Superoxide dismutase protects osteoprogenitors from irradiation with low LET but not high LET species

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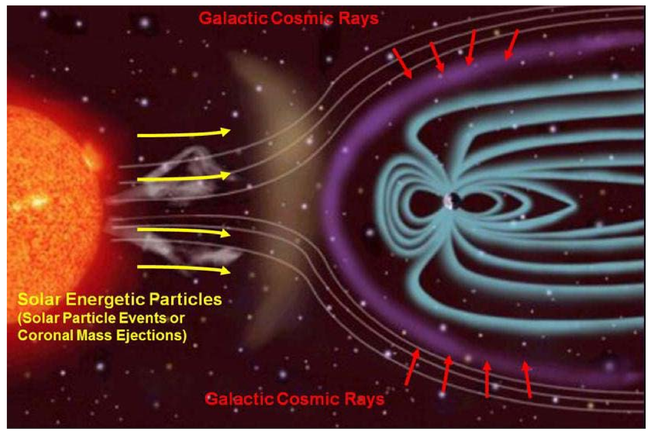
ABSTRACT

Ionizing radiation-induced bone loss appears to be a two-stage process: first an early increase in pro-resorption cytokines and increased bone resorption by osteoclasts, followed by a decrease in bone formation by osteoblasts. This results in a net loss of mass in mineralized bone tissue. The molecular mechanisms underlying the imbalance in bone remodeling caused by exposure to radiation are not fully understood. We hypothesized that the radiation-induced rise in reactive oxygen species (ROS) damages osteoblast progenitors, leading to a decrease in number and activity of differentiated progeny. We have shown that a diet high in antioxidant capacity prevents radiation-induced bone loss in adult mice (Schreurs et al. 2016) by reducing the early increase in pro-resotption cytokines. Here, we investigated the damaging effects of radiation exposure on cells in the osteoblast lineage, testing if addition of the exogenous antioxidant enzyme, superoxide dismutase (SOD) can mitigate radiation damage. Osteoprogenitors were grown *in vitro* from the marrow of 16wk old, male C57Bl/6 mice. Cells were irradiated 3 days after plating (day 0) with either gamma (^{137}Cs, 0.1-5Gy) or iron (^{56}Fe, 600 MeV/n, 0.5-2Gy), and then grown until day 10. SOD or vehicle was added 2 hours before irradiation (SOD at 200U/ml), twice a day and up to day 5, for a total of 2 days treatment. Cell behavior was assessed by: (a) colony number (counted on day 7), (b) DNA content (surrogate for cell number) to assess cell growth (percent change between day 3 and day 10) and (c) alkaline phosphatase activity (osteoblast differentiation marker). Results show that SOD protected cells from the adverse effects of low-LET ionizing radiation, but not high-LET radiation. These novel results provide an interesting platform to explore further diverse effects and damages caused by low-LET and high-LET, pointing toward different mechanisms and possible intervention strategies for radiation-induced bone loss.

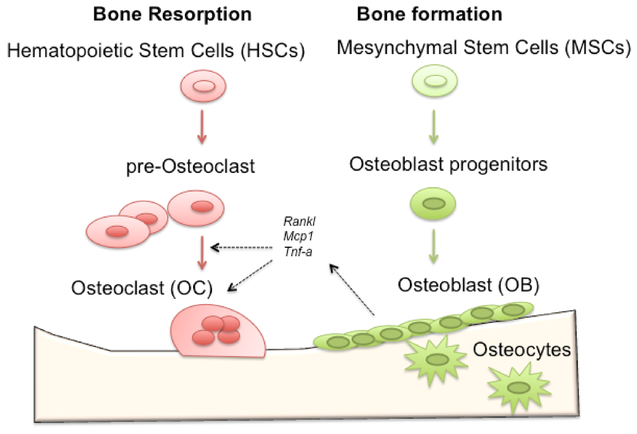
PROBLEM

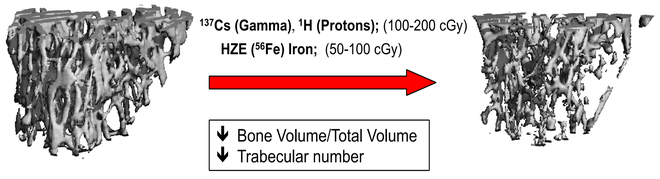
Future long-duration space exploration beyond the earth's magnetosphere will increase human exposure to space radiation and associated risks to skeletal health.



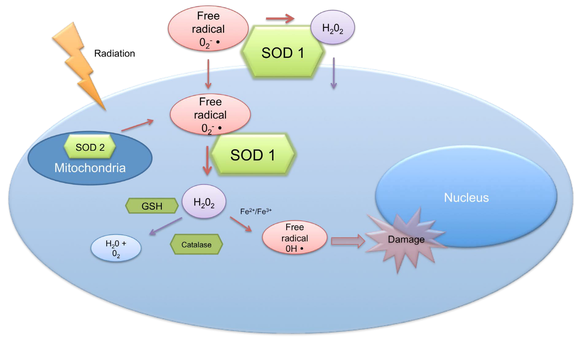
BACKGROUND

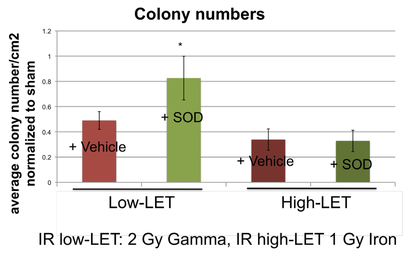
Bone remodeling: a balance between bone resorption by osteoclasts and bone formation by osteoblasts.





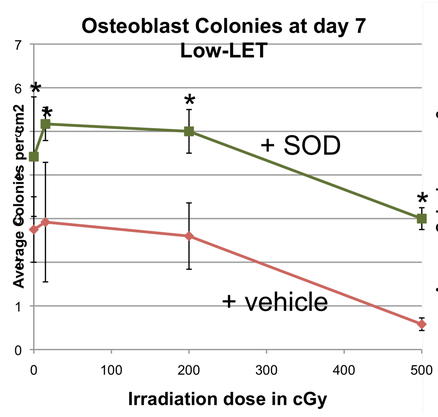
RESULTS

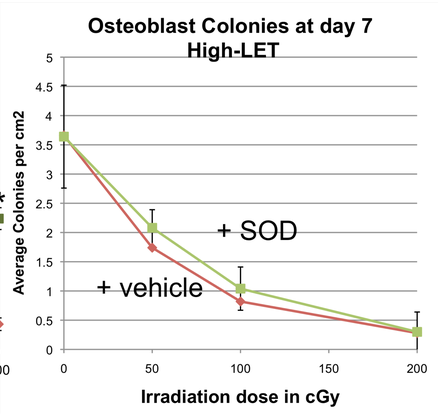


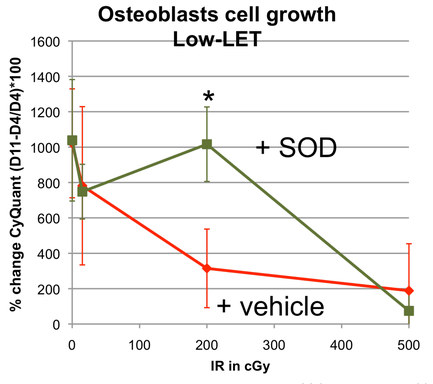


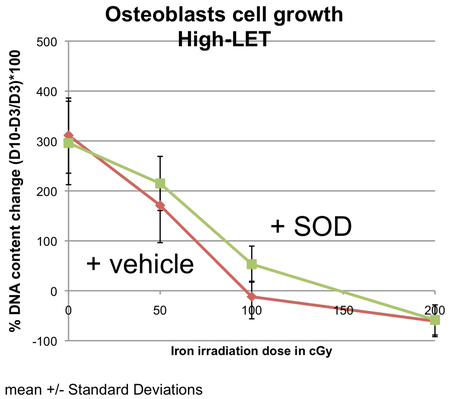
IR low-LET: 2 Gy Gamma, IR high-LET 1 Gy Iron

SOD protects osteoblast progenitors in low LET irradiation but not high LET radiation









Values expressed in mean +/- Standard Deviations

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