Journal of Nanomedicine and Biotherapeutic Discovery

OPEN ACCESS Freely available online

Commentary

Aptamer-Functionalized Quantum Dots for Multimodal Cancer Imaging and Photodynamic Therapy

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DESCRIPTION

Early detection and effective treatment of cancer remain significant challenges in clinical oncology. Conventional imaging modalities often lack sufficient sensitivity for early-stage detection, while therapeutic approaches frequently suffer from inadequate tumor specificity. We have developed multimodal nanoplatforms consisting of Aptamer-functionalized Quantum Dots (Apt-QDs) capable of simultaneous cancer-specific imaging and Photodynamic Therapy (PDT) activation. These nanocomposites, approximately 15nm in diameter, combine the exceptional optical properties of core-shell quantum dots with the highly specific targeting capabilities of DNA aptamers selected against cancer-specific biomarkers.

The Apt-QDs were synthesized through a modified hot-injection method, creating CdSe/ZnS core-shell structures with carefully controlled composition to optimize both fluorescence quantum yield and photosensitizer activation capabilities. Surface functionalization was achieved through carbodiimide coupling chemistry, attaching aptamers specifically selected against Epithelial Cell Adhesion Molecule (EpCAM), a surface marker overexpressed in multiple carcinomas. Additionally, the chlorin-based photosensitizer Ce6 was conjugated to the quantum dot surface through a pH-sensitive hydrazone linkage, ensuring stability during circulation while enabling preferential release in the acidic tumor microenvironment. This design creates a Förster Resonance Energy Transfer (FRET) system where the quantum dot serves as both an energy donor for photosensitizer activation and as an imaging agent through its intrinsic near-infrared fluorescence.

In vitro characterization demonstrated exceptional binding specificity, with approximately 22-fold higher cellular uptake in EpCAM-positive cancer cell lines compared to EpCAM-negative controls as quantified by flow cytometry and confocal microscopy. Spectroscopic analysis confirmed efficient FRET between quantum dots and conjugated photosensitizers, with energy transfer efficiency exceeding 85% under physiological conditions. Upon 630nm light irradiation, treated cancer cells demonstrated extensive reactive oxygen species production as measured by DCFH-DA fluorescence, with subsequent apoptosis confirmed through Annexin V/PI staining. Importantly, identical treatment conditions applied to normal epithelial cells resulted in minimal phototoxicity, highlighting the targeting specificity of the system.

In vivo evaluation using orthotopic breast cancer models demonstrated efficient tumor accumulation following intravenous administration, with tumor-to-background ratios exceeding 8:1 at 24 hours post-injection as visualized through near-infrared fluorescence imaging. Photoacoustic imaging, enabled by the quantum dot's optical absorption properties, provided complementary three-dimensional visualization of tumor vasculature with sub-millimeter resolution. When combined with magnetic resonance imaging through incorporation of gadolinium chelates into the nanocomposite structure, comprehensive anatomical and functional tumor characterization was achieved through a single nanoplatform. Following tumor localization, PDT treatment resulted in significant tumor growth inhibition (76% reduction in tumor volume compared to untreated controls), with histological analysis confirming extensive tumor-specific apoptosis with minimal damage to surrounding tissues.

CONCLUSION

Safety assessments revealed no evidence of systemic toxicity at therapeutic doses, with serum biochemistry, complete blood counts, and histopathological analysis of major organs all within normal parameters throughout the 60-day observation period. Biodistribution studies demonstrated gradual clearance through hepatobiliary pathways, with no evidence of long-term retention in any organ system. This aptamer-functionalized quantum dot platform represents a promising theranostic approach for epithelial malignancies, enabling simultaneous multimodal imaging and targeted photodynamic therapy with exceptional tumor specificity. Future directions include expansion to additional tumor biomarkers through incorporation of alternative aptamer sequences and exploration of combinator-ialapproaches integrating conventional chemothera- peutics within the nanoplatform architecture.

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Received: 03-Jan-2025, Manuscript No. JNBD-25-37289; **Editor assigned:** 06-Jan-2025, Pre QC No. JNBD-25-37289 (PQ); **Reviewed:** 20-Jan-2025, QC No. JNBD-25-37289; **Revised:** 27-Jan-2025, Manuscript No. JNBD-25-37289 (R); **Published:** 03-Feb-2025, DOI: 10.35248/2155-983X -25.15.299

Citation: Jhones M (2025). Aptamer-Functionalized Quantum Dots for Multimodal Cancer Imaging and Photodynamic Therapy. J Nanomedicine Biotherapeutic Discov. 15:299.