Author's response to reviews

Title: Biomarkers of peripheral muscle fatigue during exercise

Authors:

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Author's response to reviews: see over
Dear Prof. Reeves,

Thank you for your email dating 13th September, your and the reviewers’ valuable comments and the possibility to revise the manuscript. According to these comments the manuscript was revised with particular regard to the following points:

Reviewer #1:

The manuscript is improved, but in the abstract I still am a bit confused. It is stated that muscle fatigue is among others related to immunological and genetic responses. I think these two factors make the muscle more or less susceptible to fatigue but are not factors that themselves cause muscle fatigue. It might, however, be that the immunological response is associated (and may thus indeed be used as markers) with muscle fatigue, but I have reservations that it is the cause of muscle fatigue. I suggest to make this clearer in the Introduction and the Abstract.

Abstract and introduction were appropriately revised.

In the Introduction the fatigue definitions are clear, but they are, I think, not split out enough. I would rather have the exercise-induced fatigue and pre-exercise fatigue (or is it weakness, or a greater muscle fatiguability) split. Also the causes of the two are different, and I think should be distinguished as you seem to have done in Table 1 and 2. Disease states, like COPD, are generally associated with an earlier onset of muscle fatigue. It is for me hard to speak about a fatigued muscle pre-exercise. I therefore find it still hard to understand the role of the BMPFs, when there is a relatively easy measure of muscle fatigue resistance, such as the rate of reduction in force/power generating capacity during ongoing contractile activity.

Exercise-induced muscle fatigue is now clearly delineated from pre-exercise fatigue. It is also mentioned that both may have similar or different causes.

On page 5 inflammation is mentioned as a mechanism of fatigue, but I doubt whether that would be the case. It may create conditions that make the muscle more susceptible to fatigue and be associated with muscle fatigue, but I believe it is not a cause of fatigue.
Inflammatory responses to exercise on page 5 are now mentioned only under less well-defined causes of muscle fatigue.

**Altered Ca-release is, however, an important factor contributing to muscle fatigue (see work by Westerblad in the 90's).**

It is stressed that also impaired Ca-release may contribute to exercise-induced fatigue.

**ROS are not electron scavengers but do have an electron in excess.**

Thank you. Was corrected appropriately.

We hope that all these changes adequately meet all objections raised by the reviewers and the Editor and that readability and content have improved from these changes.

Please confirm receipt of the manuscript.

Sincerely Yours,

Vienna, 15th August 2012

J. Finsterer, MD, PhD