Exposure to ^{56}Fe radiation induces persistently increased serum levels of known colorectal cancer biomarkers in C57BL/6J mice

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Abstract:
Purpose: Radiation is a known risk factor of colorectal cancer (CRC) and ^{56}Fe radiation has been shown to enhance intestinal tumorigenesis in mouse models. Here, we investigated ^{56}Fe-induced changes in serum levels of established biomarkers reported to be associated with CRC risk and correlated the results at the receptor level in the intestinal tissues.
Materials and Methods: Six- to eight-week-old female C57BL/6J mice (n= 8/group) were exposed to whole body ^{56}Fe radiation (1.6Gy, 1 GeV/n), at the NASA Space Radiation Laboratory. Serum and gastrointestinal tissues were collected two and twelve months after radiation and analyzed for insulin like growth factor 1 (IGF-1), IGF1R, leptin, and adiponectin levels by ELISA, and their corresponding receptors IGF1 receptor (IGFR1), Adiponectin receptor-R1 (AdipoR1), Adiponectin receptor-R2 (AdipoR2) and Ki67 by immunohistochemistry in intestine and colon.
Results: ^{56}Fe radiation exposure caused a significant increase in serum IGF1, insulin-like growth factor binding protein 3 (IGFBP3) and leptin levels at two months post-exposure. The levels of free leptin and free IGF1 measured by calculating leptin/adiponectin and IGF1/IGFBP3 ratio showed a distinct pattern at 2 and 12 months post-exposure, with significantly high free leptin at 2 months and higher free IGF1 at 12 months, respectively. Further, the immunohistochemical analysis in intestine and colon tissues demonstrated increased expression of IGF1R and decreased expression of AdipoR1/R2 receptors at both two and twelve months post-exposure.
Conclusions: Increased levels of known CRC biomarkers in mice serum correlates with the increased expression of receptors in the tissues and are supportive of our ^{56}Fe-induced increased intestinal tumorigenesis data in $APC^{Min/+}$, a well-studied mouse model of CRC. When considered with increased Ki67 staining, data presented in this study has potential implication for ^{56}Fe-induced cancer risk estimation.