Reviewer’s report

Title: Corticotropin Releasing Factor 2 Receptor Agonist Treatment Significantly Slows Disease Progression in MDX Mice

Version: 1 Date: 20 January 2007

Reviewer: Jeffrey Chamberlain

Reviewer’s report:

General: The manuscript by Hinkle et al reports studies of the effects of an agonist against corticotrophin releasing factor 2 receptor (CRF2R) on diaphragm muscle structure and function in the mdx mouse model for Duchenne muscular dystrophy. This drug was also compared against vehicle only, and against prednisone and the combination of the agonist and prednisone. The authors also studied effects on gene expression in the various cohorts. The results were very dramatic, with a clear improvement in diaphragm muscle function and morphology. Both prednisone and the agonist worked well, but the best results appear to have been obtained with the combination of prednisone and the agonist. This work provides important data on this interesting new compound and should stimulate additional research that could lead directly to human trials of the agonist. Overall the data are clear and the results explained well. I have only a few general comments.

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

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. In the introduction the authors mention that mdx hearts undergo rapid and continual deterioration. While this is true of the diaphragm, I do not believe this is true of the heart. The hearts in mdx mice do slowly develop fibrosis and a cardiomyopathy, but they do not lose many myocytes and I would argue their deterioration is slower than in limbs muscles.

2. When prednisone and PG-873637 were combined it appears that muscle TPT and HRT were significantly lower than the time zero control. Is there any particular significance to this finding? This may have only been seen in experiment one.

2. There sees to be a typo on page 8 where there is a reference to experiment 3, I believe this should be experiment 2?

Discretionary Revisions (which the author can choose to ignore):

1. Will the expression profiling data be made available on a publicly accessible web site?

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:
I declare that I have no competing interest