Reviewer's report

Title: Biomarkers of peripheral muscle fatigue during exercise

Version: 2 Date: 17 August 2012

Reviewer: Hans Degens

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Major compulsory revisions:

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.

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.

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

I like the section ‘ATP metabolism’ and subsequent sections dealing with mechanisms of muscle fatigue.

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

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.