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LETTER TO THE EDITOR

Comment on Sirtuin 1 in skeletal muscle of cachectic tumour-bearing rats

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Dear Sir,

We read with interest the recent article by Toledo et al. [1]. In their study, the authors found that mRNA levels for SIRT1 were increased in muscle from tumor-bearing rats and that SIRT3 mRNA levels were unchanged. In the discussion of the results, the authors stated that the observation of unchanged SIRT3 "is in contrast with that of Alamdari et al. [39] showing an upregulation of SIRT3 in skeletal muscle during sepsis". This was a surprising statement since we did not examine or report on SIRT3 expression in our study [2]. We did examine the effects of sepsis on the mRNA levels for the histone deacetylases HDAC3 and 6 and nuclear protein levels for the same HDACs as well as for SIRT1. Importantly, protein levels for HDAC6 and SIRT1 were decreased (not increased) and muscle HDAC activity was reduced during sepsis.

We think the misquotation of our work in the article by Toledo et al. [1] was unfortunate, not only because it was erroneous but also because it suggests that the expression of a histone deacetylase (SIRT3) may be increased during sepsis, implying increased deacetylase activity and reduced levels of acetylated cellular proteins. This is opposite to the conclusions in our paper [2] and in other recent reports from our laboratory [3–7] in which we found evidence that muscle wasting caused by sepsis and glucocorticoids is associated with, and probably at least in part regulated by increased acetylation of cellular proteins. These conclusions were also supported by experiments in which treatment of cultured muscle cells [4] or rats in vivo [2] with histone deacetylase inhibitor increased the expression of atrogin-1 and stimulated protein breakdown. In more recent experiments, we found evidence for a role of reduced (not increased) SIRT1 expression and activity in glucocorticoid-induced muscle wasting [7]. It was surprising to see that SIRT1 mRNA levels were increased in muscle from tumor-bearing rats in the study by Toledo et al. [1]. It would have been interesting to have information about SIRT1 protein levels and HDAC activity in the same muscles.

Sincerely,
Nima Alamdari,
Per-Olof Hasselgren

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