Mitigating HZE radiation-induced deficits in marrow-derived mesenchymal progenitor cells and skeletal structure

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

We showed previously that a diet supplemented with Dried Plum (DP) prevents short term bone loss caused by total body irradiation (Schreurs et al. Scientific Reports, 2016 Feb 11;6:21343).

HYPOTHESIS
DP diet mitigates persistent, damaging effects of HZE radiation on bone structure and marrow-derived osteoprogenitors and stem cells.

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

METHODS
Animals: Male C57Bl/6J mice, 16 wk old at time of total body irradiation (TBI) Study design: ZG2 study design: Control diet X Dried Plum (25%) and (60Gy-sham vs IR); Radiation: Total Body Irradiation (TBI); single exposure, > 50 Gy
-IR: 0.86 Gy/min
-Dual (1Gy total dose) Sequential: proton (0.25Gy)- Fe(0.5Gy)-proton(0.25Gy): E = 600 MeV/n
-LET: 6Fe(1Gy)
-TimeFrame: - prefused 14-21 days with control diet (CD) or Dried Plum diet (DP)
-Samples recovered 1d, 11d or 30d post TBI
Gene expression: qPCR
Statistics: data shown are Mean ± S.D., 1-factor or 2-factor ANOVA, Takey-Kramer post hoc

RESULTS
DP reduced expression of pro-osteoclastogenic cytokines 1d after TBI (137Cs)

DP reduced serum oxidative stress marker (serum TBARS) 11d days after TBI (137Cs)

DP prevented damage to marrow-derived osteoprogenitors 30d after TBI (56Fe)

SUMMARY/CONCLUSIONS
• DP diet fully protected radiation-induced bone loss from low LET or high LET radiation
  -relevance for spaceflight and radiotherapy
• Possible mechanisms for DP radioprotective effects:
  -mitigate early increase in pro-osteoclast cytokines
  -reduce oxidative damage, in bone and systemically
  -prevent damage to osteoprogenitors and mesenchymal stem cells

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