Biological Space Radiation Countermeasures to Enable Long Duration Exploration Missions

Brock J. Sishc[1], Janice A. Zawaski[2], Janapriya Saha[3], Gregory G. Nelson[4], S. Robin Elgart[5]

Aegis Aerospace Inc.1, NASA's Johnson Space Center2, Leidos Inc.3, KBR Inc.4, University of Houston5

Abstract

NASA's career radiation limit for astronauts is 600 mSv. Currently planned missions beyond low Earth orbit (LEO) will expose crew to at least double that amount of radiation (for Mars missions). Therefore, to enable long duration exploration, countermeasures need to be deployed to reduce the long-term health outcomes of space radiation exposure. Limitations to the ability of spacecraft to shield against the high energy charged particles of the space radiation environment necessitate alternative methods to reduce overall space radiation risk for carcinogenesis. Recent successes in the arenas of Acute Radiation Syndrome (ARS) and clinical radiotherapy have demonstrated the efficacy of compound-based/biologicals in reducing the detrimental long term health outcomes associated with space radiation exposure. In recent years, the Space Radiation Element has funded the investigation of several such compounds including Avasopasem Manganese, CDDO-Me, Metformin, and γ-tocotrienol. The demonstrated efficacy of these compounds in reducing carcinogenesis, central nervous system, and cardiovascular disease risks demonstrate the need for, and potential benefit of, a robust countermeasure identification and development program with an initial starting suite of compounds available to validate others. The authors would also like to present highlights of a recent Space Radiation Element sponsored issue of Life Sciences in Space Research entitled "Breaking the Limit" on this specific topic.

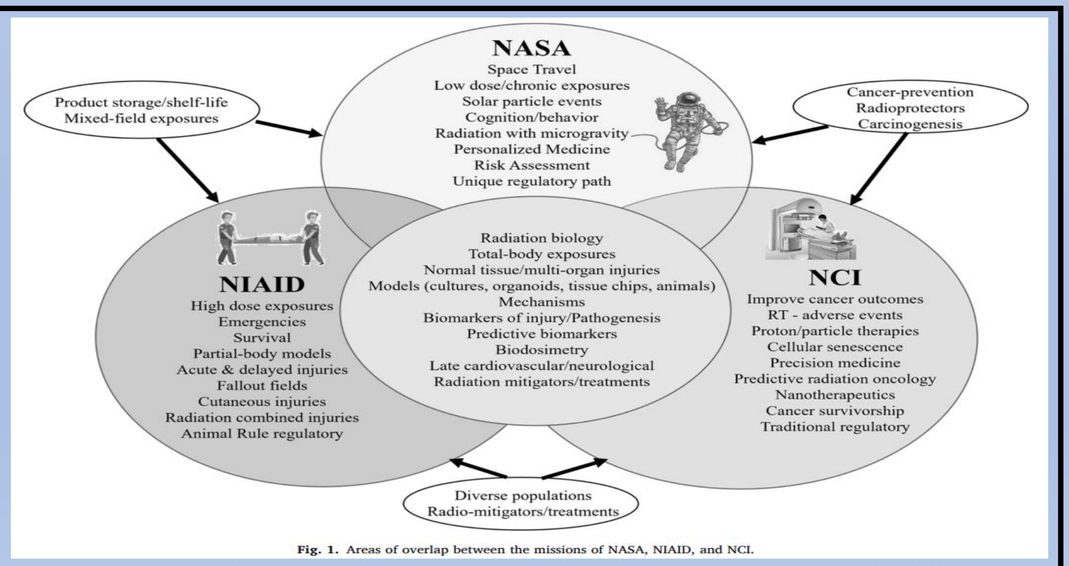
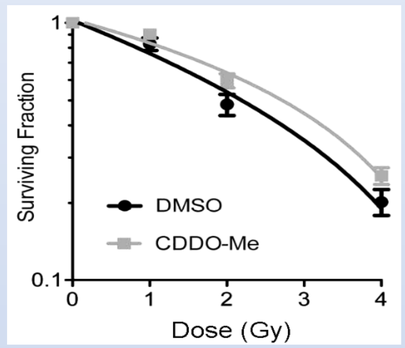
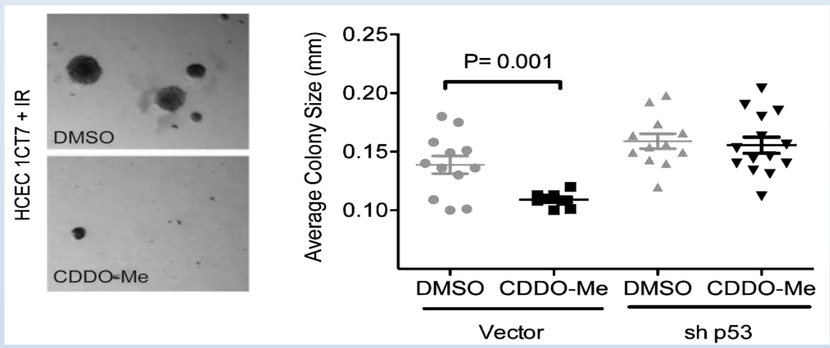


Fig. 1. Areas of overlap between the missions of NASA, NIAID, and NCI.

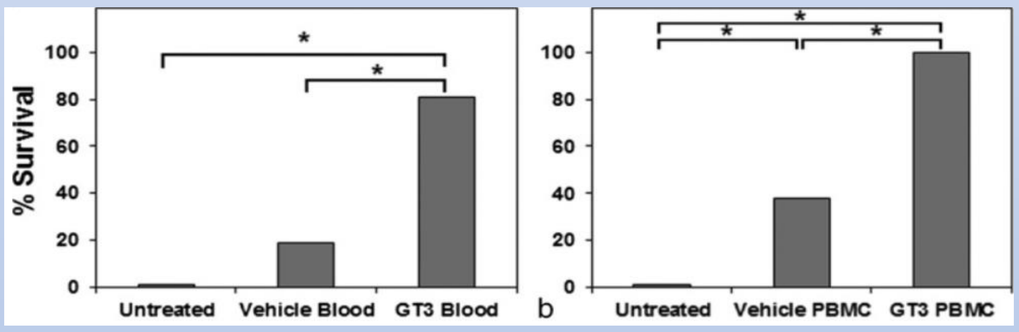
Schematic depicting the individual missions and overlap of various imperatives of the different U.S. Federal Government Agencies responsible for identifying and developing countermeasures against ionizing radiation induced health effects. NASA is responsible for identifying and operationalizing countermeasures against the chronic low dose rate accelerated particle environment of space. NAIAD is responsible for identifying countermeasures (radioprotectors and mitigators) to moderate the effects of ARS from accidental exposure events. The NCI is interested in identifying radiation countermeasures (radioprotectors, radiomitigators, and radiomodifiers) that can be utilized to improve clinical cancer therapy and prevention. ***DiCarlo et. al. 2022. Life Sciences in Space Research.***

Countermeasures Being Tested For Efficacy Mitigating Space Radiation Carcinogenesis

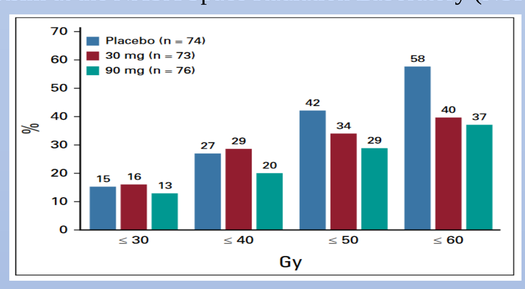


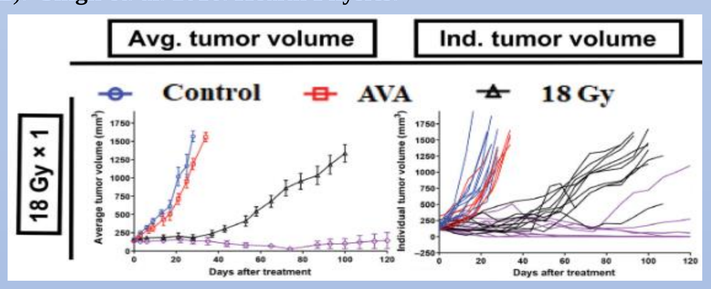


CDDO-Me, an activator of the Nrf2 endogenous antioxidant signaling pathway has demonstrated efficacy in both protecting colonic epithelial cells from radiation exposure based on clonogenic cell survival assays (Left Panel). Additionally, CDDO-Me reduced the frequency of HZE irradiated cells as indicated by a larger colony forming capacity in soft agar assays (right panel). Taken together, results indicate that CDDO-Me is not only an effective radioprotector for colonic epithelial cells, but that it may also have anti carcinogenic properties, making it an appropriate candidate for further testing as a space radiation countermeasure. **Eskiocack et. al. 2010. Radiation Research.**



Γ-tocotrienol, a derivative of the tocopherol family of antioxidant compounds, chemically modified to increase oral bioavailability was used to test the effect of irradiation on whole blood (left panel) and peripheral blood mononuclear cells (PBMC, right panel) in cell cultures. Γ-tocotrienol was effective at increasing the survival of both whole blood and PBMC's, indicating it's efficacy as a potential space radiation countermeasure. The same compound is currently being tested for efficacy in mitigating the consequences of exposure to GCRsim at the NASA Space Radiation Laboratory (NSRL). **Singh et. al. 2016. Health Physics.**





Avaseopasem Manganese (AVA,GC4419) has shown efficacy in reducing the incidence of radiation induced oral mucositis (RIOM) in patients being treated with radiation therapy for head and neck cancer. This indicates potent radioprotective properties in human clinical trials (left panel). In animal studies, not only did AVA not protect tumors from radiation therapy, but it sensitized the tumors to high dose per fraction IR exposure by altering their oxidative metabolism. Unpublished data also suggests that AVA is effective at reducing the rate of radiation induced mutation frequencies *in vitro.* **Anderson et. al. 2019. Journal of Clinical Oncology., Sishc et. al. 2021. Science Translational Medicine.**

Please feel free to explore the open access, Space Radiation Element sponsored issue on Countermeasures to Mitigate the risks of Space Radiation Exposure at the link below.

https://www.sciencedirect.com/journal/life-sciences-in-space-research/vol/35/suppl/C

References

- **DiCarlo er. Al. 2022. Life Sciences in Space Research.**
- **Eskinoack et. al. 2010. Radiation Research.**
- **Singh et. al. 2016. Health Physics.**
- **Anderson et. al. 2019. Journal of Clinical Oncology.**
- **Sishc et. al. 2021. Science Translational Medicine.**