Reviewer's report

Title: Atherosclerosis, Inflammation and Lipoprotein Glomerulopathy in Kidneys of ApoE-/-/LDL-/- double knockout mice

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Reviewer: Antti Saraste

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This study describes renal artery atherosclerosis (histology), renal vascular volume (micro-CT vascular imaging) and kidney pathology (histology) in aged atherosclerotic double knockout (ApoE-/- and LDLR-/-) mice. The results show atherosclerotic lesions in the renal artery, reduced total intrarenal vascular volume, perivascular inflammation, and glomerular changes consistent with lipoprotein disease/emboli in the atherosclerotic model. The results are interesting in providing careful description of kidney disease in this particular animal model.

- Major Compulsory Revisions

1) The manuscript introduces quantitative micro-CT imaging. I assume that the vascular volume consists mainly of venae. The manuscript would be improved by showing data on tracking/segmentation of the arteries and venae separately. Otherwise, this needs to be discussed.

2) The conclusion is “The reduced intra-renal total vascular volume is associated with renal inflammation, suggesting a direct relationship between atherosclerosis, inflammation and glomeruli alterations.” The manuscript would be strengthened by data correlating imaging data with quantitative data on inflammation, glomerular disease, and severity of atherosclerosis (renal artery or aorta). If no correlative data is shown, the discussion and conclusions should be reformulated accordingly.

3) The presence/significance of superficial “plaque rupture” and superficial “intraplaque haemorrhage” in mouse vs. man remains a controversial issue. This needs to be discussed.

4) The authors found vasa vasorum in the renal arteries of hypercholesterolemic mice, but these were not quantified. Were there any vasa vasorum in control animals?

5) Methods: what kind of diet did the mouse have?

Discretionary Revisions

1) Were there anatomically severe stenoses in renal arteries?

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.