Analysis of the molecular mechanisms of organ specific metastasis by orthotopic implantation of a human colon cancer cell in nude mice

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Cancer cell metastasis to distant organs is the major cause of death in cancer patients. However, the molecular mechanisms that control the spread of cancer to distant organs including the lymph nodes are unknown. Tumor metastasis to regional lymph nodes is a crucial step in the progression of cancer. Detection of tumor cells in the lymph nodes is an indication of the spread of the tumor, and is used clinically as a prognostic tool and a guide to therapy. A number of metastasis-related factors have been implicated in the cancer metastasis. Experimental studies with VEGF-C and chemokines have recently shown that they can induce direct metastasis to the lymph nodes.

To clarify the molecular mechanisms regulating the organ specific metastasis, we established an experimental model by orthotopic implantation of a human colon cancer cell in nude mice. This model developed distant metastasis by 6 weeks after tumor injection into the cecum. 100% of nude mice developed primary tumor. 30% of mice with local tumor produced the liver metastasis. 90% of mice produced lymph nodes metastasis.

We now started to investigate the mRNA expression of metastasis related factors (VEGF-isoforms, basic FGF, MMP-2, -7, -9, TIMP 1, MT1-MMP, c-MET) and chemokines (CCR7, CXCR4) using RT-PCR method in the primary site, metastatic sites. In preliminary examination, we observed overexpression of one of VEGF-isoform, VEGF-165, in the metastatic liver tumor. On the other hand, there were no significant differences of the mRNA expression of other VEGF-isoforms (VEGF-121, VEGF-189), basic FGF and VEGF-C among those metastatic sites.

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