Methionine intake modulates radiation damage in the gut

Sarita Garg[1], L. Clai Morehead[1], Henrique Rodrigues[2], Oscar Zuniga[2], Lokesh Akana[2], Kimberley Krager[3], Nükhet Aykin-Burns[3], Adam R. Wolfe[2], Isabelle R Miousse[1],

Departments of Biochemistry and Molecular Biology[1], Radiation Oncology[2], and Pharmaceutical Sciences[3]

University of Arkansas for Medical Sciences

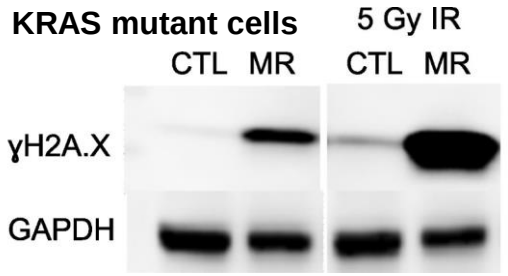
Problem: Normal tissue damage limits the radiation dose used in radioresistant KRAS mutant rectal tumors

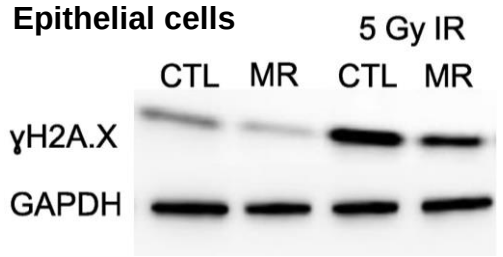
1. KRAS mutant cells show differences in the metabolism of methionine

Biochemical	
S-1-pyrroline-5-carboxylate	sphingosine
1-methylhistidine	hexadecasphingosine (d16:1)*
S-methylmethionine (SAM)	heptadecasphingosine (d17:1)
S-adenosylhomocysteine (SAH)	uracil
cysteine	flavin adenine dinucleotide (FAD)
N,N,N-trimethyl-alanylproline betaine (TMAP)	beta-guanidinopropanoate
sphingadienine	thioproline

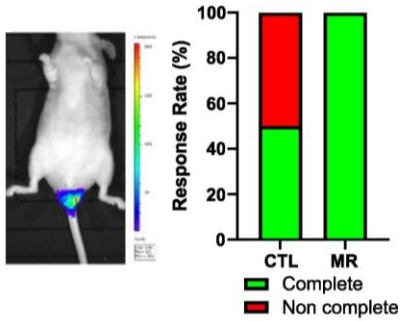
Human colorectal cancer cell CRISPR-engineered to express either KRAS wildtype or G13D

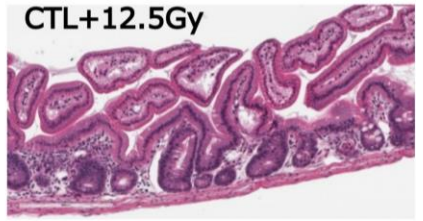
2. KRAS mutant cells and normal epithelial cells have opposite phenotype in response to low methionine

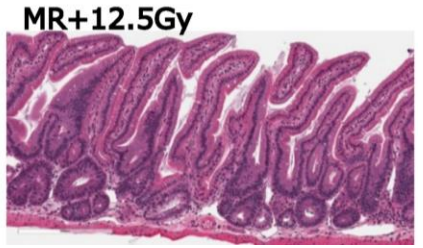




3. Low methionine intake sensitizes tumors and protect the epithelium







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