

## **Methionine intake modulates radiation damage in the gut**

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The use of radiation therapy in cancer is limited by normal tissue toxicity. Our goal is to increase the differential between the damage inflicted to the tumor relative to the normal surrounding tissue. Our previous work showed that high levels of dietary methionine exacerbate radiation damage in the gut. Methionine is an essential amino acid that also has a role as a methyl donor and in the synthesis of the antioxidant glutathione. Lower levels of methionine intake are associated with an increase in longevity in animal models. We also showed that reducing dietary intake of the essential amino acid methionine sensitizes tumors to radiation therapy without inducing weight loss. Furthermore, methionine restriction decreases markers of inflammation and increases markers of tight junction in the healthy murine gut. In this experiment, we irradiated the abdominal area with a single dose of 12.5 Gy X-ray using a Small Animal Radiation Research Platform (SARRP). Half of the mice remained on a standard diet (0.65% methionine) while the other half received a methionine-restricted diet (0.12% methionine) for one week preceding and one week following radiation. At one week after radiation, we observed evidence of gut protection from radiation in animals that were consuming a methionine-restricted diet versus a control diet. This indicates that lowering the amount of methionine in the diet of patients receiving cancer radiotherapy may help in mitigating side effects.