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A Superficial Colon Tumor Model Involving Subcutaneous Colon Translocation and Orthotopic Transplantation of Green fluorescent Protein-Expressing Human Colon Tumor

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Background: The orthotopic transplantation model of human tumor has been demonstrated to be more patient-like animal tumor model. However, observations of tumor progression and metastasis are limited by the deep location of the colon or limited deep penetration ability of fluorescence through tissue. The purpose of this study is to establish a superficial orthotopic model to allow easier real-time visualization and more sensitive monitoring of fluorescent orthotopic colon tumor.

Methods: Human colon cancer HT-29 cells were transduced with a pLPCX expression retroviral vector containing GFP and neomycin resistance genes. For superficial orthotopic transplantation model, the cecum was identified and pulled out of the peritoneal cavity, the space between the cecum and peritoneum was sutured, the cecum was pulled to subcutaneous tissue, an incision was made on the cecal serosa followed by the implantation of a 1-mm tumor tissue to the cecum. For comparison, a conventional orthotopic transplantation model was established in a separate group of mice simultaneously. When tumor sizes reached 5 mm in diameter, half the mice in each model received 5-FU treatment. Primary tumor and metastases were monitored by fluorescent imaging or caliber measurement.

Results: Tumor fluorescence was observed as early as three days (median time of 4.7 ± 1.3 days) post-transplantation in the superficial orthotopic transplantation model, which was much earlier than 21 days (median time of 26.2 ± 9.9 days) in conventional orthotopic transplantation model. Although tumor growth of 5-FU treated mice in conventional orthotopic model were lower than those of the untreated mice, the difference was not significant. However, in superficial orthotopic model tumor growth was significantly inhibited in 5-FU treated mice relative to the untreated mice. Fluorescence imaging showed similar metastasis incidence between the superficial and conventional orthotopic transplantation models.

Conclusion: The fluorescent superficial orthotopic transplantation colon model allows easier real-time visualization and more sensitive monitoring of tumor growth as well as convenient repeated sampling. It is a valuable orthotopic implantation model for evaluating colon cancer.