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Biology in Space (8)

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TISSUE ENGINEERING AND MICROGRAVITY

Abstract

Purpose: Tissue engineering under real and simulated microgravity conditions represents a new technology in gravitational biology and translational regenerative medicine. The purpose of this presentation is to summarize recent findings in the field observed when different cell types (thyroid cancer cells and endothelial cells) were exposed to real microgravity in space or to simulated microgravity using ground-based facilities.

Methodology: Follicular thyroid cancer cells and endothelial cells were investigated during international spaceflights in space or on the International Space Station (ISS) and were cultured in newly developed automated hardware for several days in orbit. Post-flight the cells were analysed by histological and molecular biological methods (proteomics, gene array, quantitative rtPCR, multianalyte profiling). In addition, cell biological experiments using the three-dimensional (3D) Random Positioning Machine (RPM) or the two-dimensional (2D) Fast Rotating Clinostat (FRC) were performed.

Results: Exposing the cells to real and simulated microgravity two phenotypes occurred: one part of the cells of both investigated cell types detached from the culture flask bottom and grew in form

of 3D multicellular spheroids (MCS), the other one continued growing as 2D monolayer. Interestingly, this formation occurred scaffold-free. MCS formed by thyroid cancer cells were more round aggregates, whereas endothelial cells exhibited a tube formation (intima constructs) and 3D MCS. The density of the monolayers exposed to microgravity revealed an impact on the results. Genomic and proteomic alterations were induced by altered gravity conditions. Biological processes such as proliferation, migration, the composition of the extracellular matrix proteins (ECMP), cell adhesion, focal adhesions, and apoptosis are influencing 3D growth under microgravity conditions. Growth factors, ECMP and cytokines such as vascular endothelial growth factor A (VEGFA), epidermal growth factor (EGF), connective tissue growth factor (CTGF), fibronectin, nuclear factor kappa-light-chain-enhancer of activated B cells (NF-B), interleukin-6 (IL6), IL8, caveolin-1 (CAV1), monocyte chemoattractant protein-1 (MCP1) and intercellular adhesion molecule 1 (ICAM1) were differentially regulated in space and under simulated microgravity and have shown to be involved in spheroid formation in microgravity. Moreover, RPM exposed FTC-133 monolayer cells or MCS incorporate vinculin, paxillin, focal adhesion kinase 1, and adenine diphosphate (ADP)-ribosylation factor 6 in different ways into the focal adhesion complex.

Conclusions: Cultivation of human cells on the ISS or a simulated microgravity-exposure of these cells induced 3D growth. Different phenotypes occurred and multicellular spheroids displayed a different gene expression profile involving important biological processes compared to monolayer cells.