Reviewer’s report

Title: Role of the ABCG8 19H risk allele in cholesterol absorption and gallstone disease

Version: 1 Date: 4 December 2012

Reviewer: Nigel Bird

Reviewer’s report:

This paper examines cholesterol absorption and the ileal cholesterol transporters ABCG5 / 8 and NPC1L1 stratified by the p.D19H allele. 168 patients were recruited from colonoscopy lists of which 34 were found to have gallstones. The paper represents a thorough examination of these transporters with largely negative results, which nevertheless do not detract from the value of the work.

Major Compulsory Revisions

I found that the presentation of the results made the paper difficult to follow at times. I felt that the stratification of patients by BMI was not particularly well justified. The WHO categorises a BMI of less than 25 as normal weight, 25-29.9 as overweight and >30 obese but the authors stratify their patients into <25 and >25 and also use the terms 'overweight' and 'obese' interchangeably. In the Results section values for the BMI’s are wrongly reported as BMI +/- 25.2 and +/- 26.6, Table 2 has the correct values and SEM's. These are reported as being significant, although it is hard to reconcile this clinically.

On page 12 it is inferred that the differences in HNF1alpha expression are different but they present a p value of 0.0564 which is not significant. The values reported for the overweight group in Table 2 also are reported as being significant at the 0.047 level whereas the levels of 7667 +/- 1295 versus 7274 +/- 1759 suggest otherwise. Throughout the paper I would like to see the statistical test that was used to generate the probabilities reported explicitly. A number of statistical tests were used and it would help the readers if they knew which test applied to what data. It would also add to the credibility of the paper if Power calculations could be included since the possibility of a Type II statistical error is always a risk in these types of studies.

Minor Essential Revisions

I would like to see a Table showing the diagnoses / indications for colonoscopy since chronic constipation is a known risk factor for the generation of gallstones. The patients did not suffer from gallstone disease and so this term should not be used interchangeably with gallstone carriers. Similarly, some of the patients in the overweight group may have been obese, but not all and therefore this term should not be used interchangeably.

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Not suitable for publication unless extensively edited

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests.