Reviewer's report

Title: Possible involvement of caveolin in attenuation of cardioprotective effect of ischemic preconditioning in diabetic rat heart

Version: 1 Date: 10 April 2011

Reviewer: Edward Lesnefsky

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General Comments:
The manuscript by Ajmani and colleagues explores the impact on infarct size in the Langendorff perfused rat heart of caveolin dependent interactions with endothelial nitric oxide synthase in the loss of preconditioning responses in the diabetic rat heart. The use of a second marker of release (both CKMB and LDH) to assess myocardial infarction is a strength. The assessment of infarct size using both tissue staining and marker release is a strength. The manuscript is of appropriate length.

Major Compulsory Revisions:
• The statistical analysis must be described in greater detail. The use of many groups requires an overall one-way ANOVA with the subsequent use of secondary multiple comparisons. It appears that this has been done, but should be more explicitly stated and demonstrated. The significance values of the overall one-way ANOVA followed by the significance values of the secondary comparisons should be explicitly stated.
• The conclusions are dependent solely on the previously published specificity of the pharmacologic agents used. The potential specificity and limitations of specificity, of the agents used should be discussed. Dose response studies should be performed where appropriate.
• Cellular data that supports the mechanistic interpretation of the infarct size data should be included. Thus, the proposed caveolin-eNOS protein-protein interactions should be assessed by co-immunoprecipitation studies. Alternatively, caveolae can be isolated from heart tissue as described by many investigators and alterations in eNOS content in the isolated caveolae shown.
• The investigators should demonstrate that L-NAME blocks protection in groups that would support the role of NO as proposed.

Minor Essential Revisions:
• Is caveolin-1 or caveolin-3 the key caveolin involved in interaction with eNOS?
• The use of the appropriate caveolin knockout mouse in these studies would add experimental rigor to the proposed conclusions.
• Alternatively, the use of the eNOS knockout mouse in these studies would add experimental rigor to the proposed conclusions.
• Cardiac functional data should be shown, in addition to the cell death data.
• Diastolic contracture data should be shown to begin to address if a similar extent of ischemic damage was observed in all the groups.
• An expanded discussion of the role of caveolins in cardiac protection should be included.

Discretionary Revisions:
• None.

**Level of interest:** An article whose findings are important to those with closely related research interests

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

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interest in completing this review.