Reviewer’s report

Title: Molecular Testing for Adult Type Alport Syndrome

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Reviewer: Judy Savige

Reviewer’s report:

This is an interesting report that summarises the commonest mutations in adult-onset Alport syndrome in the US.

Major Compulsory Revisions

Could the authors please provide evidence that these 3 mutations account for 50%, 40% and 5% of all adult-onset Alport syndrome in the US? Have these or similar common mutations been described in non-US populations? Are they or analogous mutations common in these populations?

More clinical information – and the variation in different family members would be useful since few series comprise so many different family members with the same mutations.

The authors quote their test sensitivity and specificity as >99% and 90% respectively but these measures were determined in family members (who will be positive or negative) and a comment should be added to the effect that this precision is very biased. The true precision of the test is best determined from a population with Alport syndrome demonstrated on renal biopsy where mutations are not known.

Minor Essential Revisions

Are the authors saying that amino acid substitutions in the NC1 domain usually result in mild disease? This was not my understanding.

The names of genes are usually written in italics.

These authors say more than 300 COL4A5 mutations have been described but most publications say more than 400.

What is UNG denaturation?

Although the authors stated that polymorphisms were unlikely, did they identify any in their patients?

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 I have no competing interests.