Reviewer's report

Title: Review: Ischemic Renal Injury

Version: 2 Date: 12 September 2010

Reviewer: Maarten Snoeijjs

Reviewer's report:

The manuscript is a brief review of ischemic acute renal injury and highlights some recent advances in this field. The review is well written and I agree with the focus of the review on acute and chronic microvascular injury and the therapeutic potential of HIF induction and preconditioning. However, I have major concerns with the section on preconditioning.

MAJOR REVISIONS

The section on preconditioning starts with a paragraph on S1PR agonists and Dicer inhibition. Although these are interesting discoveries, I would recommend to focus on preconditioning in this section. The next paragraph on preconditioning may be expanded by discussing (1) other methods of conditioning such as remote conditioning and postconditioning, (2) results of renal conditioning in large animals and clinical trials in aortic surgery which have not always been able to replicate the positive findings in small animals, (3) describe the underlying mechanisms of conditioning in more detail (I do not think the focus on Tregs is justified), and (4) possibly briefly discuss the positive findings of conditioning in clinical trials on acute myocardial infarction.

MINOR REVISIONS

1. In the section 'Pathobiology of ischemia', I would add that the corticomedullary junction is particularly vulnerable to ischemia because the increased metabolic demands of sodium reabsorption and the limited potential for anaerobic metabolism in this part of the tubular epithelium.

2. In the section 'Progression to chronic kidney disease', I would discuss the debate on the origin of progressive renal fibrosis: does tubular atrophy cause fibrosis which leads in turn to capillary rarefaction, or does capillary rarefaction cause fibrosis which leads to tubular atrophy. The paper by Higgins that is referred to in the manuscript seems to support the latter theory.

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.