

Serial In Vivo Imaging of the Lung Metastases Model and Gene Therapy Using HSV1-tk and Ganciclovir

鄧文炳

Deng WP*;Wu CC;Lee CC;Yang WK;Wang HE;Liu RS;Wei HJ;Gelovani JG;Hwang
JJ;Yang DM;Fu YK..

Abstract

Noninvasive imaging in lung metastatic tumor models is used infrequently because of technical limitations in detecting metastases. We have previously used 2'-fluoro-2'-deoxy-5-iodo-1-beta-d-arabinofuranosyluracil labeled with (131)I ((131)I-FIAU) and demonstrated the applicability of noninvasive imaging for monitoring cancer gene therapy in an experimental animal model of herpes simplex virus type 1 thymidine kinase (HSV1-tk)-expressing tumor xenografts. 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 the lung metastases model. METHODS: To improve the detectability of lung metastases, an experimental blood-borne lung metastases model in mice was established using intravenously administered HSV1-tk-expressing NG4TL4 fibrosarcoma cells (NG4TL4-TK) and simulated the clinical application of HSV1-tk plus ganciclovir (GCV) prodrug activation gene therapy. The efficacy of noninvasively monitoring the sites of development of lung metastatic lesions and their GCV-induced regression were assessed by SPECT with (131)I-FIAU. RESULTS: The results of this study showed that the lung metastases model of NG4TL4-TK cells could be successfully detected as early as 24 h after intravenous injection of tumor cells radiolabeled with (131)I-FIAU and also subsequently detected by extended monitoring with the intravenous injection of (131)I-FIAU on day 10. In mice treated with GCV, gamma-camera imaging demonstrated a significant growth inhibition of NG4TL4-TK cells of primary tumors and lung metastases on day 7 after initiating treatment. CONCLUSION: We conclude that this in vivo imaging approach will be useful for future studies of the lung metastases model and for the assessment of novel anticancer and antimetastatic therapies.