Reviewer’s report

Title: Assessment of Surfactant Protein A (SP-A) dependent agglutination

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Reviewer: Timothy E. Weaver

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The authors describe a relatively simple assay to measure the ability of SP-A in biological fluids (serum and BAL) to self-associate into higher order structures (agglutinates). When applied to BAL from patients with CF or bronchitis, the assay detects significantly smaller agglutinates in disease samples compared to controls.

Major

1. While this finding is reproducible, it is not clear what it means. This is an important issue as there is no clear indication of when or why this assay should be used. Indeed the authors state "it will be important to investigate for correlations of this assay for SP-A function with lung function and meaningful lung disease outcome variables to completely appreciate its value" (second to last paragraph of discussion).

2. Reduced agglutinate size in disease BAL is interpreted as a change in SP-A function. In fact a link between SP-A function and agglutinate size is not investigated in this study. Decreased agglutinate size could reflect a qualitative change (e.g. altered SP-A1:SP-A2 ratio) or a quantitative change (there is less SP-A in disease BAL compared to control).

3. There is some confusion regarding the dose-dependence of the assay. BAL from controls contains 391X more SP-A than serum (table 1) yet forms the same size agglutinates (~ 500 pixels, Fig 4).

Minor

1. What is the evidence for the antiparallel association of CRD domains in Fig 1a?

2. The order of presentation in the methods section should be revised e.g. in the description of the assay (second paragraph of methods) the statement "final concentration of SP-A derived from the peak fractions was 100 ng/ml SP-A" is very confusing because SP-A purification is discussed much later.

Level of interest: An article of limited interest

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:

I declare that I have no competing interests