

Correspondence

Circulating fibrocytes: Will the real fibrocyte please stand up?

To the Editor:

We read with interest the recent article by Dupin et al¹ showing increased levels of circulating fibrocytes during an acute exacerbation of chronic obstructive pulmonary disease (COPD) and congratulate the authors on thoroughly addressing this overlooked but important area of research. On a technical note, the authors use a previously published technique whereby they discard adhered cells after 1 hour and use a nonadherent, CD3-depleted, fraction of PBMCs from which the proportion of fibrocytes was measured. There is a general consensus that fibrocytes are adherent, and Pilling et al² have shown that manipulation of culture conditions, such as cell density, can affect fibrocyte frequency. Can the authors confirm that fibrocytes were not lost during adhesion and that PBMCs from each of the study groups were plated at an equal cell density during this time? It would be informative to determine the likely effect of these variables on the fibrocyte frequencies and levels observed among the 3 groups.

Furthermore, from the flow cytometric plots presented,¹ there appears to be heterogeneity in the side scatter (SSC) signal for type 1 collagen positive cells, with SSC low cells contributing mostly to the final fibrocyte frequency measurement (see Fig E1 in Dupin et al). Heterogeneity could be due to different developmental stages of the same cell or unrelated cells with a similar phenotype (CD45⁺ type 1 collagen positive), both of which are difficult to disentangle in human studies but are nevertheless analyzed as a homogenous population here and elsewhere.³ Can the authors comment on whether it is possible to identify 2 populations of fibrocytes on the basis of their differential light scatter properties (FSC-A vs SSC-A), and whether separate analysis of each “subpopulation” leads to different or similar conclusions?

As alluded to in the discussion,¹ it remains unclear whether the association between lung function/mortality and fibrocytes reflects their (detrimental) pr remodeling properties, which should be prevented, or simply reflects a host response to damage in an attempt to reduce inflammation (perhaps as a myeloid derived suppressor cell [MDSC]),⁴ which is ultimately unsuccessful. As Dupin et al¹ correctly point out, further work needs to be performed to address this important question. We believe that to further understand the role of fibrocytes in COPD and asthma we must first understand the developmental

lineage of circulating fibrocytes (and other type 1 collagen positive cells), their relationship with (type 1 collagen negative) monocytes and heterogeneous MDSCs, in mice and humans. Allied to this, although culture and flow cytometry continue to play an important role when used together, an identification procedure that uses direct flow cytometric staining and minimizes cell processing will ultimately prove to be more sensitive but only if new approaches to flow cytometric set-up (eg, Fluorescence minus one controls⁵), reagent utilization (eg, live/dead exclusion dyes^{5,6}), and data curation (MIFlowCyt)⁷ are embraced into the analysis and dissemination pipeline. We will then be able to shed more light on their properties, which will ultimately provide the foundation to manipulating their role during disease.

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