Abstract:
Cancer cachexia is a progressive wasting syndrome and the most prevalent characteristic of cancer in patients with advanced pancreatic adenocarcinoma. We hypothesize that genes expressed in wasted skeletal muscle of pancreatic cancer patients may determine the initiation and severity of cachexia syndrome. We studied gene expression in skeletal muscle biopsies from pancreatic cancer patients with and without cachexia utilizing Real-Imaging cDNA-AFLP-based transcript profiling for genome-wide expression analysis. Our approach yielded 183 cachexia-associated genes. Ontology analysis revealed characteristic changes for a number of genes involved in muscle contraction, actin cytoskeleton rearrangement, protein degradation, tissue hypoxia, immediate early response and acute-phase response. We demonstrate that Real-Imaging cDNA-AFLP analysis is a robust method for high-throughput gene expression studies of cancer cachexia syndrome in patients with pancreatic cancer. According to quantitative RT-PCR validation, the expression levels of genes encoding the acute-phase proteins \( \alpha \)-antitrypsin and fibrinogen \( \beta \) and the immediate early response genes Egr-1 and IER-5 were significantly elevated in the skeletal muscle of wasted patients. By immunohistochemical and Western immunoblotting analysis it was shown,
that Egr-1 expression is significantly increased in patients with cachexia and cancer. This provides new evidence that chronic activation of systemic inflammatory response might be a common and unifying factor of muscle cachexia.