Reviewer's report

Title: Newborn screening for citrin deficiency and carnitine uptake defect using second tier molecular testing

Version: 2 Date: 25 September 2012

Reviewer: Takeyori Saheki

Reviewer's report:

The authors describe importance of second tier mutation testing for improvement of newborn screening for citrin deficiency and carnitine transporter defects. Plasma citrulline is the most sensitive marker for newborn screening for CD so far, but it is not so sensitive enough to detect the patients. Newborn screening for CD is useful for the patients to prevent incorrect therapy if they suffer from CTLN2.

Decrease in plasma carnitine is the best marker for CUD, but shows false-positive or false-negative under various conditions. However, newborn screening has big effects since carnitine administration ameliorates all the symptoms of CUD. To improve the new-born screening of CD and CUD, the authors showed importance of second tier mutation testing.

A possible novel finding the author didn’t mention is that even heterozygotes of CD may show slight increases in citrulline in newborn screening, although there is still possibility that they might be homozygotes of CD. Heterozygotes might be found if the authors tested the rest showing low citrulline levels, so that the carrier rates and the predicted incidences the authors calculated should be minimum ones. There is no such discussion.

Otherwise, the results and discussion are well written.

Some minor points;
In Results, Screening for citrin deficiency, line 10, the authors describe “six of the patients”. I suggest that they are not patients, so this should be neonates, newborn or subjects.
In Discussion, line 23, (19.52 microM) should be (19.5 microM)?

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:
'I declare that I have no competing interests'