Universität Basel

Research Project

Effect of exercise and exercise factors on cancer cachexia

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Project title Effect of exercise and exercise factors on cancer cachexia
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Cachexia, defined as loss of muscle and fat mass, is a major complication in cancer that not only massively increases morbidity and mortality, but also reduces the tolerance to radio- and chemotherapy. In fact, cachexia is estimated to constitute the actual cause of death in 22%-40% of all cancer patients, and not the tumor itself. Despite this obvious clinical importance, the molecular mechanisms leading to cancer cachexia are poorly understood. Furthermore, no effective treatment exists for this pathology. Intriguingly however, many of the key symptoms of cachexia are highly reminiscent of the plastic changes observed in trained skeletal muscle, yet in an inversed manner. Therefore, exercise has been speculated to constitute a possible therapeutic intervention for cachexia. Unfortunately, cancer patients, in particular those undergoing radio- and chemotherapy or those already suffering from cachexia, often exhibit a relative exercise intolerance, e.g. due to frailty, fatigue, nausea or time-consuming and restricting cancer treatment regimes. To overcome these hurdles, a better understanding of exercise-mediated effects in cancer could help to identify specific factors that harbor an anti-cachectic potential. In addition, so-called “exercise mimetics”, pharmacological agents that elicit training-like effects in muscle, could also benefit cancer patients. Our project is aimed to systematically assess the outcome of endurance exercise on cachexia in tumor-bearing mice. Second, we will study how the peroxisome proliferator-activated receptor γ coactivator 1α (PGC-1α) affects changes in body weight and muscle mass in sedentary and trained mice with ectopic tumors. PGC-1α is a key regulator of endurance training adaptation in skeletal muscle and sufficient to attenuate muscle wasting in various pathological contexts. Moreover, PGC-1α is thought to constitute the target for most currently described experimental exercise mimetics. Finally, state-of-the-art genomic and proteomic techniques will be combined with computational analysis methods to identify exercise and tumor-derived factors in cachectic animals in an unbiased manner. Collectively, the data will provide novel insights into the role of exercise in the treatment of cancer cachexia, and should reveal molecular mediators of such a therapeutic effect that could be used in the treatment of cancer patients.

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