

学 位 論 文 の 要 旨

三 重 大 学

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<p>主論文の題名</p> <p>Intravital imaging of the effects of 5-fluorouracil on the murine liver microenvironment using 2-photon laser scanning microscopy</p> <p>主論文の要旨</p> <p>5-fluorouracil (5FU) is often used in the treatment of colorectal cancer. 5FU can improve the median overall and disease-free survival rates and reduce recurrence rates in patients who have undergone curative surgical resection. But, in the adjuvant setting, whether 5FU eradicates clinically undetectable micrometastases in target organs such as the liver or inhibits the adhesion of circulating tumor cells has not been established. 5FU was administered after the inoculation of red fluorescent protein-expressing HT29 cells to examine its inhibitory effect. 2-photon laser scanning microscopy was performed at select time points for time-series imaging of liver metastasis of green fluorescent protein-transgenic mice. We quantified the cell number in vessels to evaluate the response to chemotherapy of the tumor microenvironment. HT29 cells were visualized in hepatic sinusoids at the single-cell level. In a few hours after injection (early stage), time-series imaging revealed that the number of caught tumor cells gradually decreased over time. In the 5FU treatment group, there was no significant difference in the cell number in the early stage. At the time of 1 week after injection (late stage), a difference in morphology was observed. 5FU eradicates clinically undetectable micrometastases in liver tissues by acting as a cytotoxic agent opposed to preventing adhesion. Time-series intravital 2-photon laser scanning microscopic imaging of metastatic tumor xenografts may facilitate the screening and evaluation of new chemotherapeutic agents with less interindividual variability.</p>			