Reviewer's report

Title: Early Innate Immune Events Induced by Prolonged Cold Ischemia Exacerbate Allograft Vasculopathy

Version: 1 Date: 15 November 2010

Reviewer: Vivek Rao

Reviewer's report:

Dr. Hancock-Friesen and colleagues from Halifax have submitted a well written manuscript describing the role of innate immunity in early lesion formation after aortic transplantation in a murine interposition model employing either 20 or 60 min of cold ischemia. I have a few minor requests for essential revisions.

1. The authors employed a fairly high dose of Cya (50mg/kg/day). Is there a rationale for such high dose? Several authors have employed as little as 5mg/kg/day for both cell and solid organ transplants. As CyA is in itself deleterious to the endothelium, the impact of such a high dose may exacerbate the differences between the two ischemic time periods tested.

2. This group has repeatedly demonstrated that SMC loss is a pivotal step in the development of CAV. In this study, they demonstrate impaired SMC recovery in the 60min group, despite higher proliferation seen at the 2wk mark. Do they have proliferation data at the 4wk mark, when the 60min group finally appears to recover SMC numbers?

3. The mTOR inhibitors (sirolimus and everolimus) have been unique in their clinical ability to attenuate CAV. Both drugs have been repeatedly shown to inhibit SMC proliferation in vitro and in-vivo. How do the authors reconcile this finding with their results? Do they plan to repeat studies using mTOR inhibition as an immunosuppressant?

In summary, the authors have performed a series of elegant and well designed experiments. A revised manuscript addressing the above comments would be a welcome addition to the literature.

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