**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.

Ionizing radiation & bone loss: clinical and space relevance
- Radiation Therapy Sequelae
  - Osteoradionecrosis (rare)
  - Contributes to weakening: post-menopausal and age-related osteoporosis
  - Secondary tumor induction outside magnetosphere and long durations

Prior evidence shows that total body irradiation stimulates osteoclastogenesis and impairs both osteoclastogenesis and bone formation by mature osteoblasts.

**Methods**

Animals: Male C57Bl/6J mice, 16 wk old at time of total body irradiation (TBI)
Study design: 2x2 study design: Control diet x Dried Plum (25%) and (0Gy-sham vs IR);
Radiation: Total Body Irradiation (TBI); single exposure, 2 Gy
+137Cs
-Dual (1 Gy total dose) 0.86 Gy/min
-Sequential: proton (0.25Gy/y) = Fe(0.50Gy/y)-proton (0.25Gy/y)
-IR: E = 600 MeV/n
-LET: Fe(10 Gy)
Timeframe: 

- preleft 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, Tukey-Kramer post hoc

**Results**

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

DP reduced serum oxidative stress marker (serum TBARS) 11d 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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