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Special issue: Exercise redox biology from health to performance

In order to support the energy demand during physical exercise, temporary acute *responses* occur in our organism to meet the homeostatic challenge imposed by the working muscles. As a result of the accumulation of exercise bouts the organism adapts. Exercise *adaptations* refer to the long-term changes that occur in our body as a consequence of training. The molecular bases of skeletal muscle adaptations to exercise such as mitochondrial biogenesis, hypertrophy, angiogenesis, and cytoprotection, are mediated by signaling events regulating transcriptional and translational processes and the activity of proteins involved in the maintenance of homeostasis [1].

Several signaling molecules are involved in these exercise-induced adaptations among them, in this special issue, we will deal with the importance of the oxidants, antioxidants and the balance between them.

First evidence showing that living cells contain free radicals was reported in 1954 in Nature [2]. It was not until the early 80's that researchers identified the first link between muscle function and free radical biology when they reported an increase in radical content in isolated frog limb muscles stimulated to contract repetitively [3]. Shortly afterwards two pioneering works in the area were published pointing to the role of free radicals in exercise-induced muscle damage and muscle fatigue [4,5]. This stimulated the interest of many laboratories to study whether the administration of antioxidant compounds could reduce both exercise-induced tissue damage and muscle dysfunction (Gómez-Cabrera et al., 2015). An interest that has remained until today. Thus, since the discovery of their existence radicals were considered damaging to tissues and this idea prevailed in the mind of exercise physiologists for years. However, in the redox biology field, a paradigm shift started within the ruling hypothesis of the negative role of radicals in exercise in the 90's [6]. Since then, our view of the role of radicals changed from merely harmful molecules that caused damage during exercise to physiological signals that modulate gene expression in skeletal muscle. This new functional role does not mean these reactive species are harmless. We have learned that reactive oxygen species (ROS) can act as a double edge sword in the skeletal muscle. The amount of ROS, the differences in the time course of their production, its compartmentalization, transience, and even the nature of the species can modulate their effects in skeletal muscle.

Deciphering the complexity of this redox balance in skeletal muscle in the context of exercise is what has encouraged us to gather the contribution of specialized laboratories in different areas of redox biology in this Special Issue entitled: “Exercise redox biology from health to performance”. The reader will find cutting edge contributions coming from very prestigious researchers in the field. We include the work from 14 different research groups dealing with the main topics in the area. Dr. Nikolaidis' laboratory give us an overview of the central role of redox regulation in exercise physiology by reviewing the redox signaling pathways involved in acute exercise-induced responses and chronic exercise-induced adaptations. Dr. Lanner's research team proposes an innovative review on the implication of ROS and inflammatory pathways in the overtraining syndrome (OTS) in sports. OTS may have devastating implications on an athlete's career and by deciphering the mechanisms underlying skeletal muscle weakness in OTS in this review, this research team opens up room for potential interventions to mitigate it. Dr. Jackson and colleagues discuss the importance of H_2O_2 in redox signaling during muscle contraction and the mechanisms by which hydrogen peroxide might act to stimulate adaptations even at the low intracellular concentrations found in contracting muscle fibres *in vivo*. Dr. Jensen's research team puts the focus on the compartmentalization of the muscle redox signals controlling exercise metabolism. The study of redox signaling is moving towards a growing appreciation that ROS do not signal in a global unspecific way, but rather elicit their effects in distinct subcellular compartments. Two compartments, the mitochondria and the cytosol are discussed in depth in its contribution. Another contribution examining the mitochondria comes from Dr. Calbet's research group. The mechanisms regulating mitochondrial respiration, particularly during high-intensity exercise are reviewed in the manuscript. The authors analyze the factors that limit mitochondrial respiration and those that determine mitochondrial efficiency during exercise. Dr. Brooks, in a contribution entitled: “Lactate as a fulcrum of metabolism” discusses the short and long-term effects on cell redox and other control systems modulated by lactate dynamics during exercise. Dr. Brooks pays special attention in his review to the regulation of enzymes involved in mitochondrial respiration and glycolysis by lactate during muscle contraction. Dr. Wadley and his team summarize in their contribution the endurance exercise-related redox signaling and the adaptations that occur not only in skeletal muscle but also in the vascular function. After a comprehensive review of the literature they discuss the impact of supplementation with diverse antioxidant compounds on different exercise-related outcomes and endurance performance. In another manuscript examining supplementation in exercise, Dr. Navas-Enamorado and co-workers review the role of zinc in muscle regeneration and in the regulation of proteostasis after exercise. The consequences on health and athletes' performance of a zinc deficiency are also discussed in their manuscript.

Dr. Caporossi's laboratory provides an overview of a new and exciting area in the exercise redox biology field, the epigenetics. The role of ROS in modulating DNA methylation, post-translational histone modifications, and non-coding RNA transcripts in the context of exercise-related adaptations is elegantly reviewed by this research team. Dr. Radak and co-workers’ review deals with the systemic role of SIRT1 in exercise mediated adaptations and more specifically in muscle repair and hypertrophy. The interactions between SIRT-1 and the transcriptional co-activator PGC1-α during exercise are also discussed in depth.

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Dr. Powers' group provides an excellent examination of the mechanisms of exercise-induced preconditioning in skeletal muscle and discuss from a biochemical point of view the bases of the exercise-induced cytoprotection against harmful events such as doxorubicin-provoked damage and inactivity-induced fiber atrophy. In another manuscript examining muscle atrophy Dr. Viña's team gives us and overview of the molecular mechanisms involved in disuse muscle wasting, a condition that will likely affect every sport practitioner in his or her lifetime. The sources of ROS in muscle atrophy, the mechanism through which they regulate protein synthesis and proteolysis and the potential interventions to prevent it, are reviewed in detail in the manuscript.

Finally, and exploring other areas of exercise physiology and disease this special issue includes works relevant to aging and cancer. First, Dr. Rodriguez-Mañas' research group contributes with an excellent review article summarizing the beneficial effects of exercise in the management of age-associated frailty. The main mechanism regulated by exercise training in the elderly are discussed, including the reduction of age-associated oxidative stress through physical interventions. Next, Dr. Rebillard and her co-workers provide a discussion on the exercise-induced redox modulation as a potential therapeutic target in cancer. Clinical and preclinical studies supporting the exercise practice as an adjuvant therapy to improve cancer outcomes are included in their comprehensive review.

To sum up the reader has here an excellent summary of state-of-the-art contributions in the field of redox regulation of muscle function. We thank the contributing authors for their efforts and the reviewers for their expert reports and assistance in preparing this Special Issue for Redox Biology.

It has been our pleasure as editors to make this project see the light. We hope that it is useful to both senior and younger researchers who have an interest in the fascinating area of exercise redox biology.

References

[1] J.A. Hawley, et al., Integrative biology of exercise, Cell 159 (4) (2014) 738–749.
[2] B. Commoner, J. Townsend, G.E. Pake, Free radicals in biological materials, Nature 174 (4432) (1954) 689–691.
[3] A. Koren, M. Schara, M. Sentjurc, EPR measurements of free radicals during tetanic contractions of frog skeletal muscle, Period. Biol. 82 (1980) 399–401.
[4] M.J. Jackson, D.A. Jones, R.H. Edwards, Vitamin E and skeletal muscle, Ciba Found. Symp. 101 (1983) 224–239.
[5] K.J. Davies, et al., Free radicals and tissue damage produced by exercise, Biochem. Biophys. Res. Commun. 107 (4) (1982) 1198–1205.
[6] M.B. Reid, F.A. Khawli, M.R. Moody, Reactive oxygen in skeletal muscle. III. Contractility of unfatigued muscle, J. Appl. Physiol. 75 (3) (1993) 1081–1087.

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