Introduction: Cachexia exists in approximately 50% of cancer patients and accounts for at least 20% of deaths from cancer. It is characterized by progressive weight loss, metabolic alterations, depletion of lipid stores, and severe loss of skeletal muscle protein, all of which significantly impair quality of life and response to treatment. Currently, there is no known cure for cachexia, since mechanisms underlying its manifestation are not defined clearly enough to identify and design effective therapeutic strategies. The complexities of cancer, and cachexia induced by cancer, dictate the necessity of studying this disease in the context of its microenvironment as well as in the context of interactions between the tumor and the body, i.e., the ‘macroenvironment’. We are applying molecular and functional imaging to understand cancer cachexia and develop clinically translatable indices for early detection of this condition. In our efforts to better characterize the metabolism of cachetic tumor, we performed in vivo ¹H MRSI and detected a high level of total choline in cachetic tumors compared to non-cachetic ones.

Results and Discussion: Despite the absence of differences in lactate concentrations between both tumor types, ¹⁸F-FDG PET imaging revealed a significant increase in glucose uptake in the cachetic MAC16 tumors compared to the non-cachetic MAC13 tumors (Figure 2). C2C12 myoblasts were stably transfected to express green fluorescent protein (GFP) as shown in Figure 3B. Expression of RFP was induced by dexamethasone (Figure 3C). Stably transfected C2C12 myoblasts will be used as cell-based optical biosensors. Regulatory changes occurring in engrafted C2C12 muscle cells in mice inoculated with cachexia inducing tumor cells are being compared to analogous grafts on non-cachexia tumor bearing mice to identify the sequence of events in the cachexia-cascade. These studies are part of our ongoing work to obtain a comprehensive characterization of the ‘cachectic phenotype’ using noninvasive multimodality imaging that will allow us to detect cancer-induced cachexia and identify new targets to prevent or reverse this condition.

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