Reviewer's report

**Title:** Familial hypomagnesaemia with hypercalciuria and nephrocalcinosis (FHHNC): 2 heterozygous mutations in the claudin 16 (CLDN16) gene.

**Version:** 1  **Date:** 13 November 2007

**Reviewer:** Kenji Fujieda

**Reviewer's report:**

**General**
This work describes a heterozygous mutation in the claudin 16 (CLDN16) gene, such as a nucleotide substitution in exon 4 (C646T) on one allele and a nucleotide substitution in intron 4 (784+1 G to T) on another allele from a patient with familial hypomagnesaemia with hypercalciuria and nephrocalcinosis (FHHNC).

In FHHNC, it is still unknown why renal failure develops and a clinical heterogeneity exists even in the same family. As pointed out by authors, clinical severity may be determined by the genotype of CLDN16.

The result, findings, and conclusion of the data appear to be appropriate and add to the understanding of the genetic basis of FHHNC.

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**Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)**

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**Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)**

The following is the queries and suggestions.

1) For readers, a figure of family tree is easy to understand.

2) **Results/ Legend**

In results, authors mentioned that lanes1 and 4 represented the affected children, and lanes 2, 3, and 5 corresponded to unaffected family members. But, in legend to figure, lanes 2 and 5 were affected cases. In Figure 1, lanes 1 and 4 showed the identical pattern to lane 6 (control).

3) On p8, line 11. This sentence is incorrect.

4) On p11, the style of ref 15 is different from others.

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**Discretionary Revisions (which the author can choose to ignore)**
What next?: Accept after minor essential revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

no competing interests