学 位 論 文 の 要 旨

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主論文の題名

In vivo optical pathology of paclitaxel efficacy on the peritoneal metastatic xenograft model of gastric cancer using two-photon laser scanning microscopy

主論文の要旨

Background We previously visualized in vivo responses to chemotherapy in a colorectal liver metastatic xenograft model using in vivo real-time and time-series intravital two-photon laser scanning microscopy (TPLSM). In this study, we established the method for evaluating the response of peritoneal xenografts to chemotherapy of metastatic gastric cancer using intravital TPLSM.

Methods Red fluorescent protein-expressing gastric cancer cells (NUGC4) were inoculated into the peritoneal cavity of green fluorescent protein nude mice.

Results Laparotomy revealed that 2 weeks after inoculation, macroscopic peritoneal metastatic nodules were formed. The first intravital TPLSM session revealed that they were composed of red tumor cell clusters and green surrounding stroma. Paclitaxel was administered intraperitoneally after the first TPLSM three times a week for 7 days in the treatment group. At the second laparotomy, there were significantly fewer and smaller nodules in the treated mice than in the controls. The second intravital TPLSM session showed tumor cell fragmentation, swelling, and nuclear condensation in the metastatic nodules—a response to chemotherapy. There were multinuclear tumor cells in the paclitaxel-treated living mice.

Conclusions Our method may become a powerful tool for evaluating the efficacy of novel anti-gastric cancer drugs in a preclinical murine model with minimum interindividual variation.