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SPACE RESEARCH FOR IMPROVEMENTS OF TREATMENT CANCER DISEASE

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Introduction. Real and simulated microgravity (μg) created either by spaceflights or by special Earth-based devices provide an exceptional environment for studying and influencing tumor cell activities. By investigating growing cancer cells in μg, scientists have shown that μg-conditions change the microtubules and mitochondria of cancer cells, modify the production and structure of cytoskeletal and extracellular matrix proteins, induce apoptosis and change the secretome [3].

One of the main aims of the current research on space medicine is to evaluate the effects of microgravity on human cells. Therefore, investigations of the primary molecular mechanisms of how microgravity might affect cell signaling are currently of interest.

Materials and methods. The ability to achieve unrestricted 3D growth in suspension on Earth, as occurs in microgravity, is a problem that was concentrated by NASA through the development of the rotating wall vessel (RWV) bioreactor. The RWV is a horizontally rotating vessel with no internal mechanical agitator. A central silicone membrane is present in the RWV that delivers oxygen via diffusion, avoiding the production of bubbles that are disruptive to the growing cells. The vessel is completely filled with culture media and thus has no air–liquid interface. Because there are no internal moving parts, the vessel provides a culture environment that is characterized by low shear and low turbulence. The Random Positioning Machine also, known as the 3D clinostat can support certain conditions of the space microgravity environment, including the lack of sedimentation to facilitate cell colocation and growth of multicellular spheroids. As opposed to the RWV in which cells are cultured entirely in suspension, in the RPM a tissue culture flask containing a sub confluent monolayer of cells is affixed to the center of a platform in an interconnected framework that is comprised of two perpendicular arms that rotate independently of each other, to create continuous random directional adjustment of the culture flask. The RPM has been used to develop culture models of malignant glioma, thyroid carcinoma and leukemic cells.

Results. In particular, microgravity has been shown to have far-ranging effects on cell functions [2] including:

- “Programmed” cell death;
- Secretion of cytokines and growth factors;
- Arrangement of the cytoskeleton;

- Composition and structure of the extracellular matrix (ECM).

During exposure to the RPM thyroid cancer cells detached from the surface of the culture flasks and formed multicellular spheroids. Grimm [2] detected an increase of extracellular matrix proteins and TGF-β 1and found hints of early programmed cell death, such as chromatin condensation, membrane blebbing, loss of nuclear envelope and cellular fragmentation into apoptotic bodies. In this stage, the amount of cytoskeletal intermediate filament protein vimentin was increased and this finding was consistent with previously discovered abnormalities in actin stress fibers and microtubuli in Jurkat cells flown on the Space Shuttle. Further investigations showed elevated amounts of the apoptosis-associated Fas protein p-53 and Bax. Caspase-3 was clearly upregulated.

This was a clear hint that simulated microgravity induces early programmed cell death using different pathways of apoptosis. By using a mitochondria-rich carcinoma cell line could show that gravitational unloading affects the mitochondria and thereby may trigger apoptosis.

Space-based research has been part of the theory shift in the field of cell biology, for which new tools have been created for culturing cells in three dimensions. It is now well understood that 3D growth environments that facilitate unrestricted cell–cell interactions are significant for defining the biology of cancer cells and tissue, including tumor formation [1].

Conclusions

Findings in space environment managed to conjectures that weightlessness could also trigger cancer cells to change the expression of numerous proteins, which could be the basis for the development of new targets for drugs.

Results from microgravity research can be used to rethink conventional cancer research and may help to pinpoint the cellular changes that cause cancer. This in turn could lead to novel therapies that will enhance the quality of life for patients or potentially develop new preventive countermeasures.

References:

1. Eiermann W, Robert NJ, Pienkowski T, Translational Research in Oncology BCIRG 006 Trial Investigators.Oncologist. 2013;18(7):812-8. DOI: 10.1634/theoncologist.2013-0091.

2. Grimm D, Wehland M, Pietsch J, Aleshcheva G, Wise P, van Loon J, Ulbrich C, Magnusson NE, Infanger M, Bauer J (2014) Growing tissues in real and simulated microgravity: new methods for tissue engineering. Tissue Eng Part B Rev 20(6):555–566. DOI: 10.1089/ten.TEB.2013.

3. G. Ruyters et al., Biotechnology in Space, Springer Briefs in Space Life Sciences, DOI 10.1007/978-3-319-64