Author's response to reviews

Title: Cardiac involvement in Beagle-based canine X-linked muscular dystrophy in Japan (CXMDJ): electrocardiographic, echocardiographic, and morphologic studies

Authors:

Naoko Yugeta (yugeta@b-star.jp)
Nobuyuki Urasawa (urasawan@amber.plala.or.jp)
Yoko Fujii (fujii@dc4.so-net.ne.jp)
Madoka Yoshimura (yoshimur@ncnp.go.jp)
Katsutoshi Yuasa (yuasa@ncnp.go.jp)
Michiko R. Wada (wadarin@ncnp.go.jp)
Masao Nakura (nakuramso@chugai-pharm.co.jp)
Yoshiki Shimatsu (shimatsu@ncnp.go.jp)
Masayuki Tomohiro (tomhromy@banyu.co.jp)
Akio Takahashi (akio_tk@ncnp.go.jp)
Noboru Machida (machida@cc.tuat.ac.jp)
Yoshito Wakao (wakao@azabu-u.ac.jp)
Akinori Nakamura (anakamu@ncnp.go.jp)
Shin’ichi Takeda (takeda@ncnp.go.jp)

Version: 5 Date: 27 November 2006

Author's response to reviews: see over
November 27, 2006

Senior Assistant Editor,
The BioMed Central Editorial Team
BMC-series journals

Dear Ms. Iratxe Puebla,

Thank you very much for your having accepted our manuscript (MS: 1681285926109043) “Cardiac involvement in Beagle-based canine X-linked muscular dystrophy in Japan (CXMD): electrocardiographic, echocardiographic, and morphologic studies”, by Naoko Yugeta et al, for publication in BMC Cardiovascular Disorders.

We have attempted to address two questions raised by the reviewer, and have prepared the reply letter. The added sentences in the manuscript have been indicated by red color. We have also changed the points raised by the editor.

Once again, thank you very much for your consideration of our manuscript. Please convey our special thanks to the reviewer.

Sincerely yours,

Shin’ichi Takeda, M.D., Ph.D.
Department of Molecular Therapy,
National Institute of Neuroscience,
National Center of Neurology and Psychiatry,
4-1-1 Ogawahigashi, Kodaira,
Tokyo 187-8502, Japan.
Tel: +81-42-346-1720
Fax: +81-42-346-1750
E-mail: takeda@ncnp.go.jp
Reply to the editor

1. Highlighting/Tracking

*Please remove any highlighting/Tracking from your manuscript text. Please also remove the ‘post-it’ style notes from the manuscript.*

> We have deleted the highlighting/Tracking and ‘post-it’ style notes from the manuscript.

2. Abstract

*Abstracts must be structured into Background, Methods, Results, Conclusions.* Please remember to also update the Abstract details on the submission page.

> We have changed “Conclusion” into “Conclusions” and updated the Abstract details on the submission page.

3. Figure title

*The image file should not include the title (e.g. Figure 1... etc.) or figure number. The legend and title should be part of the manuscript file after the reference list. The figures are numbered automatically in the order in which they are uploaded.*

> We have deleted figure title or figure number from each image file.

4. Figures

*It is important for the final layout of the manuscript that the figures are cropped as closely as possible to minimize white space around the image.*

> We have cropped all of the figures as closely as possible to minimize white space.
Reply to the reviewer, Dr. Luca Ferasin:

We, indeed, appreciate the reviewer’s enormous efforts to improve the quality of our manuscript. Thank you.

Discretionary Revisions

1. Methods

*Did you calculate the M-mode parameters based on a single measurement or multiple measurements (e.g. 3 or 5 consecutive heart cycles).*

> We calculated the M-mode parameters based on multiple measurements of 5 consecutive heart cycles, or 3 or 5 representative heart cycles. We, therefore, added the sentence in the **Methods** as follows.

**The sentence has been added in the Methods (p9; line 21-22):**

We calculated the M-mode parameters based on multiple measurements of 5 consecutive heart cycles, or 3 or 5 representative heart cycles.

2. Methods

*If the new reference reports a normal FS (%) in Beagles as 40 +/- 10 (Mean +/- SD), then the normal range (95% confidence interval) would be 20-60 (Mean +/- 2SD). Would the Authors be prepared to change their statement based on this comment?*

> We have recognized that ‘reference interval’ would be decided based on Mean +/- 2SD of the data of large numbers of normal healthy controls (usually more than 120 individuals). In the original reference that we mentioned [28, Crippa et al. 1992], they examined FS of 25 healthy Beagle males. They have not decided ‘the reference interval’ of FS of Beagle male, but other references cited their paper [28], and described a range of values of normal healthy dogs; 20-70% [Boon JA. Evaluation of Size, Function, and Hemodynamics. In: Cann CC ed. Manual of Veterinary Echocardiography, 1st ed. Baltimore, Williams and Wilkins, 1998, p189]. In addition, a recent paper has described that 25% of FS could provide a useful dividing line, because 95% of the apparently normal dogs had FS > 25% [Cornell et al. J Vet Intern Med 2004; 18: 311-21]. Taken these reports, as the reviewer addressed, 27.3% of FS in III-302MA at 21 months of age was within normal range, although 27.3% is lower than the value of a
normal littermate. We have changed the statement in the **Results** and **Discussion** as indicated below. We have deleted the description from the **Methods**, **Figure legends in Figure 3** and the bar indicating lower limit of normal FS from **Figure 3**.

1. We have deleted the sentence from the **Methods** of Echocardiographic findings (p9; lines 21-22 in the 2nd revised version).

   **The sentence deleted from the Methods:**
   We considered the normal range of FS as more than 30% based on a previous report [28].

2. We have changed the description in the **Result** (p12; lines 21-22) and cited a new reference [29, Cornell et al.] together with the reference [28]

   **The sentence has been changed in the Results (p12; lines 20-22):**
   FS in III-302MA decreased with advancing age, and the value (27.3%) at 21 months of age was lower than that of the normal littermate, but was within normal range reported previously [28, 29].

3. We have changed the statement in the **Discussion** (p16; lines 2-4)

   **The sentence has been changed in the Discussion:**
   Echocardiography did not reveal particular left ventricular dysfunction in any CXMD1 dog by 21 months of age, but a mild hypokinesis of the left ventricular wall was observed in III-302MA at 21 months of age (Fig. 3B).

4. We have deleted the sentence from the **Figure legend of Figure 3** (p26; line12 in the 2nd revised version), and also deleted the bar indicating lower limit of normal FS from **Figure 3**.

   **The sentence deleted from the Figure legend of Figure 3:**
   In FS, the normal range has been recognized as > 30% based on a previous report [28].