Review of: "The Mechanism of Hyperammonemia Triggered by Corticosteroid Administration in Late-Onset Ornithine Transcarbamylase Deficiency"

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Imoto and collegues report two patient cases of late-onset OTC defects manifested by hyperammonaemic coma after treatment with corticosteroids. This is a known phenomenon. But the present article excells by substantiating the reports by an ambitious study of OTC-deficient mice that develop hyperammonaemia after dexamethasone treatment.

Due to several issues I cannot recommend publication in its present form. I do, however, strongly encourage the researchers to continue to investigate this interesting topic and expand the present experimental set-up.

Major issues:

1. The enzyme expression profile of urea cycle enzymes as effect of dxa treatment in this study is the exact opposite of what has previously been reported in the literature. This discrepancy is worrying. Corticosteroids would normally induce urea cycle enzymes. This may be due to the very high dxa-doses used? - see below

2. Lower dxa doses should be investigated and thus I suggest including more dxa groups.

3. Sample size is to small (3 in control groups and 5 in OTC deficient animals).

4, In line with 3), I do not think that parametric students ttest is appropriate for this sample size and I do not think the assumption of equal variance is met. Non-parametric testing should be used in the present set-up. But as mentioned, instead, more animals should be included.