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研究报告

$\alpha_v\beta_3$受体显像剂$^{99}Tc^m$(N)(PNP6)(Cys-RGD)的制备及动物实验

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摘要　目的 探讨99Tcm标记的小分子环形Cys-RGD肽用于αvβ3受体阳性肿瘤显像的可行性。方法 以99Tcm(N)核通过二膦基胺类化合物PNP6（PNP6＝二[二(乙氧基丙基膦)-乙基]-乙氧基乙基胺）标记环形Cys-RGD肽（c(Arg-Gly-Asp-D-Tyr-Lys)-Cys）；采用HPLC法测定标记物的放化纯，并考察标记物的体外稳定性；进行正常小鼠和荷FWK-1胰腺癌裸鼠模型的体内生物分布试验及平面显像。结果 在优化的标记条件下，标记率大于92%，且具有良好的体外稳定性；生物分布实验表明标记物在血液中清除较快，主要通过肾脏排泄，99Tcm(N)(PNP6)(Cys-RGD)在肿瘤中的摄取值为2.92±0.71% ID/g (注药后1h)，肿瘤/血和肿瘤/肉的比值分别为11.0和3.1（注药后4 h）；注药后1h，肿瘤显像清晰。结论 99Tcm(N)(PNP6)(Cys-RGD)具有成为αvβ3受体阳性肿瘤显像剂的潜在应用价值。

关键词

分类号

Preparation and Biological Study of $^{99}Tc^m$(N)(PNP6)(Cys-RGD) for Integrin $\alpha_v\beta3$-positive Tumor Imaging

Abstract Objective To investigate the possibility of Radiolabelled Cys-RGD peptides for tumor αvβ3 integrin receptor scintigraphy. Methods The Cys-RGD peptide conjugate Cys-RGD（c(Arg-Gly-Asp-D-Tyr-Lys)-Cys） was radiolabelled with 99Tcm-nitrido core combined with PNP6 ligand (PNP6=bis(diethoxypropylphosphino ethyl)ethoxy ethylamine), and the radiochemical purity was measured with HPLC. The in vitro stability was investigated at room temperature and incubated in the cystein and serum solution. Biodistribution studies and gamma camera imaging were performed in normal mice and nude mice bearing FWK-1 pancreatic tumor xenografts. Results The radiolabelling yield was over 90% under optimized preparation condition. The high in vitro stability was found for 99Tcm(N)(PNP6)(Cys-RGD). In vivo biodistribution studies indicated the radiolabelled peptides was cleared rapidly from blood and mainly excreted via urinary system. Tumour uptake was 2.92±0.71% ID/g at 1h post injection. The ratios of tumor/blood and tumor/muscle were 11.0 and 3.1 at 4h post injection, respectively. Scintigraphic imaging allowed contrasting visualisation of αvβ3-expressed tumors at 1h post injection. Conclusion The results suggest 99Tcm(N)(PNP6)(Cys-RGD) would be the potential agent for αvβ3-positive tumor imaging.

Key words

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