Title: Candidate nutritional countermeasure to mitigate adverse effects of spaceflight

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Problem statement: *During spaceflight, astronauts are subjected to microgravity as well as radiation, both of which have adverse effects on bones, soft tissues and organs, possibly by shared mechanisms. For this reason there is a need to identify broad-spectrum countermeasures to protect multiple tissues from both insults.*

The spaceflight environment poses multiple challenges to homeostasis, including microgravity and ionizing radiation. Together, these factors contribute to cellular stress, and effects include increased generation of reactive oxygen species (ROS), oxidative and DNA damage, cell cycle arrest and cell senescence. We have shown that a purified diet supplemented with dried plum (DP, 25%) conferred full protection of cancellous structure from the rapid bone loss caused by exposure to ionizing radiation (*Schreurs et al. 2016*). Based on these promising results for a new countermeasure to prevent space radiation induced-tissue damage, we will conduct additional studies to advance the potential countermeasure to a higher CRL level. We will test the DP diet for its ability to prevent bone loss caused by simulated microgravity as well as exposure to radiation. This will be achieved by exposing mice to each factor (simulated microgravity and radiation) alone and in combination. We **hypothesize** that spaceflight conditions lead to oxidative damage and bone loss, and that DP, a dietary additive rich in antioxidant and polyphenolic compounds, is an effective countermeasure for multiple tissues, including bone. To test this hypothesis we will accomplish the following aims:

Aim 1 *Determine if the antioxidant rich diet DP prevents simulated microgravity-induced bone loss.*

Aim 2 *Determine if DP prevents simulated spaceflight-induced bone loss (microgravity and radiation combined).*

Aim 3 *Determine if DP is effective as a countermeasure for adverse effects of simulated microgravity and radiation on non-skeletal tissues (brain, eye).*