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靶向 **GD2** 的核素多肽探针的设计优化及应用研究

摘要

目的：肿瘤作为人类重大健康问题，具有极高发生率和死亡率。精准检测肿瘤进展并通过手术根治性切除病灶，能够极大提高患者的生存率和改善预后。双唾液酸神经节苷脂 GD2 在神经母细胞瘤等多种肿瘤细胞表面表达异常上调，是一种极具潜力的生物标志物。本研究旨在开发 GD2 靶向的核素多肽探针，以实现泛癌种精准诊断。

方法：以那昔妥单抗和伤寒毒素 B 亚基为配体，结合计算机辅助药物设计技术，设计并筛选 GD2 靶向肽。通过细胞实验验证候选肽与 GD2 的结合特异性，并在动物模型中评估其靶向性能。进一步修饰后，将高亲和力优选肽与放射性核素耦合，构建适用于 SPECT 成像的核素多肽探针。

结果：成功设计并筛选出具有高特异性和高亲和力的 GD2 靶向肽，细胞实验证实其能够有效识别并结合表达 GD2 的肿瘤细胞。动物模型研究表明，构建的核素探针在肿瘤部位具有良好的靶向富集和显像效果，能够清晰显示肿瘤病灶。此外，同配体荧光探针能够辅助肿瘤切除手术导航。

结论：本研究成功构建了靶向 GD2 的 SPECT 核素探针，该探针具有泛癌种诊断潜力，可应用于神经母细胞瘤、乳腺癌等多种肿瘤的早期诊断和术中导航，为肿瘤的精准诊疗提供了新的分子影像学工具。

关键词

SPECT，放射性诊断，GD2，多肽探针，肿瘤

Abstract

Objective: Cancer represents a major global health challenge characterized by high incidence and mortality rates. Accurate detection of tumor progression and radical surgical resection of lesions can significantly improve patient survival and prognosis. Disialoganglioside (GD2) is aberrantly overexpressed on the surface of neuroblastoma and various other tumor cells, representing a highly promising biomarker. This study aims to develop GD2-targeted radiolabeled peptide probes for pan-cancer precise diagnosis.

Methods: Using naxitamab and cholera toxin B subunit as ligands, GD2-targeted peptides were designed and screened through in silico molecular docking and virtual screening. The binding specificity of candidate peptides to GD2 was validated through cellular experiments, and their targeting performance was evaluated in animal models. Subsequently, high-affinity optimized peptides were conjugated with radioactive nuclides to construct radiolabeled peptide probes suitable for SPECT imaging.

Results: GD2-targeted peptides with high specificity and affinity were successfully designed and screened. Cellular experiments confirmed their effective recognition and binding to GD2-expressing tumor cells. Animal model studies demonstrated that the constructed radiotracer exhibited excellent tumor-targeting accumulation and imaging performance, enabling clear visualization of tumor lesions. Additionally, the corresponding fluorescent probe with the same ligand provided effective navigation assistance for tumor resection surgery.

Conclusion: This study successfully developed a GD2-targeted SPECT radiotracer with pan-cancer diagnostic potential. The probe can be applied to precise diagnosis and intraoperative navigation for various tumors including neuroblastoma and breast cancer, providing a novel molecular imaging tool for precision oncology.

Keywords

SPECT, Radionuclide imaging, Disialoganglioside, Peptide probe, Tumor

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