AN EXTRA COPY OF P53 SUPPRESSES INITIATION OF KRAS-DRIVEN TUMORS BUT NOT RADIATION-INDUCED LYMPHOMAS

E. J. Moding[1], H. D. Min[2], K. D. Castle[1], C. L. Lee[2], D. G. Kirsch[1,2]
[1]Department of Pharmacology and Cancer Biology (everett.moding@duke.edu), [2]Department of Radiation Oncology (david.kirsch@duke.edu), Duke NASA Specialized Center of Research, Duke University Medical Center, Durham, NC 27708

The tumor suppressor p53 has been shown to block tumor progression in multiple tumors types. Radiation-induced cancer following exposure to space radiation represents a major risk for astronauts traveling into deep space. Although the mechanisms of space radiation-induced cancer are poorly understood, p53 has been shown to regulate many cancers initiated by terrestrial radiation. To investigate the role of p53 in lung carcinogenesis and lymphomagenesis in the presence and absence of radiation exposure, we exposed *LA-1 Kras*^{G12D} mice with wild-type p53 or an extra copy of p53 (super p53) to whole body irradiation with five daily 1.2 Gy fractions of 320 kVp X-rays or five daily 0.2 Gy fractions of 600 MeV/nucleon ^{56}Fe and compared tumor formation in these mice with unirradiated controls. We found that an additional copy of p53 suppressed both lung tumor and lymphoma initiation in the absence of radiation. Exposure to X-rays accelerated lymphoma formation, but neither X-ray nor ^{56}Fe exposure affected lung tumor burden at six months after irradiation. In contrast to unirradiated mice, super p53 and wild-type p53 mice developed lymphomas at similar rates following X-ray or ^{56}Fe radiation exposure. These results demonstrate that although p53 suppresses initiation of Kras-driven tumors, an extra copy of p53 does not protect against radiation-induced lymphomas.