Reviewer’s report

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

Version: 1 Date: 15 November 2007

Reviewer: Nine Knoers

Reviewer’s report:

General
This manuscript involves a simple case-report of a patient with FHHNC caused by compound heterozygosity of CLDN16 mutations.

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

1) There is very little news in this manuscript. Patients with FHHNC caused by CLDN16 mutations have been described several times and the role of claudin-16 as a tight-junction protein involved in paracellular transport of calcium and magnesium in the TAL is very well known. This report does not add anything new to that knowledge. The only novelty is the finding of one not earlier described mutation.

2) Detailed clinical data on the affected sibling of the index patient are missing

3) There is discrepancy between the text (results section) and the figure legend of figure 1 with respect to which individual is in which lane. This makes interpretation of the figure impossible.

4) The discussion is far too long in relation to the small message of this case report.

5) In the discussion it is suggested that the severity of the presentation of FHHNC in the patient and the sibling points to a complete loss of function of claudin-16. This is nonsense. The only way to get an idea about the function of claudin-16 mutants is by functional analysis.

6) The whole discussion about possible genotype-phenotype correlations is speculative and weak and not supported by earlier studies.

7) The methods section is rather limited. The method of sequencing is not mentioned.

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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)

1) 'tds' should be spelled out fully

2) In the discussion section page 8, line 11, text is missing and therefore the sentence makes no sense.

3) In the legend on figure 2 "PCLN1" is suddenly introduced without mentioning that this is another (old) name for Claudin-16

4) The acronym TAL is used in the abstract already but explained only later in the manuscript.

5) There are a few spelling errors in the manuscript:
   FHNNC instead od FHHNC
   In section background page 3 line 13 "encodes for claudin16", should be "encodes claudin-16"

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Discretionary Revisions (which the author can choose to ignore)

**What next?:** Reject because too small an advance to publish

**Level of interest:** An article of insufficient interest to warrant publication in a scientific/medical journal

**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