Pulmonary Fibrosis in the New Millennium

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This second monographic issue of BRN Reviews for 2021 is focused on a field in respiratory medicine that is evolving fast: interstitial lung diseases (ILD) and specifically the different faces of the development of lung fibrosis. Several international authors, experts in different aspects of lung fibrosis have participated in this issue.

The first review is an exhaustive revision of the cellular mechanisms involved in the pathogenesis of idiopathic pulmonary fibrosis (IPF). The paper has been co-authored by Mauricio Rojas, from the Davis Heart & Lung Research Institute, Ohio State University, Columbus, USA, and Sandra Cuerpo/Nuria Albacar, from the Servei de Pneumologia, Hospital Clínic, Barcelona. Current evidence suggests that the fibrotic response in IPF arises due to accelerated aging of the lung after repeated injuries to the alveolar epithelium, which causes the production of inflammatory mediators that induce the recruitment and activation of lung fibroblasts. These cells are responsible for the secretion of excessive amounts of collagen fibers, destroying the normal lung architecture leading to decreased lung compliance, disrupted gas exchange, and, ultimately, respiratory failure. Different alterations of cellular function have been proposed to be related to the premature aging of pulmonary tissue in IPF, such as defects in DNA repair, mitochondrial dysfunction, telomeric shortening, loss of protein homeostasis, and cellular senescence. The authors nicely review all the cellular mechanisms involved in the development of lung fibrosis.

The second paper, authored by Hongwei Han and David Lagares from the Fibrosis Research Center, Harvard Medical School, USA, is focused on the use of "mechanotherapeutics" for the treatment of IPF. IPF is an age-related progressive lung disease characterized by excessive deposition of extracellular matrix (ECM) produced by activated myofibroblasts. Traditionally, myofibroblast activation has been thought to be exclusively driven by soluble biochemical stimuli, such as pro-fibrotic growth factors and cytokines. However, the mechanical properties of the fibrotic ECM including matrix stiffness have recently gained more attention given its ability to drive myofibroblast activation independently from soluble mediators. In this review, the authors summarize the molecular mechanisms promoting mechano-activation of myofibroblasts in lung fibrosis and the potential of treating IPF with "mechanotherapeutics", a novel class of anti-fibrotic therapeutic agents.

The third and fourth review are focused on a complicated association: lung cancer and pulmonary fibrosis. Martina Armati, representing the IPF team from Siena University, Italy, summarizes the evidence related to the role of non-invasive biomarkers in lung cancer and IPF, to better understand the point in common of these two conditions, to better understand and define these diseases individually and together. and to give other information about the severity and the prognosis in IPF patients.

In the fourth review, Theodoros Karampitsakos and Argyris Tzouvelekis from the University of Patras (Greece), and Demosthenes Bouros from the University of Athens (Greece) explore the diagnostic and therapeutic challenges in IPF and lung cancer. Patients with IPF present with an increased risk for lung cancer development compared to the general population, while lung cancer development has a major impact on patients' prognosis. Importantly, lung cancer development has an increased risk during the IPF course. Nonetheless, well-designed prospective studies for patients with IPF and lung cancer are currently lacking. The review aims to address the main challenges for patients with IPF and lung cancer

The fifth review is written by Joel Francesqui, from the Servei de Pneumologia, Hospital Clínic, Barcelona and Sanjay Kalray/Eva M Carmona from the Division of Pulmonary and Critical Care Medicine, Mayo Clinic, Rochester, USA. Sarcoidosis is a systemic granulomatous disease with an intrathoracic involvement in about 90% of the cases. 10-20% of sarcoidosis cases may progress to fibrotic forms. Recognition of this phenotype is important as it carries a poor prognosis and a limited response to treatment. The authors reviewed the diagnosis and therapeutic options in pulmonary fibrosis secondary to lung sarcoidosis.

The novel aspects of the present monographic will be valuable and interesting for those clinicians and researchers with a huge interest in lung fibrosis and personalized medicine. Although the development of this monographic issue has been difficult in this pandemic time, the authors have done an extra effort to obtain the different reviews for this issue on time.

I hope you enjoy the reading!

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