Reviewer's report

Title: The rat STSL locus: characterization, chromosomal assignment, genetic variations in sitosterolemic hypertensive rats

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Reviewer: Timothy J Aitman

Level of interest: A paper whose findings are important to those with closely related research interests

Advice on publication: Other (see below)

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The manuscript describes studies of the Abcg5 and Abcg8 genes in rats and follows on from previous work by the manuscript's authors on the corresponding genes in humans and mice. The authors conclude that a missense substitution in Abcg5 accounts for sitosterolemia in a small number of sensitive rat strains.

Major Comments

1. There is no linkage data that definitively links sitosterolemia in the rat strains to the determined location of the Abcg5 and Abcg8 genes on rat chromosome 6.

2. There is no biochemical data to indicate that the missense mutation at codon 583 alters the activity or function of the Abcg5 gene product.

3. The possibility that the proposed causative missense mutation is an epiphenomen appears not to have been considered. There is almost no discussion of the functional consequences of the missense mutation, for example, discussion of effect on protein structure or activity.

Minor Comments

1. In their quantitative PCR assays, the use of GAPDH as a control is inappropriate as the
expression of this gene alters between different inbred rodent strains.

2. The Coomassie stain and Transferrin assessment of protein loading on the gels, in Figure 8, give contradictory results, raising doubts about the conclusion that Abcg5 expression is increased two-fold in SHR. More robust data should be presented or Figure 8 deleted from the manuscript.

**Competing interests:**

None declared.