MINIMIZING CHEMOTHERAPY SIDE EFFECTS: CALCIUM SONOPORATION

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In chemotherapy, the main goal is to eliminate cancerous cells by inhibiting their proliferation and metastasis to other organs. Chemotherapy can lead to adverse short-term and long-term side effects such as infertility, alopecia [1]. **Calcium (Ca^{2+}) ions** are significant for signal transduction pathways, due to being one of the most common intracellular signal transmitters between various signal compartments of the cell [2]. The disruption of intracellular Ca^{2+} homeostasis in a cell could play a crucial role in the destruction of cancer cells. It has been shown that Ca^{2+} serves an essential role in electroporation and demonstrates a potential for anti-cancer treatment [3]. In attaining spatio-temporally controlled delivery of anticancer drugs, sonoporation (SP) employs non-invasive application of medical ultrasound (US) in conjunction with microbubbles (MBs). SP might prove more efficacious than electroporation, however, Ca^{2+} delivery and application for sonotherapy has not been sufficiently studied. The utilization of Ca^{2+} in cancer treatment presents a promising avenue for the substantial mitigation of adverse side effects associated with conventional cytotoxic agents.

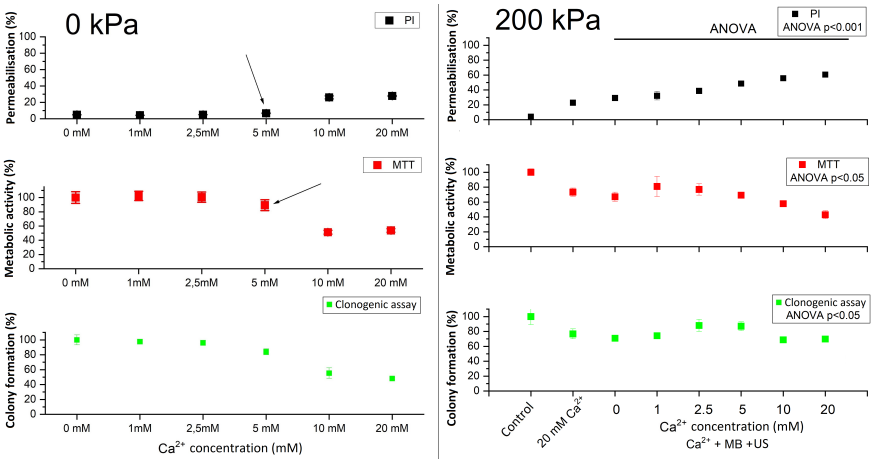

Fig. 1. Membrane permeabilization (propidium iodide (PI) assay, 20 min), metabolic activity (MTT test, 48h) and cell viability (clonogenic assay, 6 days) evaluated in different groups without US (left panel) and after Ca^{2+} delivery via US (right panel).

During the experiment, by using of PI, MTT and clonogenic assays, it was determined that the mortality of mouse breast cancer (4T1) cells increased from 5mM Ca^{2+} concentration, which was a turning point for the metabolic activity of cells and their viability. Our preliminary data indicate that Ca^{2+} transport, induced by MB cavitation, for 4T1 cells is not lethal in the presence of 200 kPa US, as the results of the clonogenic assay indicate the recovery of cell viability after 6 days (Fig. 1). The ANOVA test showed that increasing the Ca^{2+} concentration at 200 kPa US has a tendency to increase cell death. Moreover, the differences between the control (0 mM Ca^{2+}) and the therapeutic (Ca^{2+} +SP) group are up to 30’(according to PI and MTT tests), which indicates the permeabilization of the cell plasma membrane and the disturbance of metabolic activity.

This work was supported by the grant: “The development of controlled cancer treatment modality based on Ca^{2+} delivery via ultrasound (S-PD-22-51)” from the Research Council of Lithuania.

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