



Study of orthotopic transplantation model of human gastrointestinal cancer and detection of micrometastases

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Abstract

AIM: To establish a relevant animal model of human gastrointestinal cancer, which can be used for repetitive investigations and may improve our understanding of carcinogenesis and cancer metastasis.

METHODS: Intact tissue of human colorectal and pancreatic cancer was transplanted in nude mice. The biological characteristics of the original and corresponding transplanted tumors were investigated by HE staining, PAS staining and immunostaining. The metastases in livers and lungs of the nude mice were investigated by immunostaining with biotinylated mab KL-1 and by RT-PCR using CK20 specific primers.

RESULTS: Nine of 16 surgical specimens grew in the nude mice subcutaneously and/or orthotopically (4 of 6 colorectal and 5 of 10 pancreatic cancer). Tumor cell content of the specimens and freezing of tissue specimens are important factors influencing the growth of

transplanted tumor. In the group of fresh tumor tissues with greater than 50% tumor cell content, transplantation rate was 100% (3 cases of pancreatic cancer and 3 cases of colorectal cancer). The orthotopically transplanted tumors resembled the original tumor morphologically and biologically, including TAA expression such as CEA by immunohistochemistry, and CEA level in the serum of mice. Ki-67 labeling index and the expression of TAA especially K-ras, 17-1A and RA-96, were associated with the potential of tumor growth in nude mice. Micrometastases in the lungs and livers of tumor bearing mice could be detected by immunostaining with biotinylated mab KL-1 and CK20-specific RT-PCR.

CONCLUSION: An orthotopic transplantation model for human colon and pancreatic cancer in nude mice has been established. The sensitive detection methods with CK-immunohistochemistry and CK20-RT-PCR were also established to study xenotransplanted human cancer and its metastatic cancer cells in the liver and lung of nude mice. This study may be helpful in understanding the mechanism of cancer metastasis and in developing new diagnostic methods and therapeutic strategies for metastases.

Key words: Gastrointestinal neoplasms; Neoplasm metastasis; Polymerase chain reaction; Mice, Nude; Immunohistochemistry; Orthotopic transplantation

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