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CELL CANCER STRESS IN SIMULATED MICROGRAVITY, DO DIFFERENT SIMULATION PLATFORMS INDUCE DIFFERENT EFFECTS?

Abstract

As human presence in space is expected to endure for increasingly longer periods in the future, a primary focus will not only be on managing the immediate effects caused by space life conditions but also on developing strategies to address potential long-term health issues that may affect future space dwellers. To achieve this goal, several devices have been created in recent years to simulate the effects of microgravity on Earth. To date, the Random Positioning Machine (RPM) is probably the most widely used platform to study the effects of simulated microgravity (s-μg) in various biological systems, including cancer cells. However, each device has its own features that may have different effects on the phenotype of cancer cells. This work aimed to test, by cell imaging and qPCR, how two different devices commonly used to perform s-g, namely the RPM and the CelVivo ClinoStar, differentially affect cell viability and the expression of specific genes involved in cancer progression. We sought to determine the effects induced after 7 days of s-μg using the triple-negative breast cancer (TNBC) cell line MDA-MB-231, a highly aggressive and radioresistant in vitro model of breast cancer. To gain a better understanding we used preformed multicellular spheroids (MCS) for our experiments. MCS are the most important cell population that can be isolated from an s-μg culture. Moreover, these 3D structures provide a more effective tool to mimic cancer progression then common 2D cell cultures. Our qPCR analysis focused on the expression of genes involved in the following processes: Cell survival and proliferation (MKI67 and AKT); apoptosis (BCL2 and BAX); epithelial to mesenchymal transition (VIM and CDH1); aggressiveness and stemness

(MMP9 and CD133). A differential and significant (p¡0.01) expression of the EMT markers vimentin and E-cadherin was found in the group of MCS isolated after s-g generated by both the RPM and the ClinoStar. Specifically, in MCS cultured in the RPM we found an increased expression of vimentin and decreased expression of E-cadherin. On the contrary, a decreased expression of vimentin and an increased expression of E-cadherin was found in MCS cultured in the ClinoStar. Finally, an increased expression of the pro-apoptotic marker Bax was found in MCS isolated from the ClinoStar cultures. Hence, our results show that different platforms to simulate gravity unloading may have a different additional impact on cell response and behavior.