Reviewer's report

Title: Exercise training with dietary counselling increases mitochondrial chaperone expression in middle-aged subjects with impaired glucose tolerance

Version: 1 Date: 12 September 2007

Reviewer: Allan Vaag

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In this manuscript, the authors have measured the expression of several key mitochondrial chaperones and level of oxidative stress in skeletal muscle in 22 subjects with impaired glucose tolerance before and after a 2-year intervention programme with exercise and dietary counselling. Briefly, they report an upregulation of mitochondrial Heat Shock Proteins and decreased oxidative stress after the intervention. Somewhat surprisingly, the beneficial changes in mitochondrial Heat Shock Proteins and oxidative stress were not related to the changes in HOMA insulin resistance and degree of oxidative stress.

The questions posed by the authors in the manuscript are indeed new and well defined, and the methods are well described and in general appropriate. One draw back, however, is that insulin resistance was not measured using the gold standard hyperinsulinaemic clamp technique, which in fact may explain the lack of any association of the changes in heat shock proteins with degree of HOMA insulin resistance. Thus, HOMA insulin resistance is more likely to represent hepatic - and not muscle - insulin resistance, given that HOMA insulin resistance is based only on fasting plasma glucose and insulin measurements, and that the main "target" of insulin in the basal state is the liver, and not skeletal muscle. The authors should explain and discuss this important issue in a revised version of the paper. Apart from this somewhat minor issue, the data appears sound and well controlled, the paper is well prepared and clearly written, and the discussion and conclusions are well balanced and supported by the data. All together, this is indeed an interesting and potentially very important paper.