Reviewer's report

Title: Dystrophin deficiency in canine X-linked muscular dystrophy in Japan (CXMDJ) alters myosin heavy chain expression profiles in the diaphragm more markedly than in the tibialis cranialis muscle.

Version: 1 Date: 18 October 2007

Reviewer: Gordon Lynch

Reviewer's report:

General

This paper represents a comprehensive assessment of myosin heavy chain analysis in two different muscles in a unique beagle model of muscular dystrophy. The work is of interest to muscular dystrophy researchers and to others involved in the study of musculoskeletal diseases.

Overall, the paper was clear and well written and the findings make a novel contribution to the field. While there are few such colonies in the world, characterizing their skeletal muscles is important for those studying the progression of the dystrophic pathology, comparative models, and their relevance to human muscle disease.

The aim was to characterize the fiber composition of tibialis cranialis (TC) and diaphragm muscles from a colony of beagle-based canine X-linked muscular dystrophy in Japan (CXMDJ), a model for muscular dystrophy.

The results show an effect of dystrophy on MyHC expression; with a reduction in the expression of MHC fast type fibers and an increase in the expression of MHC slow type fibers in the diaphragm. This effect was increased with advancing age. In contrast, in the TC, dystrophy was associated with an increased expression of hybrid (slow and fast type) fibers that was consistent over different ages. Thus, dystrophic fibers from CXMDJ¬ dogs show altered phenotype, with the alterations being both muscle- and age-specific. Since MyHC expression in canine skeletal muscle is closer to that seen in human skeletal muscle compared with murine skeletal muscle, it was also concluded that dystrophic dogs may be a better model for human DMD compared with mdx mice.

The effect of a lack of dystrophin on MyHC expression was compared between adult normal (10 month) and affected CXMDJ dogs (11 month). However, this study also showed an effect of age (even a difference in age of 1 month) on MyHC expression. Therefore is there any reason to suggest that some of the differences seen between MyHC expression in muscle from normal and affected adult dogs was due to the difference in age between these groups (10 vs 11 months?).

It would be important to present data (or state clearly within the manuscript)
confirming that there is no difference in MyHC expression in normal dogs aged 10 vs 11 months and/or in affected dogs aged 10 vs. 11 months.

Methods:

Page 8, lines 11-12. Details of the anesthesia procedures should be provided.

Results:

Figure 2 is complex due to the considerable amount of data. It would be better to split it up so that Figure 2A (table showing fiber number) is removed and made into a Table, thereby leaving only the 6 graphs in Figure 2.

Figure 6. The authors are to be commended for attempting to quantify the relative expression of the different MyHC types between groups and muscles. However, some important information is lacking in this figure with respect to sample size and statistical analyses. The number of fibers analyzed is shown, but from how many dogs? Also, were statistics performed to analyze the differences in MyHC expression between groups (normal vs affected: eMyHC (-) vs affected: eMyHC (+)) and/or muscles (TC vs diaphragm)? If so, this information should be included. If not, why was a statistical analyses not performed?

Figure 7B and C. Same as above – provide information on the number of animals used as well as the outcome of any statistical analyses.

Figure 6B. It is interesting to note that although TC from 2 and 11 month old dogs showed a majority of slow MyHC fibers, TC from 4 month old dogs showed a majority of fast (~75%) MyHC fibers. It would be helpful to describe why 4 month old dogs are different to 2 and 11 month old dogs in this regard.

Discussion:

The authors do a good job of suggesting an explanation for the differences in MyHC expression with dystrophy between different muscles. However, no explanation is given for the differences in MyHC with dystrophy between different ages. This should also be discussed briefly, especially with retrospect to any age-specific signaling pathways involved in MyHC expression.

What next?: Accept after minor essential revisions

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