Reviewer's report

Title: Modulation of the oscillatory mechanics of lung tissue and the oxidative stress response induced by arginase inhibition in a chronic allergic inflammation model

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Reviewer: Nicholas Kenyon

Reviewer's report:

Aristoteles and colleagues have investigated the effects of NOS and arginase inhibition, alone and in combination, on oxidative stress and the resistance and elastance of the lung parenchyma in a guinea pig allergic inflammation model. A specific hypothesis is not stated in the introduction, but the authors state this work build upon prior studies focusing on iNOS inhibition and lung responsiveness. The arginase inhibition is a new approach here. Besides the unique methods measuring lung resistance and elastance in peripheral lobar lung strips, the majority of the data is from immunohistochemistry. The manuscript is clear and well written, while the results are primarily descriptive. Major comments:

1. Is the arginase activity assay specific for arginase 2 or is it total arginase activity? Was staining done for arginase 1 on these lung strips? A significant increase in arginase 1 in alveolar macrophages would be expected with OVA?

2. What were the inflammatory cell counts in the lungs ever counted in any of these animal experiments? What is the extent of iNOS and arginase staining in the inflammatory cells versus the resident lung cells in this model? One would expect iNOS staining to be evident in a variety of compartments in these sections, including inflammatory and alveolar macrophage cells?

3. Some studies suggest that arginase 2 is constitutively expressed in the lungs of animals, and change little with antigen challenge. The results here suggest that this is not the case, and this contention should be discussed more completely.

4. The addition of measurements of L-arginine content in these lung strips by HPLC or MS would help support their hypothesis. Perhaps an alternative would be to perform NOx measurements. Was lung lavage collected in these animals? NOx measurements would be interesting to measure with the two inhibitors. Some quantitative evidence of NO flux or L-arginine level alteration would be more convincing for the “competition” hypothesis.

Level of interest: An article of importance in its field

Quality of written English: Acceptable
**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests.