

GENE EXPRESSION CHANGES IN MOUSE INTESTINAL TISSUE FOLLOWING WHOLE-BODY PROTON- OR GAMMA-IRRADIATION

Ashley Purgason^{1,2}, Ye Zhang^{1,3}, Lingegowda Mangala⁴, Ying Nie⁵, Daila Gridley⁵, Stanley R. Hamilton⁴, Derek V. Seidel⁶ and Honglu Wu¹

¹NASA Johnson Space Center, Houston, Texas

²The University of Texas at Arlington, Arlington, Texas

³Wyle Laboratories, Houston, Texas

⁴The University of Texas MD Anderson Cancer Center, Houston, Texas

⁵Loma Linda University Medical Center, Loma Linda, California

⁶Texas A&M University, College Station, Texas

Crew members face potential consequences following exposure to the space radiation environment including acute radiation syndrome and cancer. The space radiation environment is ample with protons, and numerous studies have been devoted to the understanding of the health consequences of proton exposures. In this project, C57BL/6 mice underwent whole-body exposure to 250 MeV of protons at doses of 0, 0.1, 0.5, 2 and 6 Gy and the gastrointestinal (GI) tract of each animal was dissected four hours post-irradiation. Standard H&E staining methods to screen for morphologic changes in the tissue showed an increase in apoptotic lesions for even the lowest dose of 0.1 Gy, and the percentage of apoptotic cells increased with increasing dose. Results of gene expression changes showed consistent up- or down- regulation, up to 10 fold, of a number of genes across exposure doses that may play a role in proton-induced oxidative stress including Gpx2. A separate study in C57BL/6 mice using the same four hour time point but whole-body gamma-irradiation showed damage to the small intestine with lesions appearing at the smallest dose of 0.05 Gy and increasing with increasing absorbed dose. Expressions of genes associated with oxidative stress processes were analyzed at four hours and twenty-four hours after exposure to gamma rays. We saw a much greater number of genes with significant up- or down-regulation twenty-four hours post-exposure as compared to the four hour time point. At both four hours and twenty-four hours post-exposure, Duox1 and Mpo underwent up-regulation for the highest dose of 6 Gy. Both protons and gamma rays lead to significant variation in gene expressions and these changes may provide insight into the mechanism of injury seen in the GI tract following radiation exposure. We have also completed experiments using a BALB/c mouse model undergoing whole-body exposure to protons. Doses of 0, 0.1, 1 and 2 Gy were used and results will be compared to the work mentioned above. The most striking result preliminarily is that both strains of mice show a greater number of genes changing at the lowest dose of exposure for their respective pathways.