Chimeric Mouse Models for Space Radiation Risk Investigations

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Assessment of human health risks associated with space radiation exposure is based largely on the knowledge learned from studies in which animals, mostly rodents, are exposed to high-LET radiation on the ground. It has been recognized that translation of animal results to meaningful implications for human disease can be challenging, particularly for certain risk categories such as the high-LET radiation effects in the central nervous system (CNS). Considering limitations in utilizing non-human primates and clinical studies in humans, chimeric animals can potentially bridge the knowledge gap between rodents and humans. In a chimeric animal, a specific organ or a cell type is replaced with respective human cells that are functional. A number of chimeric mouse models have been developed in the medical research community to study human diseases, and some of the models can potentially be used for NASA applications. For instance, mice engrafted with human hepatocytes, which have been used in studies of genotoxicity from carcinogen exposures, can be used for quantification of space radiation damage. A chimeric brain model, which was shown to perform superiorly in memory and cognitive tests, can also be a candidate for studying the CNS effects of radiation. It has also been reported that mice engrafted with human hematopoietic progenitor cells were exposed to X-rays and high-LET Si ions to investigate the radiation effects in the immune system. In a pilot study, we use PXB mice whose livers contain >90% human cells. These mice are exposed to gamma rays for investigations of DNA damage and transcriptomics changes in the humanized livers. Results obtained from PXB mice will be compared non-engrafted control animals from the same background strain that are exposed to identical conditions. The aim of the study is to determine whether chimeric mouse models are suitable for investigations of space radiation risks.