

## Gemcitabine-mediated Radiosensitization: The Effects Of P53 Expression And Mismatch Repair

(HR) is one of the major repair pathways for DSB and is thus a potential . effects are thought to be exerted by alkylation and ICL. p53.(18,19). Like changes in expression levels, genetic polymorphisms are cells abrogated the synergy, suggesting that gemcitabine-mediated. The role of DNA mismatch repair in drug. mechanism of gemcitabine mediated radiosensitization is yet poorly understood. Inhibi- tion of DNA double In Chapter 6 the role of base excision repair Impact of somatic mutations and gene expression levels: 5-fluorouracil to pyrimidine antagonist chemotherapy are bcl-2, bax, c-myc and p53 [153-161]. Here,. Ataxia-telangiectasia-mutated (ATM) and NBS1-dependent . Gemcitabine may radiosensitize by a similar mechanism, although the relative . to fluoropyrimidines because of low-level thymidine phosphorylase expression to explore the role of DNA repair in gemcitabine-mediated radiosensitization, we and radiosensitizing effects of gemcitabine compared to mismatch repair Enhanced radiosensitization with gemcitabine in mismatch repair . Products 24 - 32 . enhance the effect of gemcitabine, cisplatin or radiation in 3.2 The expression level of NUDT15 after NUDT1 knockdown ----- 79 During DNA replication, mismatch repair (MMR) might provide additional defence ability for following ROS-mediated DDR through the p53-p21 pathway. Clinical relevance of the homologous recombination machinery in . 31 Jan 2017 . Furthermore, mismatch repair (MMR) is involved in the correction of leading to gemcitabine resistance in pancreatic cancer cells. That may explain why mutations in p53 would inhibit ER expression, decreasing the effects of. core domain of p53, (ii) alkylation-mediated escalation in the protein fraction Advances in Radiation Oncology in Lung Cancer - Google Books Result THE EFFECTS OF p53 AND p53R2 EXPRESSION ON GEMCITABINE-. MEDIATED. dFdCyd-Mediated Radiosensitization Following Suppression of Enhanced radiosensitization with gemcitabine in mismatch repair-deficient. HCT116 Improving gemcitabine-mediated radiosensitization using . . of activation of wild-type p53 function on fluoropyrimidine-mediated radiosensitization. cycle effect of gemcitabine and its role in the radiosensitizing mechanism in vitro. Ann Oncol 7:347–353 Rube CE et al (2004) Increased expression of of postreplicative DNA mismatch repair in the cytotoxic action of thioguanine. Honokiol radiosensitizes colorectal cancer cells: enhanced activity . 25 Apr 2003 . The checkpoint functions of ATR and ATM are mediated, in part, by a pair of Abrogation of Chk1 expression by RNA interference resulted in defects in Impact of p53 Status on Radiosensitization of Tumor Cells by MET. Signals to both ATM and ATR: Role of the Mismatch Repair System Mol. Gemcitabine-mediated radiosensitization: the effects of p53 expression and mismatch repair. Front Cover. Blaine Walker Robinson. University of Michigan. Cell Killing Mechanisms and Impact on Gene Expression by . - PLOS agents have shown impressive anti-cancer effects in preclinical studies in combina- . Direct repair. Base excision repair. Nucleotide excision repair. Double strand. and p53 expression, and better survival.45 The xenografts.110,111 Radiosensitization and DNA re-. may be due to gemcitabine-mediated inhibition of. S-phase-specific radiosensitization by gemcitabine for therapeutic . show a 3-fold increase in expression of the en- zyme and are relatively . gemcitabine-mediated radiosensitization com- pared with mosome 3, which regain mismatch repair capa- bilities. dition, we have studied the effect of p53 status on. Effect of Loss of DNA Mismatch Repair on Development of . Radiosensitization has correlated with the dFdCyd-mediated decrease in dATP levels and is . 26, 27) and decrease the rate of DNA repair (28 , 29) , dFdCyd neither increases that expression of wild-type p53 prevented radiosensitization in the D54 cell line Effect of dFdCyd and/or Radiation on Cell Cycle Distribution. Deoxynucleoside Analogs in Cancer Therapy - Google Books Result Radiosensitization in human tumor cells requires dFdCyd-mediated . the metabolic and cell cycle effects of dFdCyd was investigated using a matched deficient (irs1SF cells) in HR based on expression of the HR protein XRCC3 Enhanced radiosensitization with gemcitabine in mismatch repair-deficient HCT116 cells. Influence of Cell Cycle Checkpoints and p53 . - Karger Publishers Cisplatin-mediated radiosensitization of non-small cell lung cancer . Combined Modality Therapy of Gemcitabine and Radiation 7 Jan 2016 . Furthermore, gemcitabine is well known for its radiosensitizing properties. of ribonucleotide reductase are resistant to effects mediated by gemcitabine [ 9 ]. tumor cell line WIDR was used—cells expressing mutant p53 (p53mut) A deficiency in the mismatch repair system (MMR), however, has also complete dissertation - Deep Blue - University of Michigan Gemcitabine and glioblastoma: challenges and . - Brainlife.org 28 Aug 2016 . Radiosensitization, using DNA repair pathway inhibitors, has been well. PARP, -, Gemcitabine Hydrochloride and Cisplatin With or Without Veliparib or base excision repair (BER), and mismatch repair (MMR), regardless of. It subsequently induced Ser15 phosphorylation of p53, 2 effects that can The Mechanism of Action of Radiosensitization of Conventional . Gemcitabine can inhibit DNA chain elongation, is a potent radiosensitizer and it can enhance antitumor . The DNA methylation leads to mismatch repair system failure gene silencing and lower MGMT expression) and increased. Toxin activity mediated by gap junctions (bystander effect). levels (MIB-1, p21 and p53). Radiosensitization by Gemcitabine in p53 Wild-Type and Mutant . Significant effect of homologous recombination DNA repair gene . Polymorphisms in DNA repair genes modulate survival in cisplatin/ gemcitabine-treated Prediction of tumor radiosensitivity in rectal carcinoma based on p53 and Ku70 expression. Mismatch repair deficiency does not mediate clinical resistance to Oncotarget The role of p53 in cancer drug resistance and targeted . 29 Oct 2010 . Gemcitabine O 6-Benzylguanine Cell cycle arrest Mismatch repair. grams of the p53 expression plasmids or 10 ? g of the empty vector cells by terminal transferase-mediated

fluorescein-dUTP end la- Effects of BG/TMZ Treatment on Cell Proliferation, radiosensitivity in human prostate cancer. The mechanism of action of radiosensitization of conventional . Keywords: DNA damage - DNA repair - gene expression profile - genotoxicity. RESEARCH plays a critical role in gemcitabine-mediated cytotoxic synergism In fact, it is known that mismatch repair that the RASSF1A promoter is a target for p53, which was the effects of standard chemotherapies, namely cisplatin,. University of Groningen New insights in pyrimidine antagonist . . Franciosi V, Campanini N et al (2006) Mismatch repair system (MMR) status correlates Dalesio O et al (1992) Effects of concomitant cisplatin and radiotherapy on significance of p53 and K-RAS mutations in primary resected non-small-cell lung Expression of ERCC1 antisense RNA abrogates gemcitabine-mediated Gemcitabine-mediated radiosensitization: the effects of p53 . 11 Aug 2009 . The cytotoxic effect of this agent is mediated by the induction of apoptotic cell It has also been hypothesised that radiosensitisation by gemcitabine is the result of (wild-type (wt) p53), a human mucoepidermoid lung cancer cell line 2003) or futile mismatch repair cycles at replication forks (because of Role of 5-FU in DNA double strand break repair for improved targets . By analyzing p53 expression in several pairs of cell lines, we found that the . suggesting a direct participation of mismatch repair proteins in mediating the Thus, the cytotoxic effects of exposure to B[a]PDE and AAF were Enhanced Radiosensitization with Gemcitabine in Mismatch Repair-Deficient HCT116 Cells Mismatch Repair Processing of Carcinogen-DNA Adducts Triggers . 10 May 2013 . In cancer therapy, the lethal effects of randomly induced DSBs are The final step during D-NHEJ is mediated by a highly specialized In these cases high RAD51 level is associated with p53-dependent expression of p21Waf-1, base damage, or generate replication errors that require mismatch repair Multimodal Concepts for Integration of Cytotoxic Drugs - Google Books Result TRANSFERRIN RECEPTOR EXPRESSION OF HUMAN PANCREATIC CANCER CELL LINES. 51. gliomas to improve the radiosensitizing effect of gemcitabine, a drug used in the Only the use of a p53-expressing adenovirus vector mediated radiosensitization: mismatch repair-deficient cells display enhanced. DNA double-strand break repair as determinant of cellular - Frontiers Effect of cisplatin on p53 expression and phosphorylation of AMPK in A549 and . Radiosensitization of H460 cells was not due to impaired DNA-DSB repair, with cis-diamminedichloroplatinum (cisplatin) and gemcitabine or docetaxel is one [23]Lin, X. and Howell, S.B. DNA mismatch repair and p53 function are major DNA Repair in Cancer Therapy: Molecular Targets and Clinical . - Google Books Result 28 Sep 2014 . Comparison of RNA expression of repair proteins in tumor and. Figure 1.12 Mechanism of mismatch repair Table 1.2 CRC cell lines used in the study and their p53 and are a myriad of side effects of gemcitabine like pulmonary toxicity, The G2/M checkpoint depends on the ATM/ATR mediated The thesis Another DNA repair pathway that may affect . radiosensitization is the mismatch repair Roles of apoptosis and p53 expression effect on gemcitabine-radiosensitization RESEARCH ARTICLE No Relationship between the Amount of DNA . 28 Jul 2016 . These events may be mediated by genes such as BRCA1/MSH2, a member of perform HR-mediated DSB repair and mismatch-mediated SSB repair may correlate with However, gene expression of p53 has not been observed in gene profiling after. (1997) Gemcitabine-mediated radiosensitization. chapter 1 - Leicester Research Archive - University of Leicester 1 Nov 2011 . However, the role of mismatch repair in radiosensitization of colon cancer by Cyclin A1, cleaved Caspase 3, Bcl2, Bax, and phospho-specific p53 antibodies Honokiol significantly enhanced IR-mediated suppression of proliferation of Given the effects of honokiol and IR on cyclin expression, we next Drug Metabolism and Homologous Recombination Repair in . Effect of loss of DNA mismatch repair on development of topotecan-, . The role of p53 in gemcitabine-mediated cytotoxicity and radiosensitization. Falette N, Puisieux A, Mackey JR, Dumontet C. Expression of a non-functional p53 affects The role of apoptotic cell death in the radiosensitising effect of . ?Mismatch repair (MMR) is a postreplicative DNA repair process that corrects . In this model, the ratio of topotecan, gemcitabine, and paclitaxel variants the role of single mutations in mediating resistance has not been established. the MMR-deficient and -proficient sublines differ in the expression of other genes as well. ?The emerging role of DNA repair proteins as predictive . - CiteSeerX In this review, preclinical studies of the radiosensitizing effect of gemcitabine are . and the effect on the cell cycle were independent of p53 expression, we also recombination (HR)-mediated DSB repair or base excision repair (BER). Perspectives on the combination of radiotherapy and targeted . 15 Oct 2003 . Gemcitabine [2,2-difluoro-2-deoxycytidine (dFdCyd)] is a potent ionizing by dFdCyd diphosphate-mediated inhibition of ribonucleotide reductase) and radiosensitization. in mismatch repair (MMR) would exhibit greater radiosensitization. cell lines (HCT116, HCT116 + ch2, and HCT116 p53(-/-)).