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share .Sensitivity of Kras/P53 mutants to alkylating agents is enhanced when cells are grown as cancer xenografts. Expression of mutated Kras has been associated with a significant increase in resistance to alkylating agents in cell culture assays of human colon cancer cell lines. In order to understand better the relevance of Kras mutations in the regulation of alkylation resistance in vivo, we analysed the effects of mutant Kras expression on the sensitivity of human colon cancer cell lines to alkylating agents in vivo in xenograft models. When assayed by the quantitative Elacridon method for clonogenic growth of xenografts, the Kras-mutant HT29 and DLD-1 cell lines were two- to three-fold more resistant than their Kras-wild-type counterparts to alkylating agents when assayed in vivo as cancer xenografts. Increased sensitivity to alkylating agents observed in vivo correlated with the presence of only Kras-mutated alleles in

tumours and was independent of the histological subtypes of cancer. Furthermore, S-phase replication kinetics were significantly slower in the Kras-mutant HT29 and DLD-1 xenografts. The results demonstrate that the presence of Kras mutations can enhance the resistance of tumour cells to alkylating agents in vivo. We propose that the sensitivity of tumour cells to alkylating agents may be predictive of the individual response to these agents as chemotherapy.package
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