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## CANCER IN SPACE: EVALUATING THE IMPACT OF THE SPACE ENVIRONMENT ON CANCER PATHOGENESIS AND NOVEL OPPORTUNITIES FOR CANCER RESEARCH

## Abstract

Cancer is a universal disease that is entrenched within our genome, and is strongly linked with environmental exposures that result in cumulative DNA damage and epigenetic alterations. The space environment provides a unique set of conditions (space radiation, microgravity and decompression) that incite cellular and genetic changes related to carcinogenesis, cancer growth and progression. Furthermore, data demonstrates that different tumour tissues behave differently within the space environment. Therefore, cancer research in space has far-reaching implications for increasing our fundamental knowledge of cancer biology and for developing future cancer therapies for space and Earth applications.

Galactic cosmic rays (GCRs) can penetrate into spacecraft and overcome protective shields, even at low earth orbit (LEO). Given the well-established terrestrial risk of DNA damage with ionising radiation, even low doses of GCRs may contribute to cancer development. Microgravity itself has also been associated with inducing DNA damage, in addition to attenuation of the DNA damage response pathway, another driver of carcinogenesis. However, microgravity has also been associated with reductions in cancer migration and promotion of apoptosis. Both ionising radiation and microgravity have been implicated in cellular mechanobiological stress through promoting the release of proinflammatory cytokines, changes to the extracellular microenvironment and cytoskeletal rearrangement, which may encourage malignant transformation. Furthermore, the decrease in atmospheric pressure in the space environment results in decompression that can lead to hypotaric hypoxia, which is associated with cancer cell survival and progression. There is also evidence that the space environment dampens the immune system, which has an active and complex role in facilitating immunosurveillance, regulating cancer survival and progression. Although the incidence of cancer amongst astronauts has not been found to be increased, this may be explained by profound fitness levels and relatively short LEO space missions. Hence, with imminent long duration space missions and increase in space activity, including space tourism, these protective factors may be impeded.

The primary purpose of this study is to investigate cancer risk and the novel opportunities for cancer research presented by the space environment. In this review, we evaluate the current state of knowledge of cancer pathogenesis under space conditions, and discuss potential preventive strategies and countermeasures for successful long-term space travel. Finally, we will explore how the space environment can further our understanding of tumour biology, as well as help identify potential therapeutic targets, and contribute to drug discovery and development, for the benefit of both space and terrestrial medicine.