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 osteoblastogenesis and bone formation by mature osteocytes (Schreurs et al. Scientific Reports, 2016 Feb 11;6:21343).

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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