



Abstract

Microgravity Exposure Induces Antioxidant Barrier Deregulation and Mitochondrial Structure Alterations in TCam-2 Cells [†]

Luisa Gesualdi ¹, Marika Berardini ¹ , Francesca Ferranti ², Anna Reale ³, Michele Zampieri ³, Katsiaryna Karpach ³, Maria A. Mariggiò ⁴ , Caterina Morabito ⁴, Simone Guarnieri ⁴ , Angela Catizone ¹ and Giulia Ricci ^{5,*}

¹ Department of Anatomy, Histology, Forensic-Medicine and Orthopedics, Section of Histology and Embryology, Sapienza University of Rome, 00161 Roma, Italy; luisa.gesualdi@uniroma1.it (L.G.); marika.berardini@uniroma1.it (M.B.); angela.catizone@uniroma1.it (A.C.)

² Human Spaceflight and Scientific Research Unit, Italian Space Agency, 00133 Roma, Italy; francesca.ferranti@asi.it

³ Department of Experimental Medicine, “Sapienza” University of Rome, 00161 Roma, Italy; anna.reale@uniroma1.it (A.R.); michele.zampieri@uniroma1.it (M.Z.); karpach.1792414@studenti.uniroma1.it (K.K.)

⁴ Department of Neuroscience, Imaging and Clinical Sciences-CAST, “G.d’Annunzio” University of Chieti-Pescara, 66100 Chieti, Italy; maria.mariggiò@unich.it (M.A.M.); caterina.morabit@unich.it (C.M.); simone.guarnieri@unich.it (S.G.)

⁵ Department of Experimental Medicine, Università degli Studi della Campania “Luigi Vanvitelli”, 80138 Napoli, Italy

* Correspondence: giulia.ricci@unicampania.it

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Abstract: One of the hallmarks of microgravity-induced alterations in several cell models is an alteration in oxidative balance. Notably, male germ cells, sensitive to oxidative stress, have also been shown susceptible to changes in gravitational force. To gain more insights into the mechanisms of male germ cells’ response to altered gravity, a 3D cell culture model was established from TCam-2 cells, a seminoma cell line and the only available in vitro model to study mitotically active human male germ cells. TCam-2 spheroids were cultured for 24 hours under unitary gravity (UG) or simulated microgravity conditions (SM), which was achieved using a random positioning machine (RPM). Apoptosis and necrosis analyses performed on the UG- and SM exposed samples revealed no significant differences in all of the cell death markers. Notably, the Mitosox assay revealed significant oxidation of mitochondria, after microgravity exposure, at least at this culture time. In the SM-treated samples, gene expression levels (evaluated by real-time PCR) of the main enzymes of the antioxidant barrier, GPX1 and NCF1, were reduced, indicating an influence of SM on mitochondrial function. Notably, the expression of HMOX, involved in the heme catabolism of mitochondrial cytochromes, was increased. The SOD, XDH, CYBA, NCF-2, TXN, and TXNRD genes were not affected. The ultrastructural analysis by transmission electron microscopy revealed that SM significantly altered TCam-2 spheroid mitochondria, which appeared swollen and, in some cases, disrupted. Indeed, mitophagy, or mitochondrial autophagy, appears to be more represented in the samples exposed to simulated microgravity. This result seems to be in line with the increase, mediated by the simulated microgravity, in the enzyme HMOX. All together, these preliminary data demonstrate TCam-2 spheroids’ sensitivity to acute SM exposure, strongly indicating a microgravity-dependent modulation of mitochondrial morphology and activity and encouraging us to perform further investigations on the chronical exposure to SM of TCam-2 spheroids.

Keywords: mitochondria; simulated microgravity; cellular spheroids; TCam-2 cells; oxidative stress; mitophagy

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