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Radiation Fields, Effects and Risks in Human Space Missions (5)

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PERSISTENT ONCOGENE AND TUMOR SUPPRESSOR GENE DYSREGULATION UNDER SUSTAINED MICROGRAVITY EXPOSURE

Abstract

Space biology indicates that microgravity stressors reshape multiple physiological systems, including immune regulation and tissue homeostasis, thereby creating a unique context for disease processes such as cancer. Within this framework, "astroimmunology" demonstrates that spaceflight- and microgravity-induced immune dysregulation and reduced tumor immunosurveillance can modify cancer risk and treatment approaches. This study, conducted within the framework of the MESSAGE (Microgravity Associated Genetics) science mission, aims to investigate the molecular effects of microgravity on human biology at the transcriptomic level. Comparative analyses were performed using a short-duration Axiom-3 mission at the International Space Station (ISS) (at day 4, day 7, and day 10 after Launch), a suborbital Galactic-07 mission (at 3 hours after return), and earth-based reference samples. Microgravity is a force that modulates DNA damage and repair, cytoskeletal organization, cell cycle control, and apoptosis, processes tightly coupled to the balance between oncogenes and tumor suppressor genes. This study, therefore, focuses on a cancer biology-oriented transcriptomics subdomain that examines how microgravity alters oncogene and TSG expression. A systematic, statistically robust comparative analysis encompassing a broad panel of oncogenes and tumor suppressor genes (TSGs) -comprising approximately 480 genes and their related aliases, derived from the OncoKB cancer gene list and the COSMIC Cancer Gene Census databases - was conducted. Transcriptomic changes associated with microgravity were analyzed using RNA-seq–based differential gene expression profiling of PBMC-derived RNA from astronaut blood samples. Within the framework of the science mission, gene expression data derived from human peripheral blood mononuclear lymphocytes (PBMCs) of astronauts were collected under all these conditions. The oncogene/TSG signatures remain transient during short-duration flights but become persistent aboard the ISS, and authentic microgravity biomarkers that cannot be accounted for by ground-based simulations. This study provides a comprehensive analysis of oncogene and tumor suppressor gene expression under microgravity, defining a distinct microgravity-associated transcriptomic signature that links cancer biology with space biology. These findings complement gain-of-function-focused carcinogenesis studies and support astronaut risk assessment under microgravity stress. Future work should prioritize functional validation of key genes and multi-omics integration across tissues to elucidate cancer-related pathways during long-duration spaceflight. In addition, extending this oncogene/TSG signature to experimental designs that explicitly test the interaction between microgravity and space radiation may enable its incorporation as a parameter in "space oncology" risk models, thereby facilitating the development of more clinically meaningful predictive frameworks.