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Microgravity shapes cancer pathophysiology and progression

Abstract:

Exposure of tumor cells to microgravity, whether aboard space platforms or in ground-based simulators profoundly remodels their biology, affecting mechanotransduction, epigenetic regulation, three-dimensional architecture and intercellular communication [1]. In colorectal cancer organoids cultured in a 3D clinostat, cells adopt quiescent-cystic morphologies, hyperactivate mitotic-spindle, G2/M-checkpoint and E2F-target pathways and lose expression of TBC1D3 GTPases, doubling their proliferation rate versus 1G controls [2]. By contrast, A-172 glioblastoma lines on a 3D "microgravity-on-a-chip" exhibit smoother cell borders, reduced filopodia and lamellipodia, and inactivation of Hippo signaling—with YAP-1 down 22 % and vinculin down 20 %, culminating in suppressed growth [3]. Epigenetically, microgravity suppresses histone-deacetylase genes (HDACs) and core histones (H2B, H4, H2A) and lowers KMT2C/D/E methyltransferases, implicating genomic instability and impaired DNA repair in both colorectal and breast (MCF-7) aggregates [2,4]. Moreover, adherent cells shed into suspension spontaneously form multicellular spheroids that mimic micrometastases, displaying oxygen gradients, reduced central necrosis and differential chemosensitivity; notably, colorectal spheroids under microgravity show enhanced 5-fluorouracil efficacy, suggesting more predictive drug screens [2,4]. Exosome biogenesis is also reprogrammed: MDA-MB-231 breast cells release fewer but larger vesicles enriched in Ras-like GTPases (Ral, Rho, CDC42), modulating paracrine invasiveness, while FTC-133 thyroid cells on the ISS elevate CD63/CD81 exosomal markers and alter over 100 microRNAs tied to aggressiveness, yielding novel epigenetic targets [1]. Lineage-specific responses further illustrate microgravity's heterogeneity: A549 lung carcinoma regains E-cadherin and downregulates N-cadherin/MMP2 toward a more epithelial phenotype; PC-3 prostate spheroids show anomalous divisions, early inflammatory signals (↑IL-6, ↑CXCL8) and RPM spheroids with upregulated VEGF, integrins and cytoskeletal components endorsing angiogenesis; gastrointestinal models shift to glycolytic metabolism and modulate multidrug-resistance genes; and melanoma (HaCaT/A375) increases viability and mitochondrial activity but reduces proliferation with actin network reorganization [5]. Collectively, these findings demonstrate that microgravity redefines tumor cell behavior, provides three-dimensional models closely emulating human cancers and accelerates therapeutic target discovery and preclinical drug evaluation, establishing microgravity research as a promising catalyst in translational oncology.

Biography

Jhan Sebastián Saavedra Torres is a medical doctor from Universidad del Cauca (Colombia), with master's degrees in Palliative Care (Universidad Nebrija) and Clinical Immunology (Universidad de Vitoria-Gasteiz, Spain). He is a Family Medicine specialist from Universidad Javeriana, Cali. His current research focuses on sepsis and immunology. He is a member of the Health Research Group (GIS) and an active participant in NASA's Human Research Program (valid through 2025). He has training in neurological diving rescue and assessment (PADI and DAN), and has authored multiple scientific publications in critical care, immunology, and global health.