Reviewer's report

Title: Alteration of renal respiratory complex-III during experimental type-1 diabetes

Version: 1 Date: 14 October 2008

Reviewer: Michael T Ryan

Reviewer's report:

This manuscript reports that complex III of the respiratory chain is specifically decreased in levels and activity in rat kidney during the early stages of diabetes. This is an interesting report that has potential wide interest in the diabetes/mitochondrial community, however additional data is required to substantiate the findings.

In particular the authors indicate that the levels of complex II are decreased on BN-PAGE, yet a complex III immunoprecipitation brings down more complex III subunits than in control. The authors indicate that there could be an assembly defect/intermediate yet they do not show this. It is therefore important that they verify that the complex III seen on BN-PAGE is in fact complex III (e.g. by western blotting) and also showing that they can detect such intermediates (e.g. by BN-PAGE followed by SDS-PAGE in the second dimension and then blotting for Rieske and Core 2).

The authors should also show the entire lanes on Figure 2A. If there are other differences observed between the control and diabetic lanes, these must be mentioned and interpreted. It may be important to quantify the levels of complex III and perform a statistical analysis.

Minor essential revisions:

In discussion, change the text “(decreased expression on BN-PAGE)” to “(decreased levels on BN-PAGE”).

How do the authors reconcile a decrease in complex III levels/activity with the observed increase in ATP production? The suggested change in complex III appears to indicate that this is already in response to mitochondrial hyperpolarization and so ATP synthesis should be already affected. Might the complex V assay not be sufficiently sensitive and/or lack physiological relevance?

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

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’