Reviewer's report

Title: Pharmacologic inhibition of S-nitrosoglutathione reductase protects against experimental asthma via both bronchodilatory and anti-inflammatory activities

Version: 3 Date: 22 July 2013

Reviewer: Matthew Foster

Reviewer's report:

In this manuscript, the authors explore the effects of a S-nitrosoglutathione reductase inhibitor in the ovalbumin model of experimental asthma. Intravenous administration of the drug significantly reduced airway hyperresponsivity to methacholine as well as airway inflammatory cells and cytokines. Although there is no direct evidence that these effects are due to increasing levels of airway S-nitrosoglutathione, the data nonetheless is the most complete description to date of the effects of S-nitrosoglutathione reductase inhibition in a model of allergic asthma.

Discretionary Revisions:

1. High levels of myeloperoxidase and MMP-9 suggest that neutrophils may be elevated at the time of therapeutic intervention in this model. Differential cell counts were performed, but only eosinophil counts were reported. It would be more informative if total cell counts and differentials (e.g. eosinophils, macrophages, neutrophils) were reported. This would allow correlation between BAL cells and inflammatory cytokines/chemokines.

2. The inclusion of bioassay data from naïve rat trachea (Fig. 5) seems a little out of place, since the rest of study is focused on mouse allergic asthma model. Authors should consider removing this data.

Minor Essential Revisions:

1. Background, p.5 (paragraph 1), it is unclear what “durable” means when in reference to GSNO and SNOs. A clearer description is needed.

2. Throughout results there is no information given as to when N6022 administration occurred in reference to the last ovalbumin challenge (e.g. 24 hours post). This information should be included in main text and all relevant figure legends.

3. In the discussion (p.18-20) the authors do acknowledge some limitations of the study, namely that SNOs were not measured and that inhibition of GSNOR could not be directly detected. They should also state that collectively, their data does not rule out the possibility that the effects of GSNOR inhibition may be due to suppression of aldehyde clearance or some other function of GSNOR.

Major Compulsory Revisions:
None

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**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' below