TM Focus on Cachexia
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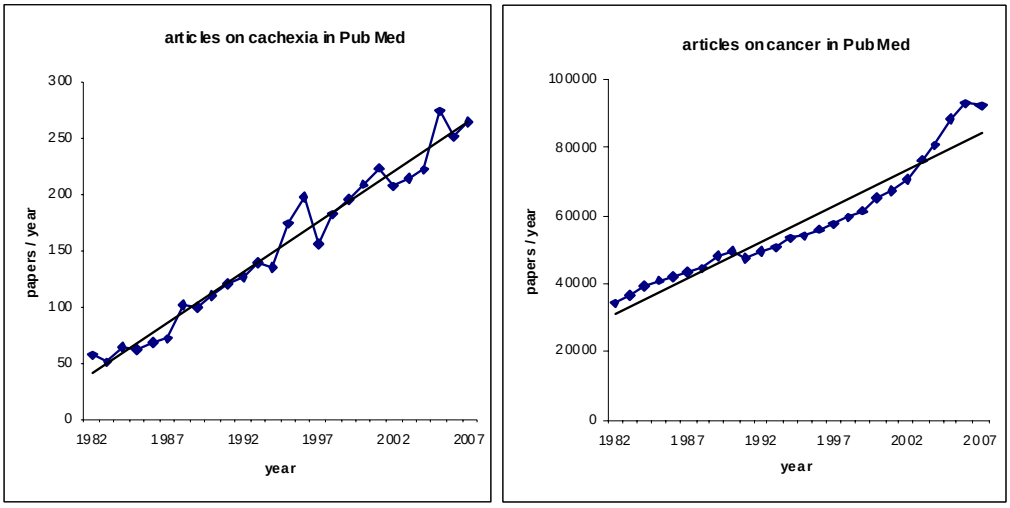
Editorial

Cachexia as a matter of meat

Cachexia is a harmful metabolic syndrome associated with underlying illness and characterized by loss of skeletal muscle with or without loss of fat mass. Being often associated with devastating chronic diseases, such as cancer and chronic cardiac failure, the clinical importance of cachexia has been neglected for decades. In the '80s the publications related to cancer summed up to the thousands per year in Pub Med, while a few dozens were those related to cachexia, even though the vast majority of cancer patients suffer from cachexia. Today, scientific publications on cancer are 2 orders of magnitude more numerous than those on cachexia (see figure). Nonetheless, a steady and significant growth in the number of scientific papers on cachexia is occurring. It is now established that cachexia negatively affects quality of life of the patients and interferes with therapy, ultimately being a primary cause of morbidity and mortality. Several reviews discussing both molecular mechanisms underlying cachexia and potential targets for intervention have been recently published [1-4]. An official definition of cachexia has become available and this will help diagnosis and clinical management, as well as basic research, by defining the criteria to recognize a patient (or an animal model) as cachectic [5].



This special issue of Basic and Applied Myology, European Journal of Translational Myology, is entirely dedicated to the pathogenetic mechanisms and the palliative management of skeletal muscle wasting. It provides a collection of several papers addressing important questions on cachexia, including basic mechanisms and possible approaches for intervention. The issue is opened by a mini-review of the major contributions from the last international congress dedicated to cachexia (4th Cachexia Conference, Tampa, 6-9 December 2007). This review concludes that in spite of the promising results of phase II clinical trials designed to combat cachexia there is a definite need for further basic and clinical research. In addition to pharmacological treatment, nutritional intervention and other approaches, such as stimulation of muscular activity, look reasonable against cachexia. A meta-analysis of the effects of exercise in cachectic patients performed by Perniconi et al. reveals that a beneficial effect from exercise can be statistically demonstrated only for patients suffering from rheumatoid arthritis. The authors also verify whether different types of physical activity have differential effects on the musculature of cachectic patients. Related to muscular activity is the observation by Cavallini et al., showing that the diaphragm is spared by muscle wasting. They also report that a severe caloric restriction may counteract sarcopenia in aging. The core of this special issue of BAM is represented by papers pinpointing the role of key cellular mediators of cachexia. In this context, Bingwen et al. report insights on the pathways leading to upregulation of the ubiquitin-ligase Atrogin-1/MAFbx in response to cytokines in models of sepsis. Nitric Oxide (NO) is implicated in the pathogenesis of muscle wasting, but the authors find that the synthesis of NO is not necessary for cytokines to elicit high levels of Atrogin-1/MAFbx expression. Recently, it has been reported a novel role for p53 in regulating muscle homeostasis, probably by affecting muscle stem cell number. Schwarzkopf et al. provide additional evidence that p53 activity is involved in promoting muscle atrophy induced by

cytokines, by exploiting a murine model with chronic p53 hyperactivation. An important mediator of p53 is PW1, which seems to regulate stem cell behavior. As mentioned above, the majority of cancer patient experience cachexia. Many of them undergo chemotherapy, a widespread approach to treat cancer. The work by Damrauer et al. strikingly shows that chemotherapies per se induce muscle wasting, which in fact persists in tumor-bearing mice in spite of tumor reduction following chemotherapy. This group also characterizes the NF-kB dependence of the phenomenon. An interesting technical paper, from Madaro et al., is closing the issue. Here the authors describe a novel model of muscle atrophy, which mimics atrophy deriving from disuse in the absence of the criticized side effects deriving from hind limb suspension. The development of a system to unilaterally induce atrophy in the musculature of mice is a potent tool to address questions on the regulation of muscle homeostasis.

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