Reviewer’s report

Title: Evaluation of the endoplasmic reticulum-stress response in eIF2B-mutated lymphocytes and lymphoblasts from CACH/VWM patients

Version: 2 Date: 10 September 2010

Reviewer: Graham Pavitt

Reviewer’s report:

Discretionary Revisions

1. In response to the recommendation of reviewer 2 that an explanation be offered for the data in the discussion, the authors may wish to look at the work of Balachandran and Barber (Cancer Cell 2004: 5:51-65). These authors noted that immortalization of mouse fibroblasts affected the ability of increased eIF2 phosphorylation to down-regulate eIF2B. They found that eIF2B expression was altered (increased) by the transformation process, this increased eIF2B activity and reduced sensitivity to eIF2 phosphorylation.

Although speculative it is possible that the differences observed between cell types in the present study could arise by a similar phenomenon. So, is it possible that elevated eIF2B expression in EIL would make the GEF assay more robust than in primary cells, and therefore easier to discern differences in activity between normal controls and patient samples? At the same time the elevated expression may make EIL cells less sensitive to changes eIF2 phosphorylation following the UPR than PL.

2. In the acknowledgements section, do the authors wish to thank ELA for any specific research grants?

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 that I have no competing interests