Reviewer's report

Title: Identification of Nephropathy Candidate Genes by Comparing Sclerosis-Prone and Sclerosis-Resistant Mouse Strain Kidney Transcriptomes

Version: 1 Date: 6 February 2012

Reviewer: Charles W heilig

Reviewer's report:

Summary: The authors have investigated the transcriptomes of sclerosis-prone and sclerosis-resistant mice by use of the SAGE method, to identify genes which may lend susceptibility to glomerulosclerosis. The OS allele was used to induce glomerular disease in the ROP mouse background, while C57BL6 mice with the OS allele do not develop significant glomerular disease. Human samples with and without FSGS were also examined for comparison with mouse samples. Multiple genes were found in renal cortex from ROP Os/+ mice which had significantly altered expression. Some correlations were found in the human FSGS samples. An initial analysis for gene expression networks suggested TGF-B signaling may be activated (though its expression was not increased).

Major Comments:

1. The study is largely descriptive, though the gene expression data may provide leads for future studies to identify and validate pathways promoting susceptibility to glomerulosclerosis in the current model.

2. Additional information examining potentially altered glomerular protein expression in the ROP Os/+ mice would be helpful in understanding what non-TGF-B pathways may contribute to glomerulosclerosis in this model.

3. A better description of what happens to albumin excretion and creatinine clearance over time in ROP Os/+ mice would also provide useful information to characterize the severity of the renal disease which develops.

4. Consideration of examining glomerular gene expression as opposed to whole cortex gene expression could prove more valuable in identifying factors which contribute to the susceptibility toward development of glomerulosclerosis in this model.

5. A better discussion of the data on glomerular numbers in the 2 strains of mice would be helpful.