Reviewer's report

**Title:** Whole exome sequencing reveals novel COL4A3 and COL4A4 mutations and resolves diagnosis in Chinese families with kidney disease

**Version:** 2  
**Date:** 22 September 2014

**Reviewer:** Richard Sandford

**Reviewer's report:**

No Major Compulsory Revisions

This is a small case series of three families with a history of a familial nephropathy. In all cases there was some uncertainty regarding the clinical diagnosis and mode of inheritance. WES was used to identify the underlying mutations which were all in AS associated genes confirming diagnoses of type 4 collagen related kidney disease (AS and TBMD). All variants are likely pathogenic and the pedigrees reveal the well described marked interfamilial variability seen in AS and the possibility of progression to ESRD in TBMD.

Current clinical practice in undiagnosed familial nephropathies would be to use a targeted gene panel or in a research setting, WES. All families had features compatible with AS and TBMD.

The manuscript is well written and contains a useful clinical message. More discussion surrounding the use of WES or targeted gene panels in the clinical or research setting should be provided along side reference to current guidelines in AS testing and the detection rates based on testing criteria.

**Level of interest:** An article of limited interest

**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