Reviewer's report

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

Version: 1 Date: 6 December 2006

Reviewer: Jill Rafael-Fortney

Reviewer's report:

General
This manuscript describes experiments designed to test the effects of an agonist of corticotrophin releasing factor 2, PG-873637, on pathological parameters of the diaphragm in the mdx mouse model of Duchenne muscular dystrophy (DMD). For comparison, this treatment was compared to treatment of mdx mice with the most prevalent drug administered to DMD patients, prednisone. PG-873637 was found to confer a similar improvement in histological and function parameters as prednisone. In addition, the combined administration of both drugs showed a slight, but significant, improvement on mdx diaphragm histological and functional parameters. Since prednisone is currently the only treatment in use for DMD and confers only a minimal short term improvement, any potential for alternative or improvements on this therapy are valuable for the treatment of this disease. Therefore, this manuscript provides novel insight into potential therapy for DMD.

There are however, a few concerns that should be addressed to clarify the data in this manuscript.

-------------------------------------------------------------------------------------------------

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)

Minor Essential Revisions:
1. Diaphragm myocyte cross-sectional area appears to be an arbitrary value based on a random-sized strip of diaphragm. It appears from the procedure described for this analysis, that the authors have numbers that would be much more meaningful. The percentage of an arbitrary area that is composed of muscle fibers would be more useful data that relates to the amount of interstitial fibrosis and inflammation.

2. Cotricotrophin is misspelled in the title.

3. "Myocyte" is defined as "a muscle cell," yet this manuscript describes the measurements of muscle fibers. Myocyte is usually used to refer to heart muscle cells or cardiomyocytes. Myoblasts and myofibers are usually used to refer to single and multi-nuclear skeletal muscle, respectively.

4. The methods sections states that male 3 month-old C57 and mdx mice were used. However, the results section states that 3 month-old mice were used for Experiment 1 and 2 month-old mice were used for experiment 2. This age difference may account for the differences in force generation between the "control" mdx groups in the 2 different experiments.

5. There is no figure legend for Figure 2. Therefore, it is not possible to know whether the two photographs shown for each label (i.e. "vehicle" or "prednisone") are 2 panels from the same sample type, or whether the two panels represent treated versus vehicle or time 0.

6. No temperature is listed in the methods at which the functional measurements were performed. Large differences in force generation occur between measurements carried out at 25 versus 37 degrees C. I would assume from the data, that the temperature was 25 or 30, but it should be stated.

-------------------------------------------------------------------------------------------------

Discretionary Revisions (which the author can choose to ignore)
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

Declaration of competing interests:

I declare that I have no competing interests.