Immune cells as biomarkers for idiopathic pulmonary fibrosis

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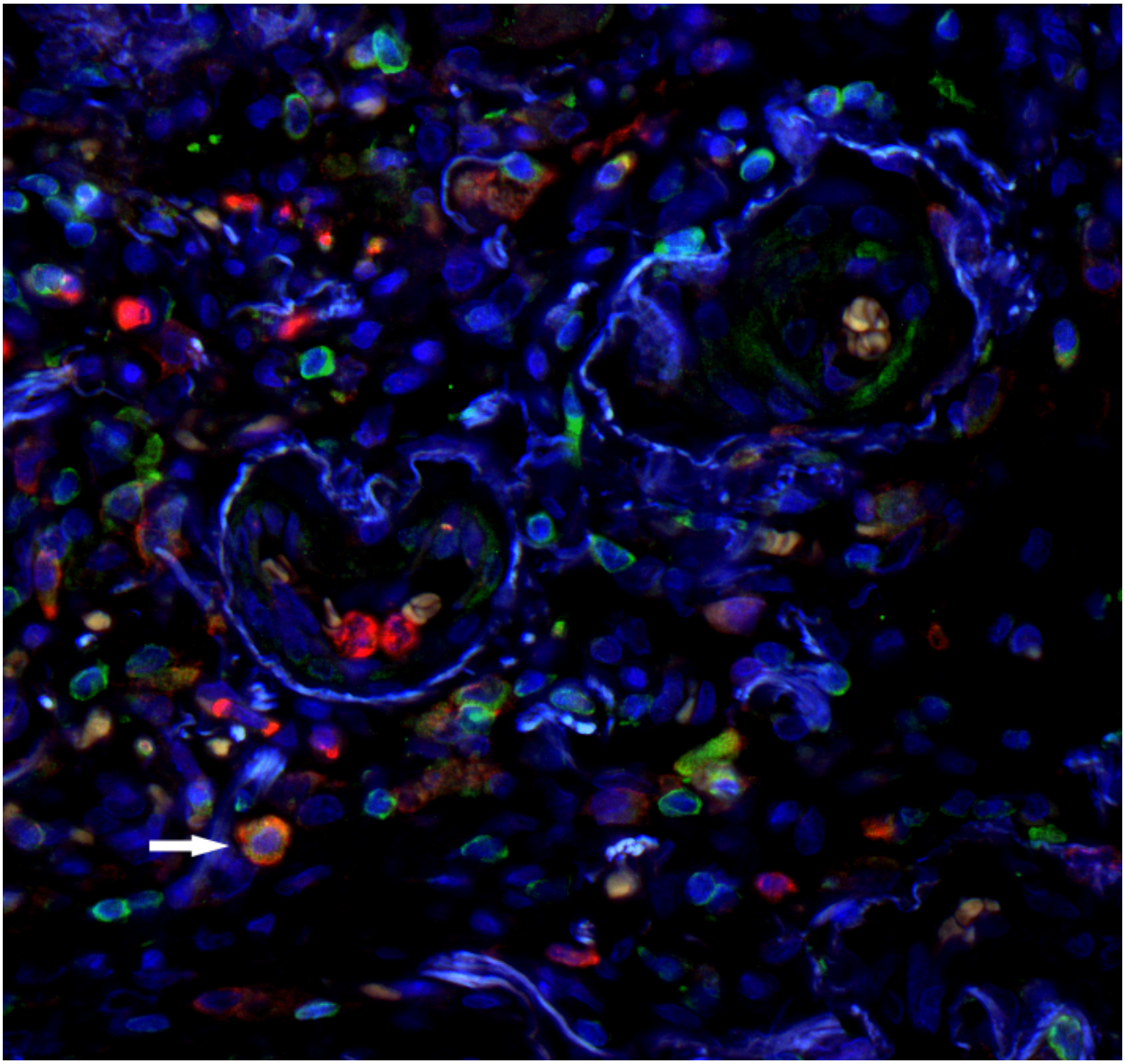

Staining of surface molecules (CD11 in red, CD33 in green) on cells in lung

tissue, nuclei in blue. MDSC are positive for both surface markers and consequently appear orange (arrow). Credit: Helmholtz Zentrum München

Researchers at Helmholtz Zentrum München, a partner in the German Center for Lung Research (DZL), have discovered that the number of myeloid-derived suppressor cells (MDSC) is increased in the blood of patients with idiopathic pulmonary fibrosis (IPF). The higher the number of MDSC, the more limited the lung function. The findings on this new biomarker have now been published in the *European Respiratory Journal*.

Patients with fibrotic lung diseases, such as idiopathic pulmonary fibrosis (IPF), show progressive worsening of lung function with increased shortness of breath and dry cough. To-date, this process is irreversible, which is why scientists are searching for novel biomarkers or indicators, which enable earlier diagnosis of this disease, with the aim to better interfere with disease progression.

A team of scientists at the Comprehensive Pneumology Center (CPC) at Helmholtz Zentrum München headed by Professor Oliver Eickelberg, Chairman of the CPC and Director of the Institute of Lung Biology as well as the DZL at the Munich partner site, have now discovered that myeloid-derived suppressor cells (MDSC) may serve as such biomarkers. "The role of MDSC has been most extensively studied in cancer, where they suppress the immune system and contribute to a poor prognosis," explained first author Isis Fernandez, MD. The current study suggests that similar mechanisms are also at work in IPF.

In collaboration with the Department of Internal Medicine V (Director: Professor Jürgen Behr) of the Munich University Hospital, the team examined blood samples of 170 study participants, including 69 IPF

patients, in terms of the composition of circulating immune cell types. In each patient, these were correlated with lung function. Strikingly, the MDSC count in IPF patients was significantly higher than in the healthy control group. At the same time, the researchers observed that there was an inverse correlation between lung function and circulating MDSC counts: the poorer the lung function, the higher the MDSC count. In control groups of patients with chronic obstructive pulmonary disease (COPD) or other interstitial lung diseases, this inverse correlation was not found. "We conclude that the number of MDSC reflects the course of the disease, especially in IPF," said Fernandez.

To obtain an indication of whether the cells themselves could be the cause of the deterioration in lung function, the researchers measured the activity of genes that are typically expressed by immune cells. They found that these genes were expressed less frequently in samples that exhibited high MDSC counts. This indicates that MDSC – similar to their role in cancer – also compromise the immune system in IPF, according to the scientists.

A look into the lung tissue of IPF patients supports this assumption. "We were able to show that MDSC are primarily found in fibrotic niches of IPF lungs characterized by increased interstitial tissue and scarring, that is, in regions where the disease is very pronounced," said Eickelberg. "As a next step, we seek to investigate whether the presence of MDSC can serve as a biomarker to detect IPF and to determine how pronounced it is." In addition, the researchers want to investigate the mechanisms of accumulation in more detail. "Controlling accumulation or expansion of MDSC or blocking their suppressive functions may represent a promising treatment options for patients with IPF," said Eickelberg.

More information: Isis E. Fernandez et al. Peripheral blood myeloid-derived suppressor cells reflect disease status in idiopathic pulmonary fibrosis, *European Respiratory Journal* (2016). DOI:

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