Neuroinflammation during cancer cachexia and molecular determinants of skeletal muscle wasting

Proposed by
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Location
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Abstract

Cancer-associated cachexia is characterized by a progressive loss of muscle mass and strength. Clinically, cachexia has a profound impact on patients' quality of life, increases the risk of surgical complications, and reduces tolerance to anticancer treatments. Although systemic inflammation induced by tumor growth is recognized as a key driver of cachexia, its effects on the central nervous system remain poorly understood.

Hypothesis and objectives. We hypothesize that tumor growth–induced systemic inflammation alters central nervous system activity and contributes to the development of cachexia. Our objectives are (1) to characterize the central inflammatory state at different stages of cachexia, and (2) to determine whether central inflammation modulate gene expression in skeletal muscle.

Experimental design. $Apc^{Min/+}$ mice, a well-established murine model of cancer cachexia, will be studied at 15 weeks (moderate cachexia), and 20 weeks of age (severe cachexia) to assess central inflammation (Objective 1). To address Objective 2, central inflammation will be induced in healthy mice via intracerebroventricular injection of an inflammatory agent. Transcriptomic analyses of skeletal muscle and assessments of muscle contractile properties (strength, contraction velocity, and endurance) will be performed to evaluate the effects of central inflammation on muscle force production and gene expression.

Candidate profile. The candidate should be motivated to develop an integrative approach of cancer cachexia, drawing on physiology as well as on cellular and molecular biology.

Keywords
Atrophy, excitation contraction coupling, force, muscle, myopathy, sex