



## Review article

## Biological effects of space radiation and development of effective countermeasures



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## ABSTRACT

As part of a program to assess the adverse biological effects expected from astronauts' exposure to space radiation, numerous different biological effects relating to astronauts' health have been evaluated. There has been major focus recently on the assessment of risks related to exposure to solar particle event (SPE) radiation. The effects related to various types of space radiation exposure that have been evaluated are: gene expression changes (primarily associated with programmed cell death and extracellular matrix (ECM) remodeling), oxidative stress, gastrointestinal tract bacterial translocation and immune system activation, peripheral hematopoietic cell counts, emesis, blood coagulation, skin, behavior/fatigue (including social exploration, submaximal exercise treadmill and spontaneous locomotor activity), heart functions, alterations in biological endpoints related to astronauts' vision problems (lumbar puncture/intracranial pressure, ocular ultrasound and histopathology studies), and survival, as well as long-term effects such as cancer and cataract development. A number of different countermeasures have been identified that can potentially mitigate or prevent the adverse biological effects resulting from exposure to space radiation.

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**Abbreviations:** ARS, acute radiation sickness; aPTT, activated partial thromboplastin time; BBI, Bowman–Birk inhibitor; BBIC, BBI concentrate; BFO, blood forming organs; BK, bradykinin; CNS, central nerve system; CT, computed tomography; DCF, dichlorofluorescein; DIC, disseminated intravascular coagulation; DMF, dose modifying factor; DNA-PKcs, DNA-dependent protein kinases; DTH, delayed type hypersensitivity; ECM, extracellular matrix; EGb76, quercetin; eSPE, simulated electron SPE; EVA, extra-vehicular activity; GI, gastrointestinal; GCR, galactic cosmic rays; G-CSF, granulocyte colony-stimulating factor; HDR, high dose rate; HS, hindlimb suspension; HZE particles, highly energetic, heavy, charged particles; ICRP, International Commission of Radiation Protection; IFN- $\alpha$ , interferon-alpha; INR, the patient's 'test' PT value divided by the laboratory 'normal' PT value, raised to the power of the International Sensitivity Index; ISS, International Space Station; LAD, left anterior descending; LBP, lipopolysaccharide binding protein; LD<sub>50</sub>, dose expected to kill 50% of the treated subjects; LDR, low dose rate; LET, linear energy transfer; LPS, lipopolysaccharide; MnSOD, manganese superoxide dismutase; NAC, N-acetyl cysteine; NASA, National Aeronautics and Space Administration; NCRP, National Council on Radiation Protection and Measurements; NK, Natural Killer; PAMP, pathogen associated molecular patterns; PBMC, peripheral blood mononuclear cell; PBS, phosphate buffered saline; PHA, phytohemagglutinin; PMN, polymorphonuclear leukocyte; pSPE, simulated proton SPE; PT, prothrombin time; PWS, partial weight suspension; RBE, relative biological effectiveness; SCR, solar cosmic radiation; SEB, surrogate endpoint biomarker; SeM, L-selenomethionine; SOBP, spread out Bragg peak; SPE, solar particle event; SWT, Si–Wu–Tang; TAS, total antioxidant status; TBI, total body irradiation; TF, tissue factor; vWF, von Willenbrand factor; WBC, white blood cell.

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## 1. Introduction

As reviewed by Hellweg and Baumstark-Khan (2007), the primary components of radiation in interplanetary space are galactic cosmic rays (GCR) and solar cosmic radiation (SCR). GCR originates from outside of our Solar System and consists of 98% baryons and 2% electrons. The baryonic component consists of 87% protons (hydrogen nuclei), 12% alpha particles (helium nuclei) and approximately 1% of heavier nuclei with atomic numbers up to 92 (uranium). These heavier nuclei include highly energetic, heavy, charged particles known as HZE particles. Although  $^{56}\text{Fe}$  ions, as a specific type of HZE particle, account for less than 1% of the GCR particle fluxes, they contribute significantly to the total radiation dose received by individual cells exposed to GCR due to the fact that the dose to an individual cell is proportional to the square of the particle's energy dependent effective charge (Katz et al., 1971).

SCR consists of low energy solar wind particles that flow constantly from the Sun and the highly energetic solar particle events (SPEs) that originate from magnetically disturbed regions of the Sun, which sporadically emit bursts of energetic charged particles (Wilson et al., 1999; Smart and Shea, 2003). SCR is com-

posed predominately of protons, with a minor contribution from helium ions (~10%) and an even smaller contribution from heavy ions and electrons (~1%). SPEs are unpredictable, develop rapidly and usually last for no more than several hours, although some SPEs may continue for several days. Since protons are the major component of SPE radiation, ground-based SPE radiation research is focused on the biological consequences of proton radiation at the appropriate energies, doses, and dose-rates expected during an SPE. A large fraction of the protons during an SPE are in the range of around 50 MeV, but there are also varying levels of protons of higher energies characterizing each individual SPE (NCRP, 1989; NCRP, 2006).

Exposure to space radiation may place astronauts at significant risk for acute radiation sickness (ARS), significant skin injury and numerous other biological effects resulting from exposure to radiation from a major SPE, which normally includes some HZE particles, or combined SPE and GCR. Doses absorbed by tissues vary for different SPEs and model systems have been developed to calculate the radiation doses that could have been received by astronauts during previous SPEs (Hu et al., 2009). For instance, it has been estimated that the August 1972 SPE could have delivered

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