High content screening of adjuvant chemotherapy in breast cancer and cancer treatment-related cardiomyopathy

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More patients are surviving cancer than ever before and this makes co-morbidity factors such as cardiotoxicity important issues in the quantity and quality of life of cancer survivors. It is important to be able to assess the cardiotoxic risk of new and existing cancer therapies. Changes in electrical impedance of cell-covered electrodes, for example, is one possible method. Alterations in the electrical impedance occur due to changes in morphology, cell contact, confluency and contractility which result from toxic effects on cells. Measurements using electrical impedance are non-invasive and can be monitored over long periods of time.

In this study, electrical impedance was used to monitor cell regrowth in breast cancer *in vitro* following chemotherapy treatment. In order to assess the cardiotoxic potential of this treatment, the same combination therapy was tested on human stem cell-derived cardiomyocytes (hSC-CMs). The combination of cyclophosphamide, adriamycin (doxorubicin) and 5-fluorouracil (CAF) administered for 4 months is a standard treatment for breast cancer patients and although often initially successful, tumor recurrence after this therapy remains a major cause of mortality in breast cancer patients. Using a murine carcinoma cell line (H8N8), we were able to investigate the effect of CAF treatment *in vitro* on untreated cancer cells and on tumor regrowth on H8N8 T3.2 cells previously treated with the regime. In addition, we tested the CAF treatment and paclitaxel on hSC-CMs. Paclitaxel caused a concentration and time-dependent reduction in viability of hSC-CMs as measured by a decrease in base impedance and caused a decrease in mean beat amplitude indicating an effect on contractility. Doxorubicin caused cardiotoxicity when present in any combination (alone or with cyclophosphamide or 5-fluorouracil) whereas cyclophosphamide or 5-Fluorouracil did not affect cell viability when applied alone or in combination with each other. Doxorubicin also caused a decrease in mean beat amplitude indicating a change in contractility.

In summary, using electrical impedance, acute and long-term effects of cancer therapy on cell proliferation of tumor cells, and cardiotoxic effects of chemotherapeutics can be identified. Such *in vitro* experiments are important to identify potential novel cancer therapeutics and also to promote cardiovascular health during cancer therapy.