Reviewer’s report

Title: Reduction in Podocyte Density as a Pathologic Feature in Early Diabetic Nephropathy in Rodents: Prevention of by Lipoic Acid Treatment

Version: 1 Date: 22 September 2005

Reviewer: Robert Nelson

Reviewer’s report:

General

Siu and co-workers examined podocyte number/glomerular section and glomerular volume/podocyte in STZ-induced diabetic male Wistar rats and in male C57BL/6J mice at 2, 6, and 8 weeks following STZ injection. They also examined the effect of treatment with insulin for 2 and 6 weeks and treatment with lipoic acid for 6 weeks on podocyte number/glomerular section and glomerular volume/podocyte in the rats. Podocyte morphometry was determined by WT1 and GLEPP1 immunoperoxidase staining. The authors reported a significant decline in podocyte number/glomerular section and an increase in the glomerular volume/podocyte in the diabetic rats and mice in comparison with controls that was substantially ameliorated in the rats by treatment with lipoic acid but not by treatment with insulin. They concluded that diabetes leads to an apparent reduction in podocyte number that may be prevented by antioxidant therapy.

A growing body of evidence points to a central role for the podocyte in the development of diabetic kidney disease. Given the difficulty of assessing the podocyte contribution to disease development and progression in humans, animal models of the disease are important. The authors demonstrate a relationship between podocyte density and diabetes and nicely outline several threats to validity in this small study. I offer a number of suggestions for consideration.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1. The first full paragraph on page 13 discusses an abrupt decline in podocyte number between 6 and 8 weeks in the diabetic rats and attributes this finding to artifact. The authors then go on to assume in spite of these data that a gradual loss of podocytes occurs after the initial steep decline in the first two weeks of STZ diabetes. I found this explanation less than compelling, since their conclusion clearly contradicts their data. I encourage the authors to revisit this issue and seek a more compelling explanation for this finding. I think some additional comments regarding their morphometric method and how it might impact these findings may be in order. Certainly, a thoughtful discussion of some of the “unintended differences” between the various rat cohorts may be helpful to the reader as well in determining the validity of the observations.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1. The authors may wish to describe in greater detail the basis for their decision to treat the rats with lipoic acid as part of the experiment. Why was this medicine chosen over others that might also have been useful?
2. The authors may also wish to describe in greater detail why they decided to include mice in this experiment as well as rats. It was not clear to me why they were included.
Discretionary Revisions (which the author can choose to ignore)

None

**Which journal?**: Not appropriate for BMC Medicine: an article whose findings are important to those with closely related interests and more suited to BMC Nephrology

**What next?**: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

**Quality of written English**: Acceptable

**Statistical review**: No

**Declaration of competing interests**: 

I declare that I have no competing interests.