



## Supplementary file

# Alveolar Epithelial Denudation is a Major Factor in the Pathogenesis of Pleuroparenchymal Fibroelastosis

Yoshiaki Zaizen <sup>1,2</sup>, Yuri Tachibana <sup>1</sup>, Yukio Kashima <sup>3</sup>, Andrey Bychkov <sup>1,4</sup>, Kazuhiro Tabata <sup>5</sup>, Kyoko Otani <sup>6</sup>, Yoshiaki Kinoshita <sup>7</sup>, Yasuhiko Yamano <sup>8</sup>, Kensuke Kataoka <sup>8</sup>, Kazuya Ichikado <sup>9</sup>, Masaki Okamoto <sup>2</sup>, Tomoo Kishaba <sup>10</sup>, Remi Mito <sup>11</sup>, Koichi Nishimura <sup>12</sup>, Mari Yamasue <sup>13</sup>, Kazuki Nabeshima <sup>14</sup>, Kentaro Watanabe <sup>15</sup>, Yasuhiro Kondoh <sup>8</sup> and Junya Fukuoka <sup>1,4,\*</sup>

<sup>1</sup> Department of Pathology, Nagasaki University Graduate School of Biomedical Sciences, 1-7-1 Sakamoto, Nagasaki 852-8501, Japan; zaizen\_yoshiaki@med.kurume-u.ac.jp (Y.Z.); y.tachibana19890221@gmail.com (Y.T.); bychkov.andrey@kameda.jp (A.B.)

<sup>2</sup> Division of Respiriology, Neurology and Rheumatology, Department of Medicine, Kurume University School of Medicine, 67 Asahi-machi, Kurume, Fukuoka 830-830-0011, Japan; okamoto\_masaki@med.kurume-u.ac.jp

<sup>3</sup> Department of Pathology, Hyogo Prefectural Awaji Medical Center, 1-1-137 Shioya, Sumoto, Hyogo 656-0021, Japan; ykismn0504@yahoo.co.jp

<sup>4</sup> Department of Pathology, Kameda Medical Center, 929 Higashi-cho, Kamogawa, Chiba 296-8602, Japan

<sup>5</sup> Division of Pathology, Department of Oncology, Kagoshima University Graduate School of Medical and Dental Sciences, 8-35-1 Sakuragaoka, Kagoshima 890-8544, Japan; tabatak.kufm@gmail.com

<sup>6</sup> Department of Pathology, Yodogawa Christian Hospital, 1-7-50 Kunijima, Higashiyodogawa-ku, Osaka 533-0024, Japan; o.kyoko303@gmail.com

<sup>7</sup> Department of Respiratory Medicine, Fukuoka University Chikushi Hospital, 1-1-1 Zokumyoin, Chikushino, Fukuoka 818-8502, Japan; y3kinoshita@gmail.com

<sup>8</sup> Department of Respiratory Medicine and Allergy, Tosei General Hospital, 160 Nishioiwake, Seto, Aichi 489-8642, Japan; yaya0630g@gmail.com (Y.Y.); kataoka@tosei.or.jp (K.K.); konyasu2003@yahoo.co.jp (Y.K.)

<sup>9</sup> Department of Respiratory Medicine, Saiseikai Kumamoto Hospital, 5-3-1 Chikami, Minami-ku, Kumamoto 861-4193, Japan; kazuya-ichikado@saiseikaikumamoto.jp

<sup>10</sup> Department of Respiratory Medicine, Okinawa Chubu Hospital, 281 Miyazato, Uruma, Okinawa 904-2293, Japan; kishabatomoo@gmail.com

<sup>11</sup> Department of Respiratory Medicine, Kumamoto University Hospital, 1-1-1 Honjou, Chuou-ku, Kumamoto 860-8556, Japan; candypinkcolor@yahoo.co.jp

<sup>12</sup> Department of Respiratory Medicine, National Center for Geriatrics and Gerontology, 7-430 Morioka-chou, Oobu, Aichi 474-8511, Japan; koichi-nishimura@nifty.com

<sup>13</sup> Department of Respiratory Medicine, Oita University Hospital, 1-1 Idaigaoka, Hasamamachi Yufu, Oita 879-5593, Japan; sai-mari@oita-u.ac.jp

<sup>14</sup> Department of Pathology, Fukuoka University School of Medicine and Hospital, 7-45-1 Nanakuma, Jonan-ku, Fukuoka 814-0180, Japan; kaznabes@fukuoka-u.ac.jp

<sup>15</sup> Department of Respiratory Medicine, Nishi Fukuoka Hospital, 3-18-8 Ikinomatsubara, Nishi-ku, Fukuoka 819-8555, Japan; watanabe@fukuoka-u.ac.jp

\* Correspondence: fukuokaj@nagasaki-u.ac.jp; Tel.: +81-95-819-7055; Fax: +81-95-819-7056

**Supplemental Table S1.** Maximum length ( $\mu\text{m}$ ) of continuous epithelial denudation in each group.

|                 | PPFE Group     | IPF Group     | Control Group | <i>p</i> -Value* | <i>p</i> -Value** | <i>p</i> -Value*** |
|-----------------|----------------|---------------|---------------|------------------|-------------------|--------------------|
| Total           | 730 (365–1465) | 580 (398–843) | 250 (100–400) | 0.086            | <0.001            | <0.001             |
| Subpleural zone | 715 (340–1278) | 475 (298–723) | 210 (100–280) | 0.077            | <0.001            | <0.001             |
| Paraseptal zone | 425 (263–688)  | 465 (290–638) | 145 (20–320)  | 0.774            | <0.001            | <0.001             |

IPF, idiopathic pulmonary fibrosis; PPFE, pleuroparenchymal fibroelastosis. \* PPFE vs. IPF. \*\* PPFE vs. Control. \*\*\* IPF vs. Control.

**Supplemental Table S2.** Percentage of epithelial denudation in the IPF group with or without PPFE-like lesions.

|                 | <b>With PPFE-like lesion</b> | <b>Without PPFE-like lesion</b> | <b><i>p</i>-value</b> |
|-----------------|------------------------------|---------------------------------|-----------------------|
| Number          | 10                           | 19                              |                       |
| Total           | 7.77 (3.23–16.50)            | 6.30 (5.33–9.78)                | 0.819                 |
| Subpleural zone | 6.64 (3.49–15.05)            | 6.57 (4.88–11.86)               | 0.819                 |
| Paraseptal zone | 8.18 (2.84–17.74)            | 5.89 (4.31–7.80)                | 0.819                 |