Bystander effect after exposure to high-LET particles encountered in cosmic radiation

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The cosmic radiation environment is significantly different from that found terrestrially. Cosmic rays primarily consist of high-energy charged particles, such as protons, alpha and heavier particles, originating from several sources, including galactic cosmic radiation, energetic solar particle events and trapped radiation belts. Some of these high-LET radiations inflict greater biological damage than that resulting from typical terrestrial radiation hazards. Future expeditions into interplanetary space will place crews at increased risk of exposure compared to the current short duration low-Earth orbit missions. Our knowledge of biological effects of high-LET particles is still developing. Research in this area may thus lead to the development of biological dosimeters and be pivotal in the design of exposure regulations and the assessment of health risks to astronaut crews. With the availability of high-energy particle accelerators and the development of microbeams the radiobiological bystander effect became of eminent interest. At low levels of exposure the communication of bioactive substances from irradiated to unirradiated cells can amplify the damage and cause significant deviations from linearity in the dose response relations. Early signal transduction events after exposure of normal human fibroblasts to high-LET particles are expected to reveal a deeper insight into the molecular mechanism controlling the cellular response to high-LET radiation. For this purpose, cells were exposed to ^{4}He, ^{12}C, ^{28}Si and ^{56}Fe ions of variable energy and LET (2.2 to 300 keV.µm^{-1}) available from the Heavy Ion Medical Accelerator (HIMAC) of the National Institute of Radiological Sciences (NIRS) in Chiba, Japan. The selection of the ion species followed their relative abundance in the cosmic radiation field. Beam intensity was tuned to ensure for all experiments a low particle fluence of ~ 7.3×10^{4} cm^{-2}, corresponding to one hit nucleus in seven cells. Absorbed doses and LET were verified by means of LiF:Mg,Ti thermoluminescence (TL) detectors, employing a method of TL efficiency correction. Immunofluorescence and immunohistochemical techniques indicated activation of ATM (ataxia telangiectasia mutated gene) and several of its substrates 2 to 3 hours after irradiation. In comparison to low-LET exposure, the number of pATM (S1981) foci per nucleus was enhanced in cells irradiated with high-LET particle beams. Especially 500 MeV/n ^{56}Fe ions yielded twice the number of foci than control or 150 MeV/n ^{4}He irradiated cells. Due to the bystander effect the number of damaged cells exceeded the number of hit cells. These data indicate that the early response of cells to high-LET radiation is modulated by the energy deposition of the particle in the cell. Thus, the correlation between the microdosimetric aspects of energy deposition and biological damage deserves further study.