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• (II)

• Stem Cell with Non-Invasive Gene-Assisted Pet Imaging for Cancer Diagnosis and Therapeutic Application (II)

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• Lung metastases model; Noninvasive imaging; Herpes simplex virus thymidine kinase; Human mesenchymal stem cell; [131I]FIAU

[131I]FIAU

• NG4TL4

NG4TL4-TK

[131I]FIAU

NG4TL4

NG4TL4-TK

[131I]FIAU

NG4TL4

24

10

[131I]FIAU

• This study is a two-year project. First year, we utilized HSV1-tk-expressing human mesenchymal stem cell to target microscopic tumors and noninvasively monitored the homing ability of human mesenchymal stem cell with micro Positron Emission Tomography (.mu.PET). We have previously employed

[131I]FIAU and demonstrated the applicability of noninvasive imaging for monitoring cancer gene therapy in an experimental animal model of HSV1-tk-expressing tumor xenografts. In this year, we have now used the same animal model to effectively and noninvasively monitor the location, magnitude, and duration of therapeutic gene expression over time for lung metastases model. Next, we utilized noninvasive imaging technique to monitor cancer treatment combined with mesenchymal stem cell and fusion protein vaccine. To improve the detectability of lung metastases, an experimental blood-borne lung metastasis model in mice was established using intravenously administered HSV1-tk-expressing NG4TL4 fibrosarcoma cells (NG4TL4-TK). The efficacy of noninvasively monitoring the 3 sites of development of lung metastatic lesions were assessed by SPECT imaging with [131I]FIAU. We subcutaneously inoculated HSV1-tk-expressing NG4TL4 fibrosarcoma cells (NG4TL4-TK) to the right flank of mice. We took advantage of the homing ability of mesenchymal stem cell combined with fusion protein vaccine, to noninvasively monitor and the treatment. The results of this study showed that lung metastases model of NG4TL4-TK cells could be successfully detected as early as 24 hours after i.v. injection of tumor cells radiolabeled with [131I]FIAU, and also subsequently detected by extended monitoring with the i.v. injection of [131I]FIAU on day 10. The combined treatment of mesenchymal stem cell and fusion protein vaccine by this study demonstrated the eradication of murine sarcoma-derived tumor. The results of planar imaging and tumor growth rate analysis showed a significant reduction in signal observed at the right flank of mice indicating the inhibition of tumor growth. We conclude that this in vivo imaging approach will be useful for future studies of lung metastases model and for the assessment of novel anti-cancer and anti-metastatic therapies.