

SPACE LIFE SCIENCES SYMPOSIUM (A1)  
Radiation Fields, Effects and Risks in Human Space Missions (4)

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HEART MITOCHONDRIAL GENOME MUTATIONS IN CB57BL/6 MOUSE DUE TO 6 GY PROTON  
RADIATION

**Abstract**

The mitochondrial genome is an ideal biomarker of diseases and environmental stressors such as proton radiation. Cardiac muscles have relatively large amounts of mitochondria, and many point mutations are linked to cardiovascular diseases. To understand the immediate effect of proton radiation on mammalian cardiovascular system at the molecular level, we sequenced the whole mitochondrial genome (16.3 kb) of C57BL/6 mouse heart tissue irradiated with 6 Gy and sacrificed after 4 hours. The sequenced mitochondrial genome was 16,301 bases, 2 bases longer than the published sequence for the same mouse strain. At the ND2 gene, one homoplasmic silent transitional mutation was found at site 04891T<sub>i</sub>C and one heteroplasmic site (C/A) at 04897. Both mutations were silent located at the 3rd codon position. A single Adenine heteroplasmic deletion at the L-strand origin of replication polyA tract between 05172 and 05182 and a two-base Adenine insertion at the tRNA<sup>Arg</sup> polyA tract between 09821 and 09830 were found. The proton-irradiated mouse mutation rate was calculated at  $1.2 \times 10^{-4}$ . Although all mutations detected were selectively neutral and not pathogenic, the rate of mutation was 8 times higher than normal, and higher than published somatic mutation rates observed in mice brain cancer cells and experimentally-induced mice tumor cells. Additional analyses substituting dominant nucleotides with variant nucleotides to account for non-dominant novel mutations suggested that the mutation rate in mice induced by proton-radiation could be as high as 12 times than normal in a relatively short period of time (4 hrs). These values predict high likelihood of fatal mutations to occur over a short period of time, suggesting that the effects of proton radiation for cancer therapy, and on biological systems during space travel, should be further evaluated.