Life Sciences as Related to Space (F)
Biological Effects of Space Radiation and Co-stressors: from Basic Research to Practical Recommendations (F2.1)
Either poster or oral presentation (no preference).

UNRAVELING ASTROCYTE BEHAVIOUR IN THE SPACE BRAIN: RADIATION RESPONSE OF PRIMARY ASTROCYTES

Mrs. Marie Denise Roggan, denise.roggan@dlr.de
Deutsches Zentrum fuer Luft-und Raumfahrt (DLR), Cologne, Germany
Jessica Kronenberg
DLR - Inst. of Aerospace Medicine, Koeln, Germany, jessica.kronenberg@dlr.de
Esther Wollert
Forschungszentrum Juelich, Juelich, Germany, e.wollert@fz-juelich.de
Sven Hoffmann
DLR - Inst. of Aerospace Medicine, Cologne, Germany, sven.hoffmann@dlr.de
Yara Nabawi
DLR - Inst. of Aerospace Medicine, Cologne, Germany, yara.nabawi7@gmail.com
Hasan Nisar
DLR - Inst. of Aerospace Medicine, Cologne, Germany, hasan.nizar@dlr.de
Bikash Konda
Deutsches Zentrum fuer Luft-und Raumfahrt (DLR), Köln, Germany, bikash.konda@dlr.de
Christian Liemersdorf
Deutsches Zentrum für Luft- und Raumfahrt, Köln, Germany, christian.liemersdorf@dlr.de
Ruth Hemmersbach
German Aerospace Center (DLR), Cologne, Germany, ruth.hemmersbach@dlr.de
Christine Hellweg
DLR - Inst. of Aerospace Medicine, Koeln, Germany, christine.hellweg@dlr.de

Exposure to ionizing radiation as part of space radiation, is a major limiting factor for crewed space exploration. Astronauts will encounter different types of space radiation, which may cause cognitive damage causing detrimental effects on learning and attention, elevated anxiety and depression. Due to its limited regenerative potential, especially the central nervous system (CNS) is very vulnerable towards radiation-induced damage. Astrocytes, the most abundant glial cells of the CNS, have different crucial functions in the CNS, e.g. maintaining normal brain function. In this work, the response of astrocytes towards low linear energy transfer (LET) X-rays and high-LET carbon ions was compared to unravel possible specific effects of space-relevant high-LET radiation. Since astronauts are also exposed to weightlessness, in addition to ionizing radiation, during space missions, the influence of clinostat-simulated weightlessness on DNA repair and reactivity after irradiation was analysed in order to consider possible combined effects of microgravity and radiation. In this study, primary murine astro-

cytes were irradiated with different doses of X-rays and carbon (12C) ions at the heavy ion accelerators GANIL, Caen, France, and GSI, Darmstadt, Germany. DNA damage and repair (γH2AX, 53BP1), NF-κB pathway activation (p65), cell proliferation (Ki-67) and reactivity of astrocytes (GFAP) were analysed by immunofluorescence and fluorescence microscopy. Cell cycle progression was investigated on the basis of DNA content, using flow cytometry. Furthermore, the induction of gene expression changes, after exposure to ionizing radiation was investigated by RT-qPCR, for the genes of interest: CDKN1A, CDKN2A, GFAP, TNF, Il1β, Il6 and Tgfβ1. Besides this, RNA-sequencing was performed for X-irradiated astrocytes. In addition, levels of the pro-inflammatory cytokine IL-6 were studied using ELISA. Furthermore, DNA damage response and astrocyte reactivity were investigated after exposure to X-rays in combination with incubation on a 2D clinostat. Our results show distinct responses of primary murine astrocytes towards the two different radiation qualities, X-rays and 12C ions. Analysis of the radiation-induced DNA double strand breaks and the respective repair revealed a clear dose- and time-dependency. With higher X-ray doses the total amount of damage increased significantly, reaching a maximum at 1 h after exposure, which subsequently was found to be decreasing, mainly due to DNA damage repair and at later time points only minor fractions of residual damage remained unrepaired. Analysis of the status of the NF-B pathway did not reveal a clear dose-, time-, or LET-dependent activation. In contrast, a LET-dependent S phase delay in cell cycle was observed, as well as time-, but not dose-dependent increase of the cytokine IL-6 and GFAP protein expression. X-irradiation and 12C ion irradiation induced a dose- and time-dependent regulation of gene expression, while proliferation of astrocytes remained mostly unaffected. Astrocytes were shown to respond to ionizing radiation with regulation of gene expression, while they were also observed to be relatively unresponsive to ionizing radiation with regards to NF-κB activation, proliferation, production of cytokine IL-6 and reactivity. Combinatory exposure of astrocytes to X-irradiation and simulated weightlessness, did not indicate a transition of astrocytes into a reactive state in any condition. Furthermore, no significant influence of simulated weightlessness on DNA damage induction and repair was observed, but only a slight tendency towards reduced DNA damage. RNA sequencing of X-irradiated astrocytes revealed downregulation of genes involved in DNA damage response and repair, Mitosis, proliferation and cell cycle. In conclusion, primary murine astrocytes are fully DNA repair proficient and simulated weightlessness did not disturb repair of X-ray-induced DNA damage. Gene expression changes after X-ray exposure were only minor and in monoculture, and reactivity was not induced. Further investigations in co-culture or in brain slices will reveal whether the rather reluctant radiation response of astrocytes is modified in presence of other cell types.