Effect of the P2X7 activating compound BzATP on myoblasts differentiation: a potential pharmacological tool to treat cachexia

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Cachexia is a complex syndrome associated to different chronic diseases, including cancer and chronic heart failure. Cachexia is characterized by weight loss, depletion of adipose and muscle tissue and weakness, and is associated with poor prognosis. Muscle mass loss typical of cachexia results from different mechanisms, i.e. reduced protein synthesis, increased protein degradation or a relative imbalance of the two, and impaired myogenesis. Purinergic (P2) receptors recognize extracellular ATP that acts as a mediator of cellular communication. ATP is released from cells following cell damage or death and non-lytic ATP release may also occur under a variety of conditions. Interestingly, intraperitoneal injection of ATP in mice with colon tumors significantly inhibits weight loss and ATP infusion to cancer patients reduces weight loss and improves performance status. Several purinoceptors are expressed on muscle satellite cells and are involved in muscle regeneration. Among these, P2X7, a membrane channel regulating Ca^{2+}/Na^{+} influx and K^{+} efflux, contributes to satellite cell proliferation and differentiation. Here, we report the effect of the P2X7 agonist Benzoyl ATP (BzATP) on the differentiation program of muscle cells, using the *in vitro* model of C2C12 myoblasts. Our results show that P2X7 is expressed both in C2C12 myoblasts and myotubes. P2X7 stimulation with its agonist BzATP robustly enhances C2C12 differentiation as revealed by myogenin and myosin induction. Accordingly, the co-treatment with the P2X7 antagonist OxoATP inhibits BzATP effect. These results suggest that P2X7 opening on muscle cell precursors enhances their differentiation into myotubes, and, based on these data, we propose that the efficacy of the pharmacological compounds activating P2X7 in the treatment of diseases characterized by muscle mass loss needs to be evaluated *in vivo*.