Editorial: Pulmonary fibrosis: One manifestation, various diseases

Barbara Ruaro1*, Marco Matucci Cerinic2, Francesco Salton1, Elisa Baratella3, Marco Confalonieri1 and Michael Hughes4

1Pulmonology Unit, Department of Medical Surgical and Health Sciences. University Hospital of Cattinara, University of Trieste, Trieste, Italy, 2Unit of Immunology, Rheumatology, Department of Experimental and Clinical Medicine, IRCCS San Raffaele Hospital, University of Florence and Division of Rheumatology AOUC & Scleroderma Unit, Allergy and Rare Diseases (UnIRAR), Milan, Italy, 3Department of Radiology, Department of Medicine, Surgery and Health Science, University of Trieste, Trieste, Italy, 4Division of Musculoskeletal and Dermatological Sciences, Faculty of Biology, Medicine and Health, The University of Manchester & Salford Royal NHS Foundation Trust, Manchester, United Kingdom

KEYWORDS
pulmonary fibrosis (PF), idiopathic pulmonary fibrosis (IPF), interstitial lung disease (ILD), familial pulmonary fibrosis (FPF), autoimmune diseases

This research topic collection entitled “Pulmonary Fibrosis: one manifestation, various diseases”, involving authors from different countries, confirms that this disease is a hot topic (Confalonieri P et al., 2022, Orlandi M et al., 2022). There are over 200 different types of pulmonary fibrosis (PF), the most common is the idiopathic pulmonary fibrosis (IPF), called idiopathic because it has no known cause. Another rare form is familial PF, for which several studies reported correlation with few genes. An important group of PF are due to other diseases, for example, autoimmune diseases such as rheumatoid arthritis, systemic sclerosis or Sjogren’s syndrome (Ruaro et al., 2022, Trombetta AC et al., 2017, Bernero E et al., 2013). PF could correlate to viral infections (e.g. COVID-19), gastroesophageal reflux disease (GERD) (Baratella E et al, 2021, Ruaro et al., 2018), and the exposure to various materials (including naturally occurring such as bird or animal droppings, and occupational such as asbestos or silica). Furthermore, smoking, radiation treatments, and certain drugs can increase risk of developing PF. In the first article (Saketkoo et al.) of the collection, the authors evaluate the use of International Classification of Functioning, Disability, and Health (ICF) approved by World Health Organization (WHO) in patients affected by interstitial lung diseases (ILD). The results of the study supported the use of ICF in ILD, as ICF may help clinicians to collect data regarding the clinical status of their ILD patients.

The second article (Ma et al.) of the collection is an interesting and comprehensive review. The authors underlined the molecular mechanisms and pathogenic factors of IPF, which would be helpful in the diagnosis, development of new drugs and the improvement
of disease prognosis. In particular, the researchers underlined the novelties regarding multiple cell types, gene mutations, epigenetic and environmental factors.

The most important message reported in the third paper (Zhou et al.) is that the assessments by high-resolution computed tomography (HRCT) pattern and scores before transbronchial cryobiopsy (TBCB) were helpful for bronchoscopists to make a better patient selection and procedure planning. The authors also reported that the multivariate analysis supported radiological probable interstitial pneumonia (UIP) pattern as an independent risk factor for moderate bleeding.

The fourth article (Zhang et al.) is a case report. The authors performed a transbronchial cryobiopsy (TBCB) assisted by extracorporeal membrane oxygenation (ECMO) in a critical case of acute respiratory failure related to an organizing pneumonia (OP) pattern. In conclusion, the paper supported that when oxygenation cannot be maintained after endotracheal intubation and surgical lung biopsy is not feasible, TBCB supported by ECMO may be a good choice to obtain lung tissue for histopathological diagnosis in patients with acute lung injury of unknown etiology.

The fifth manuscript (Zhou et al.) is an interesting case report that evaluate the treatment by pirfenidone of PF secondary to ARDS-COVID-19. Over 96 weeks after pirfenidone, the score of the mMRC dyspnea scale, the 6 min walking test distance, total lung capacity, diffusion capacity for carbon monoxide and chest CT improved. In conclusion, this case demonstrated that pirfenidone might be a potential treatment option for the post-COVID-19 pulmonary fibrosis.

The sixth article (Wang et al.) is a retrospective study that evaluate 579 patients with fibrosing ILD, of which 227 (39%) met the criteria for progression. The authors observed that clubbing of fingers and a HRCT-documented UIP-like fibrotic pattern were more frequently associated with the progressive fibrosing.

The mortality was worse in patients with PF with hypoxemia, in those with baseline diffusion capacity of the lung for carbon monoxide (DLCO) predicted ≤50%, or in those with UIP-like fibrotic pattern.

In the seventh paper (Ma et al.) the researchers provides an overview of different cytokines and growth factors involved in IPF.

The authors of the eighth article (Min et al.) demonstrated that lungs from mice with bleomycin (BLM)-induced PF were characterized by decreased expression of TNF receptor-associated factor 6 (TRAF6) in lung fibroblasts. Furthermore, the results indicate that reduced TRAF6 expression in fibroblasts is essential for the progression of PF, and therefore, genetically increasing TRAF6 expression or disrupting tribbles pseudokinase 3 (TRIB3)-TRAF6 interaction could be potential therapeutic strategies for fibroproliferative lung diseases.

In the ninth article (Xu et al.) the authors used human embryonic lung fibroblasts (HELFs) treated with different concentrations of vincristine (VCR) to study the molecular mechanism of VCR-induced PF and the possible involvement of the mitogen-activated protein kinase (MAPK) signaling pathway. In the conclusions, the researchers reported that VCR could promote the differentiation of fibroblasts into myofibroblasts by regulating the MAPK signal pathway.

In the penultimate article of the collection, the authors (Tanner et al.) used a series of in vitro and in vivo models to identify the therapeutic potential of bisphosphonate zoledronic acid (ZA) in the treatment of idiopathic pulmonary fibrosis (IPF). Furthermore, farnesyl diphosphate synthase (FDPS) was used as a potential antifibrotic target using a bleomycin mouse model. The results of the study reported that in vitro administration of ZA reduced myofibroblast transition and blocked NF-κB signaling in macrophages leading to impaired immune cell recruitment in a transwell assay. FDPS-targeting siRNA administration significantly attenuated profibrotic cytokine production and lung damage. In addition, ZA treatment of mice with bleomycin-induced lung damage displayed decreased cytokine levels in the BALF, plasma, and lung tissue, resulting in less histologically visible fibrotic scarring. Additionally, ZA polarized macrophages towards a less profibrotic phenotype contributing to decreased IPF pathogenesis.

The last research (Yu et al.) proved that catalpol (CAT) might work through Ang II/AT1/TGF-β/Smads pathway to improve lung pathological changes as well as suppress epithelial mesenchymal transition (EMT) in mice with PF. CAT may serve as a novel therapeutic candidate for the simultaneous blockade of Ang II and TGF-β pathway to attenuate PF.

In conclusion, this special issue pays particular attention to recently progress made on use of innovative tests and treatments, which is expected to provide new insights into research.

**Author contributions**

BR, MMC, FS and MH conducted the manuscript. MC and EB the final amendments and approved the final version. All authors contributed to the article and approved the submitted version.

**Acknowledgments**

The authors would like to thank Selene Lerda for her linguistic advice.

**Conflict of interest**

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.
Publisher’s note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

References

Baratella, E., Ruaro, B., Marroccoli, C., Starvaggi, N., Salton, F., Giudici, F., et al. (2021). Interstitial lung disease at high resolution CT after SARS-CoV-2-related acute respiratory distress syndrome according to pulmonary segmental anatomy. J. Clin. Med. 10, 3985. doi:10.3390/jcm10173985

Bernero, E., Sulli, A., Ferrari, G., Ravera, F., Pizzorni, C., Ruaro, B., et al. (2013). Prospective capillaroscopy-based study on transition from primary to secondary raynaud’s phenomenon: Preliminary results. Reumatismo 65 (4), 186–191. doi:10.4081/reumatismo.2013.186

Confalonieri, P., Velpe, M. C., Jacob, J., Maiocchi, S., Salton, F., Ruaro, B., et al. (2022). Regeneration or repair? The role of alveolar epithelial cells in the pathogenesis of idiopathic pulmonary fibrosis (IPF). Cells 11 (13), 2095. doi:10.3390/cells11132095

Ozlandi, M., Landini, N., Sambataro, G., Nardi, C., Tolfa, L., Beu, C., et al. (2022). The role of chest CT in deciphering interstitial lung involvement: Systemic sclerosis versus COVID-19. Rheumatol. Oxf. 61, 1600–1609. doi:10.1093/rheumatology/key130

Ruaro, B., Casabell, A., Paolino, S., Pizzorni, C., Alessandri, E., Serisolo, C., et al. (2018). Correlation between bone quality and microvascular damage in systemic sclerosis patients. Rheumatol. Oxf. 57, 1548–1554. doi:10.1093/rheumatology/key130

Ruoaro, B., Pozzan, R., Confalonieri, P., Tavano, S., Hughes, M., Matsui Cerinie, M., et al. (2022). Gastroesophageal reflux disease in idiopathic pulmonary fibrosis: Viewer or actor? To treat or not to treat? Pharmaceuticals 15, 1033. doi:10.3390/ph15081033

Saketkoo, L. A., Escorpizo, R., Varga, J., Keen, K., Fligelstone, K., Birring, S. S., et al. (2022). World Health organization (WHO) international classification of functioning, disability and Health (ICF) core set development for interstitial lung disease: Foundational steps in preparation for ICD-11 - a collaboration with the global fellowship on rehabilitation and exercise in systemic sclerosis (GFRSS). Front. Pharmacol. (accepted for publication).

Trombetta, A. C., Smith, V., Gotelli, E., Ghio, M., Paolino, S., Pizzorni, C., et al. (2017). Vitamin D deficiency and clinical correlations in systemic sclerosis patients: A retrospective analysis for possible future developments. PLoS One 12, e0179062. doi:10.1371/journal.pone.0179062

Xu, H., Yang, J., Tu, M., Weng, J., Xie, M., Zhou, Z., et al. (2022). Vincristine promotes transdifferentiation of fibroblasts into myofibroblasts via P38 and ERK signal pathways. Front. Pharmacol. 13, 901000. doi:10.3389/fphar.2022.901000