

Cytokines and Muscle Physiology

Cytokines are typically discussed in terms of their critical role in the functioning of the immune system. Their importance to other systems, especially muscle physiology, is more recently described. In this special section, the contributors present reviews of their work in the area of cytokines and muscle physiology including growth and disease.

In the immune system, the balance of cytokine expression influences whether a disease state is created or protection against disease prevails. This balance is affected by the type of cytokine produced, the availability of the cytokine to bind receptors, the expression of appropriate receptors, and the response of the target cell. Cytokines can also be expressed in an autocrine or paracrine manner. The contribution of paracrine expression is especially significant in those tissues into which leukocytes migrate, as in the case of inflamed muscle following injury or disease. In many systemic disease states, blood elevations of cytokines can be detected, thus emphasizing the encompassing involvement of cytokines in the disease.

Cytokines have been shown to have a profound role in the loss of muscle mass in many disease states. The exact mechanisms involved are being studied in muscular dystrophy, cancer, AIDS, chronic infections, and inflammatory myopathies, and will give insight into the role of cytokines in normal muscle physiology. From the current investigations, it has been shown that cytokines can affect different stages of myocyte development. Some cytokines can affect the proliferation of myoblasts, while others have been shown to affect the ability of myoblasts to differentiate, including the expression of myogenic proteins and the ability to fuse into myotubes.

The authors contributing to this section have made advances in dissecting the role of cytokines in disease states and in the normal physiology of muscle. Kurek et al. discuss the effect of cytokines on muscle growth. They focus on the role of leukemia inhibitory factor (LIF), but also include a discussion on interleukin-6 (IL-6), transforming growth factor- α (TGF- α), and insulin-like growth factor-1 (IGF-1). They conclude with a review of gene therapy and myoblast transfer therapy and the possible contributions of cytokines in muscular dystrophy therapy. Monden et al. review the *in vitro* and *in vivo* effects of IL-6 on protein balance in muscle. They include sections on the transgenic models used to study cytokine-induced protein degradation and the intracellular processes potentially affected by cytokines. Argiles et al. review the muscle wasting disorders and compare the molecular and cellular differences between different forms. They focus on cytokines produced by macrophages, especially the effects of tumor necrosis factor (TNF) on muscle protein metabolism. Cantini et al. present their latest work on identifying macrophage factors which stimulate the proliferation of myoblasts. Goebels and Hohlfeld present a review on the inflammatory myopathies and the immune mechanisms behind them. They also discuss the role of cytokines in the immunopathogenesis of myopathies.

The review articles included in this section cover a broad spectrum of the effect of cytokines on muscle physiology. We hope that these reviews offer investigators a broad appreciation of this relatively new area of cytokine research and lead to new discussions and new ideas on the possible therapeutic uses of cytokines in muscle disease as well as muscle healing and cellular therapy.

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