibrotic hypersensitivity pneumonitis; SARC: sarcoidosis; CTD-ILD: connective tissue disease-ILD; IPAF: interstitial pneumonia with autoimmune features; NSIP: non-specific interstitial pneumonia; IgG4-RD: IgG4 related disease; the last two columns indicate the availability of mRNA and/or cells from the specific patients, respectively; \* indicates a case not included in the RT-PCR studies.

**Supplementary Table 2**

Summary of means ± standard deviations of clinical parameters and of the evaluated indicators for each assessed group of patients.



DNGS: diagnosis; GNDR: gender; SMKR: smoker; TLC: total lung capacity; FVC: forced vital capacity; FEV: forced expiratory volume; DLCo: diffusing lung capacity for carbon monoxide; FF: fibroblastic foci; FC: collagen fibrosis; LY: lymphocytes; NE: neutrophils; MO: monocytes; FBRTC: progressive fibrosis; IPF: interstitial pulmonary fibrosis; fHP: fibrotic hypersensitivity pneumonitis; SARC: sarcoidosis; CTD-ILD: connective tissue disease-ILD; IPAF: interstitial pneumonia with autoimmune features; NSIP: non-specific interstitial pneumonia; IgG4-RD: IgG4 related disease; the last two columns indicate the availability of mRNA and/or cells from the specific patients, respectively.