CCL2 and T cells in pulmonary fibrosis: an old player gets a new role

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Idiopathic pulmonary fibrosis (IPF) is an incurable condition characterised by progressive extracellular matrix deposition and tissue remodelling in the adult human lung. Because 5-year mortality rates approach 70%, new approaches to treatment are sorely needed. IPF is thought to result from an abnormal wound healing response caused by an unknown insult to the lung epithelium that results in the recruitment and activation of myofibroblasts via incompletely understood mechanisms. The contribution of immune activation to these processes remains unknown. While the contribution of innate cell populations such as macrophages is gaining increased acceptance, the contribution of T cell driven adaptive immune responses remain controversial.

The paper by Milger et al represents an important step forward in our understanding of this issue. Historically, IPF has been defined as a non-immune entity due to its lack of an identifiable antigen driven immune response, lack of inflammatory infiltrate on lung biopsy, lack of benefit from conventional immunosuppressive therapies and lack of a requirement for lymphocytes for development of maximal fibrosis in commonly used animal models. However, the now seminal finding that lymphocyte modulating agents actually worsen outcomes to the lung epithelium that results in the recruitment and activation of myofibroblasts via incompletely understood mechanisms. The contribution of immune activation to these processes remains unknown. While the contribution of innate cell populations such as macrophages is gaining increased acceptance, the contribution of T cell driven adaptive immune responses remain controversial.

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and response to therapy. Nevertheless, the study by Milger et al3 firmly frames CCR2+ CD4+ cells as a new and exciting area of study of CCL2 biology as it relates to pulmonary fibrosis. Further understanding of these findings will advance the evolving understanding of the complex contribution of lymphocyte heterogeneity to IPF and related conditions affecting the adult mammalian lung.

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