INDUCTION OF CYTOGENETIC DAMAGE BY HZE ^{56}Fe PARTICLES *IN VIVO* IN BOTH DIVIDING AND NON-DIVIDING TISSUES

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INTRODUCTION

A chief concern for prolonged manned space flight is the risk associated with radiation exposure from Cosmic Rays. An important component of this radiation exposure is from Galactic Cosmic Rays containing high energy, heavy ions (HZE). Since ^{56}Fe ions are the most densely ionizing particles present in Galactic Cosmic Rays, studies are being conducted at Brookhaven National Laboratory using the Alternating Gradient Synchrotron (AGS) to define the biological effects associated with exposure to these particles. To understand the induction of genomic instability it is first important to define the total amount of cytogenetic genetic damage induced by the radiation exposure. Genomic instability has been suggested as a potential mechanism for the radiation induced cancer and as marker for cancer risk. These studies are directed toward understanding the relationships that exist between initial cytogenetic damage in important cell types and the induction of genomic instability.

METHODS

Five Wistar Rats were exposed to each of four graded doses of ^{56}Fe particles (1000 MeV/AMU) at 0.0, 0.2, 0.5 and 1.0 Gy using a dose rate of 0.2 Gy/min. Cells from regions of the respiratory tract that are known to be either sensitive (deep lung) or resistant (trachea) to the induction of cancer from high LET radiation and bone marrow cells which demonstrate genomic instability were isolated after exposure, placed in short term culture and cytogenetic damage evaluated. Indicators of cell proliferation and the frequency of chromosome aberrations and micronuclei were evaluated as a function of exposure, dose and time after exposure.

RESULTS

To date we have data which demonstrates that there was a decrease in mitotic index in the bone marrow as a function of dose (slope -0.29 X Dose) and an increase in mitotic index as a function of time (0.5- 5 hours) between exposure and sacrifice for each treatment. Since the bone marrow cells are rapidly dividing the frequency of chromatid aberrations was evaluated in the bone marrow. There was a well defined exposure related increase in chromatid deletions with a few chromatid exchanges also noted. It was also observed that the distribution of the aberrations in the cell population was very non-random with some cells containing multiple chromatid type of aberrations suggesting a non-random distribution of energy in the cell population. Micronuclei are being scored in the deep lung epithelial cells and in the tracheal epithelial cells. Such data will be compared to that derived following exposure to low LET gamma rays delivered at high and low dose rates as well as to exposure to radon exposures *in vitro* and following inhalation. Finally, the frequency of micronuclei will be compared to the frequency observed following exposure to alpha particles from a microbeam.

CONCLUSION

The frequency of initial chromosome damage is continuing to be evaluated and as tissue culture conditions are further defined will be related to the potential for the induction of genomic instability. The high Z particles induce mitotic delay and seem to produce non-randomly distributed damage in the bone marrow. Research supported by a Grant # 1 RO1 CA74053-01 from NIH/NCI and NASA with Washington State University Tri-Cities.