TACSM Abstract

Mitochondrial Dysfunction is Evident in Lewis Lung Carcinoma-Induced Muscle Wasting

CONNER BENSON[1], DAVID E. LEE[2], JACOB L. BROWN[2], MEGAN E. ROSA[2], TYRONE A. WASHINGTON[3], NICHOLAS P. GREENE[2], and MICHAEL P WIGGS[1]

[1]Integrated Physiology and Nutrition Laboratory; Department of Health and Kinesiology; University of Texas at Tyler; Tyler, TX
[2]Integrative Muscle Metabolism Laboratory; Human Performance Laboratory; Department of Health, Human Performance and Recreation; University of Arkansas, Fayetteville, AR
[3]Exercise Muscle Biology Laboratory; Human Performance Laboratory; Department of Health, Human Performance and Recreation; University of Arkansas, Fayetteville, AR

Category: Undergraduate

Advisor / Mentor: Wiggs, Michael (mwiggs@uttyler.edu)

ABSTRACT

Cancer cachexia is a paraneoplastic syndrome associated with adverse prognosis and shortened survival. The defining feature of cachexia is extensive muscle atrophy leading to progressive functional impairments. The molecular mechanisms responsible for the rapid muscle wasting are not fully elucidated. Based on emerging evidence, we developed the hypothesis cachectic muscle wasting is caused by mitochondrial dysfunction increasing reactive oxygen species production leading to global oxidative stress. To test this hypothesis we utilized the well-established Lewis-Lung Carcinoma (LLC) model of cancer cachexia. The time-course study consisted of one, two, three and four week LLC tumor bearing mice and age-matched four week saline (PBS) control (Ctrl) mice. Tumors were implanted into the hind flank at $1X10^6$ cells in 100 µL PBS. The plantaris was weighed for wet mass then teased into small fiber bundles and permeabilized for the quantification of mitochondrial function. Mitochondrial dysfunction was classified by a decrease in the respiratory control ratio (RCR), which is the ratio of state 3 (maximal ADP stimulated respiration) to state 4 (oligomycin-induced leak respiration). Muscle mass progressively declined over the time-course, reaching significance at 4 weeks (Ctrl vs 4-week, $p<0.05$). Mitochondrial function was not different among groups, however individual *a priori* comparison between groups revealed that 4wk cancer animals exhibited marked mitochondrial dysfunction compared to all other groups ($p<0.05$). These data demonstrate that late stage cancer-induced muscle wasting is associated with significant mitochondrial dysfunction.