

A novel, facilitative role of caspases in space radiation induced mutagenesis and carcinogenesisC-Y. Li¹, F. Li¹, J. Shen², X. Liu¹, J. Brogan¹, J.S. Bedford³, Y. Peng⁴¹Duke University Medical Center, Box 3135, Durham, NC 27514; ²University of Colorado School of Medicine, Aurora, CO; ³Colorado State University, Fort Collins, CO; and ⁴Purdue University, Lafayette, IN

Caspases are in general thought of as killers of cells that are barriers for carcinogenesis. However, based on our recent work showing a facilitative role for caspases in promoting epigenetic reprogramming in the induction of pluripotent stem cells (iPSC) from differentiated fibroblasts (Li *et al*, *Cell Stem Cell*, 2010, 7:508-20), we hypothesized that caspases may play a facilitative role in space radiation induced carcinogenesis. We have conducted a series of experiments to examine the effect of caspases in space radiation induced mutagenesis and carcinogenesis. Our results show that inhibition of caspases 3&7 significantly reduced radiation induced chromosomal aberrations in human IMR90 cells. On the other hand overexpression of a wild type caspase 3 increased chromosomal aberrations. Furthermore, we show caspases 3& 8 also have a significant role in space radiation induced carcinogenesis. Blocking caspases 3&8 significantly reduced 600 MeV ⁵⁶Fe ions induced anchorage independent growth in human mammary epithelial cells. These are exciting data that are counter-intuitive and may have significant implications in space radiation induced carcinogenesis. Experiments are under way to investigate the molecular mechanisms underlying these surprising observations.