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MITOCHONDRIAL GENOME MUTATIONS AFTER 24 HRS OF PROTON RADIATION

Abstract

To understand the 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 exposed to 0.1 Gy and 2.0 Gy proton radiation. Sham-irradiated served as controls (n=3 per group). The mice were then sacrificed after 24 hours. There were two transition mutations (both G to A) in two out of three mice exposed to 0.1 Gy proton. One mouse showed a homoplasmic change at the 1st codon position in COX III gene at position 9029 and constituted an amino acid change from Glycine (codon GGU) to Serine (codon AGU). The other mouse had a heteroplasmic change at the 1st codon position involving a nonsynonymous substitution from Aspartic Acid (codon GAC) and Asparagine (codon AAC) at position 15408 within Ctyb gene. All three mice that were proton-irradiated at 2.0 Gy showed mutations with animal 1 having a transition substitution (G to A), and two other mice both with transversions (T to A, and G to A). Animal 1 also exhibited an indel event at position 5943, and inferred to lead to a frameshift translation of the COXIII gene. All point mutations observed in 2.0 Gy-irradiated mice were heteroplasmic and involved nonsynonymous substitutions. The gene regions with mutations were ND2, COIII, Cytb and COX I. All observed mutations for 0.1 Gy and 2.0 Gy were expected to be deleterious, however, frameshift and transversional mutations detected at 2.0 Gy-irradiated mice appeared more consequentially fatal. Data from this study demonstrated that the number of mutations did not appear to show strict linear correlation, but the type of mutation and lethality appeared more serious as dosage increased from 0.1 Gy to 2.0 Gy.