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Author: Ms. Agata Górska
University of Wrocław(UWr), Poland

Mr. Dawid Przystupski
Wroclaw Medical University, Poland
Mr. Piotr Wawryka
Wroclaw Medical University, Poland
Mr. Leszek Kogut
Scanway sp. z o.o., Poland

THE MODULATORY EFFECT OF ALTERED GRAVITY ON DRUG RESISTANCE IN HUMAN OVARIAN CANCER CELLS.

Abstract

Some types of cancer - such as breast, colon and ovarian cancer - display multidrug resistance (MDR), which leads to failures in applied treatment. Due to significant clinical implications related to cancer treatment and the MDR phenomenon, the search for the therapies overcoming cellular MDR mechanisms or acting effectively despite their occurrence has been the subject of many studies. We believe, that implementation of the gravity-related experiments may become a new tool for the understanding of cancer cell physiology and its potential use for the development of novel therapies for tumor treatment.

Numerous studies have reported that mechanical stimuli display remarkable influence on growth and biological processes of tumorous cells; hypergravity also seems to be a factor strongly affecting cell physiology. Gravitational loading modulates expression of various genes involved in cytoskeleton rearrangements and motility, cell cycle and apoptosis, signal transduction and metabolism projecting on increased proliferation and differentiation rates and hindered migration. Hypergravity is likely to have an impact on the pharmacokinetic and pharmacodynamic of drugs through enhanced membrane fluidity which plays a key role in diffusion-controlled reactions as well as the functioning of membrane-tethered proteins. Interestingly, molecules considered to play a crucial role in graviperceptions, are well-known to be involved in MDR and cancer migration and metastasis as well.

Based on these findings we stated our hypothesis that gravitational stimuli may modify biophysical and chemical properties of cell membrane and cytoskeleton leading to modulation of MDR pathways on genetic and proteomic levels. This idea gave rise to the HyperCells project within the framework of ESA Education Spin Your Thesis! 2019 , aimed to investigate how hypergravity affects the drug sensitivity of human ovarian cancer cells (SKOV-3).

This is the first *in vitro* study revealing the relationship between hypergravity and MDR in human ovarian cancer cells. Our studies have revealed alterations in cell cycle, namely G1/G0 cell cycle arrest induced by exposure to hypergravity and simultaneous administration of cisplatin. Furthermore we observed changes in cell morphology, induction of apoptosis and autophagy indicating an occurrence of synergic effect of cisplatin and hypergravity. Thus, we believe that hypergravity may affect cell pathways involved in MDR, especially those associated with cell membrane and cytoskeleton, resulting in higher chemosensitivity of cancer cells. The investigation and clarification of these phenomena may constitute an initial step toward enhancing our understanding of the link between MDR and the response to various gravitational stimuli.