Use of anticancer chemotherapeutics as radiation response modifiers in murine hepatocarcinoma

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**Background** Radiotherapy of hepatocellular carcinoma in human has been a challenging area of oncology practice due to its radioresistance as well as complication risk of adjacent organs. However, recent studies have shown efficacy of radiotherapy in combination with chemotherapy. In this study, we investigated efficacy of anticancer chemotherapeutic agents as radiosensitizers using murine hepatocarcinoma model.

**Methods** HCa-1, a murine hepatocarcinoma was transplanted to male C3H/HeJ mice. This tumor is highly radioresistant with 50% tumor cure dose (TCD50) of more than 80 Gy. When tumors grew to 8 mm, mice were treated with 25 Gy radiation and various chemotherapeutic agents including TNF-α, 5-Fu, adriamycin, cisplatinum, paclitaxel, and gemcitabine. Tumor response to the treatment was determined by tumor growth delay assay and by enhancement factor. In case of enhancement of antitumor effect by tested drugs, underlying mechanism was investigated with regard to induction of apoptosis and its regulating molecules.

**Results** Among the tested drugs, gemcitabine appeared to enhance the antitumor effect of radiation. Other drugs, such as TNF-α and paclitaxel have shown simple additive effect while the antitumor effect of radiation plus the remaining drugs were less than additive. Underlying mechanism involved additive effect in induction of apoptosis.

**Conclusion** By searching drugs that can beneficially interact with radiation, anticancer chemotherapeutics can be used as radiation response modifier with additional advantage of their own antitumor effect and proved safety.