Reviewer's report

Title: Cell stress molecules in the skeletal muscle of GNE myopathy

Version: 2 Date: 19 November 2012

Reviewer: Aldobrando Broccolini

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Major Compulsory Revisions

The paper of Fischer and coworkers aims to explore a possible pathogenic role of stress molecules in GNE myopathy muscle. Among these, they found that the cell-stress molecules #B-crystallin and iNOS are overexpressed in GNE myopathy muscle and may identify early disease mechanisms. The experiments are well conducted and the results appear convincing in terms of expression of these proteins. However, some skepticism remains regarding the possible role of proteins such as aB-crystallin and iNOS in the pathogenic cascade of GNE myopathy. An increased expression of both proteins has been documented in a heterogeneous group of acquired and inherited myopathies (see for example the paper by Banwell and Engel, Neurology 2000, cited by the authors). Also in sporadic inclusion-body myositis, that possibly shares some pathogenic aspects with GNE-myopathy, the role of aB-crystallin in the progressive degeneration of muscle fibers is not known. I believe that overall these results lack specificity and add very little to what is already known about GNE myopathy. The discussion is speculative for the most part and there is no definite evidence that aB-crystallin accumulation leads to Amyloid-beta overexpression. Possibly, additional in-vitro studies would be needed to substantiate this hypothesis.

Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.