Electrical stimulation-induced senescence and autophagy in estrogen-receptor positive breast cancer

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Cancer is a highly aggressive and continuously evolving disease that is characterized by dysregulation of the cell cycle. The vast majority of cancer treatments involve some form of chemotherapy and radiotherapy. While these therapeutic strategies have evolved over the years, they still have some drawbacks. The main drawback to chemotherapy is that it is delivered systemically, resulting in delivery to healthy cells as well as cancer cells, which leads to a vast array of deleterious and often treatment limiting side effects. Radiotherapy, while more localized in its nature, still suffers from some penetration issues which can damage healthy surrounding tissue. In addition, radiation involves expensive equipment, hospital implementation and some difficulties in positioning for treatment. Thus, while both treatments show positive effects in treating cancer, they are often associated with many side effects that impact the patient. Electrical pulse stimulation (EPS) has been long used in skeletal muscle rehabilitation, due to the excitable nature of muscle. Previous work in our lab with EPS on myoblasts and rhabdomyosarcoma (a muscle cancer) cells in cell culture has shown to halt cell growth. When implemented using breast cancer (MCF7) cells, G2 cell cycle arrest and cellular senescence were induced in a seemingly Akt-dependent manner, suggesting the plausibility of EPS as a cancer therapy. My thesis aims to further identify the mechanisms through which EPS causes senescence on breast cancer, with focus on the role of the Akt signaling pathway. I will be stimulating MCF7 cells with the addition of an Akt inhibitor to evaluate whether this pathway is directly responsible for the induction of the previously observed effects that arise from multiple bouts of EPS (2d, 4 hr/d). Additionally, I plan to investigate whether EPS induces cellular senescence through activation of the intrinsic autophagy and mammalian target of rapamycin (mTOR) pathways, halting cell growth.