As discussed by Allden and coworkers in their article, among other hypotheses, CD71− AMs could be an expression of a subpopulation of immature monocytes recruited into the alveolar space from the bloodstream during active inflammation/tissue injury, as was previously shown in a preclinical animal model of lung fibrosis (6). We believe that the lack of specificity about the presence of CD71− AMs in IPF that we show in this brief report supports the latter interpretation. Furthermore, the reported association between the proportion of CD71− cells and the clinical course of patients with IPF may reflect the ongoing fibrotic process that characterizes the rapidly progressive form of the disease and may also characterize other, non-IPF ILDs that in some cases display an accelerated pathological/clinical evolution. Although further studies on large populations of patients with ILD will be needed to confirm these preliminary observations, we believe that the study by Allden and coworkers is very promising and reinforces the role of BAL as a potential source of fundamental information in the field of translational medicine in respiratory diseases.

Author disclosures are available with the text of this letter at www.atsjournals.org.

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Reply to Puxeddu et al.

From the Authors:

We thank Puxeddu and colleagues for their interest in our paper and for opening a dialogue regarding the role of CD71-expressing airway macrophages (AMs) in interstitial lung disease (ILD) (1). Indeed, it is interesting that the authors found a similar population of CD71− AMs in a second cohort of patients with idiopathic pulmonary fibrosis (IPF), further validating our findings. The authors describe a level of CD71− AMs in a group of patients with non-IPF ILD comparable to that observed in patients with IPF. These data raise the question of whether CD71− AMs may be an important pathogenic component of IPF as well as other fibrotic lung diseases.

To determine whether the proportions of CD71-expressing AMs were altered during non-IPF ILD, we examined BAL samples from a cohort of patients with hypersensitivity pneumonitis (n = 18), respiratory bronchiolitis-associated ILD (n = 2), sarcoidosis (n = 2), or undifferentiated connective tissue disease (n = 5), and used a multicolor flow-cytometry gating strategy identical to that described in our initial publication (1). We found that in patients with non-IPF ILD, there was an increase in the proportion of CD71− AMs compared with healthy control subjects, and furthermore, the proportions of these populations were similar to those found in patients with IPF (Figure 1). One of the key findings of our original study is that CD71− AM status was an independent predictor of survival in patients

![Figure 1. Proportions of CD71− airway macrophages (AMs) in BAL from healthy subjects (n = 11), patients with idiopathic pulmonary fibrosis (IPF) (n = 23), and patients with non-IPF interstitial lung disease (ILD) (n = 23). ***P < 0.001 and ****P < 0.0001, Mann-Whitney U test. n.s. = not significant.](image-url)

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with IPF. Importantly, in this non-IPF group, there was only one death over the period investigated, so it was not possible to investigate the relationship between CD71+ AMs and mortality in this cohort.

We agree that further studies on the role of CD71 in the pathogenesis of fibrotic lung disease are needed to confirm our observations, and we thank the authors for adding to our findings.

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Empysema Is—at the Most—Only a Mild Phenotype in the Sugen/Hypoxia Rat Model of Pulmonary Arterial Hypertension

To the Editor:

Translational research is essential to develop strategies for the treatment of pulmonary arterial hypertension (PAH) using animal models that reproduce the severity, the progressive nature, and the resistance to treatment of human PAH, including severe arterial remodeling and progressive right ventricular (RV) failure (1).

We read with interest the letter by Kojonazarov and colleagues (2), we have not only conducted a previous in the SuHx rat model of PAH. Based on the report by Legchenko and colleagues demonstrated that RV failure develops between 1 and 6 weeks after the end of 3 weeks of hypoxia in SuHx rats, together with progression of pulmonary vascular disease, loss of peripheral pulmonary arterioles, and a metabolic switch in the right ventricle (6).

The advantages of the SuHx rat versus most other rat models of PAH such as monocrotaline were highlighted by a group of experts, and include the intensification of the vascular remodeling process, leading to the appearance of human-like plexiform lesions, and the virtual unresponsiveness to current PAH treatments, correlating well with the common unresponsiveness of PAH to therapy in humans (1).

Importantly, "severe emphysema" has not been observed previously in the SuHx rat model of PAH. Based on the report by Kojonazarov and colleagues (2), we have not only conducted a search of the literature but also analyzed lung histology from different SuHx rat studies in established laboratories (Table 1 and Figure 1). In contrast to Kojonazarov and colleagues, we did not find any severe or even moderate emphysema in any of the SuHx models analyzed (Figure 1 and Table 1). Mean linear intercept (MLI) as a surrogate for alveolar enlargement was not significantly different in SuHx versus untreated control lungs from Sprague-Dawley rats obtained from Charles River (Figures 1A and 1B). The Stewart group measured MLI in Sprague-Dawley rats obtained from Harlan, and found a mild (18%) increase in MLI in SuHx...