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Multicellular Cancer Spheroids as an in Vitro Model for Localized Hyperthermia Study

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Abstract : In modern oncology hyperthermia (HT) is defined as a controlled tumor heating. HT treatment temperatures range between 40–48 °C and can selectively damage heat-sensitive cancer cells or limit their further growth, usually with minimal injury to healthy tissues. Despite many advantages, conventional whole-body and regional hyperthermia have clinically relevant side effects, including cardiac and vascular disorders. Additionally, the lack of accessibility of deep-seated tumor sites and impaired targeting micrometastases renders HT less effective. It is believed that above disadvantages can significantly overcome by the application of biofunctionalized microparticles, which can specifically target tumor sites and become activated by an external stimulus to provide a sufficient cellular response. In our research, the unique optical tweezers system have enabled capturing the silica microparticles, primary cells and tumor spheroids in highly controllable and reproducible environment to study the impact of localized heat stimulation on normal and pathological cell and within multicellular tumor spheroid. High throughput spheroid model was introduced to better mimic the response to HT treatment on tumors in vivo. Additionally, application of local heating of tumor spheroids was performed in strictly controlled conditions resembling tumor microenvironment (temperature, pH, hypoxia, etc.), in response to localized and nonhomogeneous hyperthermia in the extracellular matrix, which promotes tumor progression and metastatic spread. The lack of precise control over these well-defined parameters in basic research leads to discrepancies in the response of tumor cells to the new treatment strategy in preclinical animal testing. The developed approach enables also sorting out subclasses of cells, which exhibit partial or total resistance to therapy, in order to understand fundamental aspects of the resistance shown by given tumor cells in response to given therapy mode and conditions. This work was funded by the National Science Centre (NCN, Poland) under grant no. UMO-2017/27/B/ST7/01255.

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