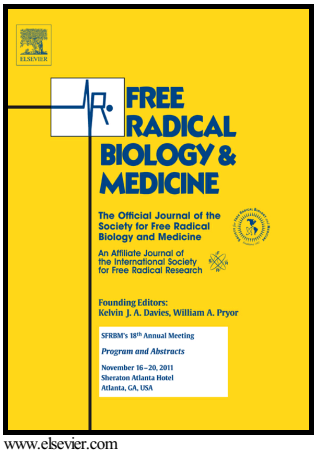

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Adaptive responses of heart and skeletal muscle to spermine oxidase overexpression: evaluation of a new transgenic mouse model

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Abstract

Spermine oxidase oxidizes spermine to produce H_2O_2, spermidine, and 3-aminopropanal. It is involved in cell drug response, apoptosis, and in the etiology of several pathologies, including cancer. Spermine oxidase is an important positive regulator of muscle gene expression and fiber size and, when repressed, leads to muscle atrophy. We have generated a transgenic mouse line overexpressing *Smox* gene in all organs, named *Total-Smox*. The spermine oxidase overexpression was revealed by β-Gal staining and reverse-transcriptase/PCR analysis, in all tissues analysed. Spermine oxidase activity resulted higher in *Total-Smox* than controls. Considering the important role of this enzyme in muscle physiology, we have focused our study on skeletal muscle and heart of *Total-Smox* mice by measuring redox status and oxidative damage. We assessed the redox homeostasis through the analysis of the reduced/oxidized glutathione ratio. Chronic H_2O_2 production induced by spermine oxidase overexpression leads to a cellular redox state imbalance in both tissues, although they show different redox adaptation. In skeletal muscle, catalase and glutathione S-transferase activities were significantly increased in *Total-Smox* mice compared to controls. In the heart, no differences were found in CAT activity level, while GST activity decreased compared to controls. The skeletal muscle showed a lower oxidative damage than in the heart, evaluated by lipid peroxidation and protein carbonylation. Altogether, our findings illustrate that skeletal muscle adapts more efficiently than heart to oxidative stress H_2O_2-induced. The *Total-Smox* line is a new genetic model useful to deepen our knowledge on the role of spermine oxidase in muscle atrophy and muscular pathological conditions like dystrophy.

[1] These authors contributed equally to the research