LET and gender are critical factors in accelerating development of lymphoma in irradiated Bax transgenic C57Bl/6 mice

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Humans are exposed to sparsely ionizing (low LET) radiation from environmental sources and radiotherapy as well as densely ionizing (high LET) radiation during radiotherapy and from cosmic radiations, particularly during space travel. To test the hypothesis that defects in mitochondrial metabolism leading to increased ROS levels could alter responses to radiation, lymphoma-prone C57Bl/6 mice over expressing the mitochondrial-acting Bax protein in thymocytes (which demonstrate increased steady-state levels of superoxide; **FRBM** 44: 1677-1686, 2008) were irradiated with both low and high LET radiations and the onset of tumor formation was monitored.

Our results show that 10 cGy of high LET iron ions (150 keV/μm, 1 GeV, generated at Brookhaven National Laboratory) demonstrated a trend toward; and 100 cGy caused a significant dose dependent 6 week acceleration of lymphoma development in Bax38/1 animals. Strikingly, in the 100 cGy group, female Bax 38/1 mice developed lymphoma faster (18 weeks) than their male counterparts (24 weeks). Low LET (^{137}Cs) 10 and 100 cGy exposed Bax 38/1 and Bax 1 mice show a slight trend toward accelerated lymphoma development that is not dose-dependent nor statistically significant at this time. These findings support the hypothesis that genetic manipulations altering mitochondrial superoxide metabolism do accelerate the onset of lymphoma development following high LET radiations in Bax transgenic mice (more so than low LET radiation) and that this effect is greater in female mice, relative to male mice. (Supported by a joint grant from DOE/NASA, DE-SC0000830).

Fig 1: Irradiation with 100 cGy of High LET (150 keV/μm) Iron ions significantly accelerates lymphoma development in Bax 38/1 Mice

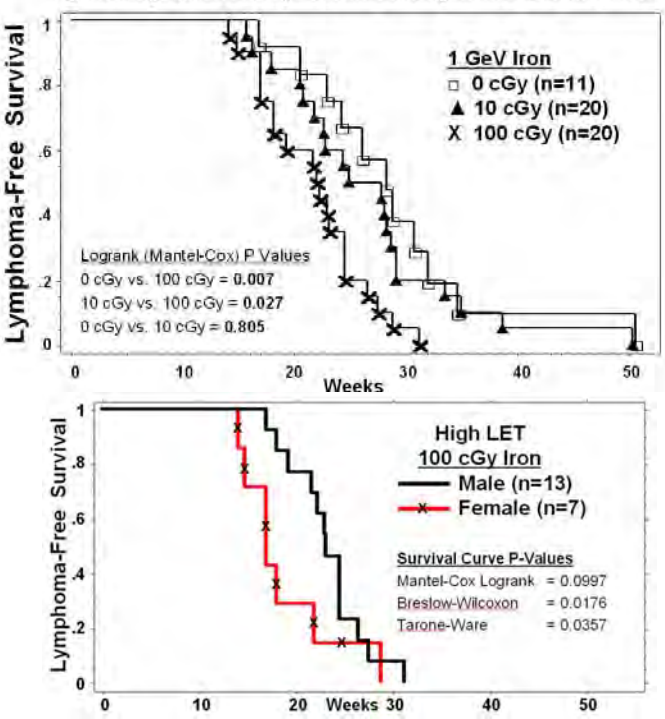
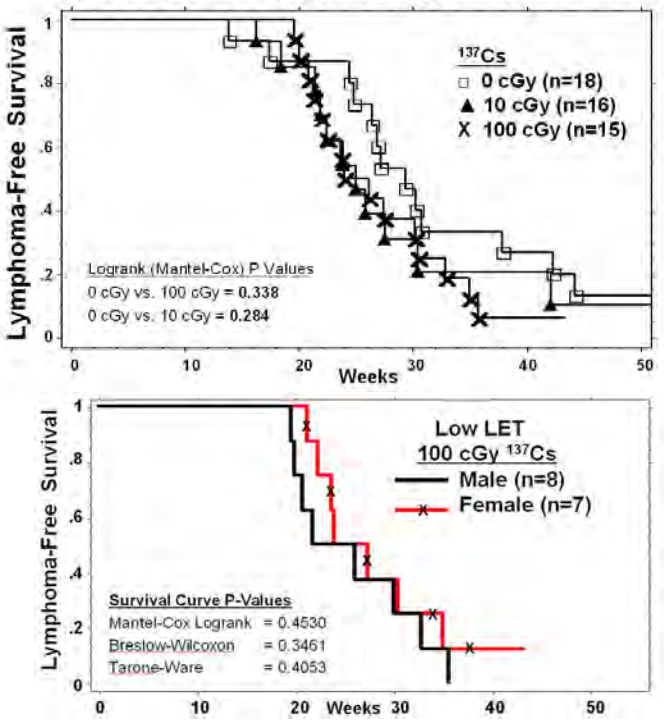
Fig 2: Irradiation with 100 cGy of Low LET (~1 keV/μm) ^{137}Cs does not significantly accelerate lymphoma development in Bax 38/1 Mice