

Nanoparticle Therapies: Targeted Treatment for Bladder Cancer With Reduced Side Effects [Letter]

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Dear editor

I am writing to comment on the recent article by Zhao et al¹ on nanoparticles as a drug delivery system for bladder cancer, which provided a comprehensive overview of the field. Despite progress in systemic therapies and surgical interventions, bladder cancer remains challenging. Nanoparticles, with their unique properties, are emerging as promising agents to improve the effectiveness of non-surgical treatment options.

One compelling aspect of the review is the exploration of targeted gene delivery using nanoparticles. A recent study² showcases a mucoadhesive mRNA nanoparticle strategy for delivering KDM6A-mRNA to orthotopic Kdm6a-null bladder cancer in mice. This approach effectively prolongs KDM6A-mRNA exposure in tumors and enhances penetration by adhering to the bladder. Nanoparticles can also silence oncogenic genes or upregulate tumor suppressors, altering the molecular landscape of bladder cancer cells.

Phototherapy, including photodynamic therapy (PDT) and photothermal therapy (PTT), offers a promising approach to cancer treatment. Explores the use of nanoparticles as delivery vehicles for photosensitizers and photothermal agents, which can accumulate more effectively at tumor sites, thereby enhancing therapeutic outcomes. Recently, a review³ delves into various nanoparticle formulations that boost the efficacy of PDT and PTT, underscoring their potential as minimally invasive treatment options for bladder cancer. Additionally, the integration of plant-based compounds with PDT is highlighted, leveraging the eco-friendly nature of these natural photoactive agents to further enhance the effectiveness of cancer treatment while promoting sustainable healthcare practices.

Moreover, the article presents a comprehensive overview of the challenges and limitations associated with nanoparticle-based therapies in cancer treatment. It delves into the potential toxicity of nanoparticles, their biodistribution, and clearance. One study⁴ developed a photoenhanced cancer chemotherapy strategy utilizing AIEgen-based multifunctional nanoparticles, which exhibited strong near-infrared fluorescence imaging and good photoenhancement performance. These nanoparticles were efficiently taken up by bladder cancer cells, reducing the release of Pt(II) under reductase and enhancing the sensitivity of bladder cancer to cisplatin chemotherapy with minimal side effects. Another study⁵ targeted the DAD1 gene using the CRISPR-Cas9 system delivered transmucosally by fluorinated polylysine nanoparticles. This approach strongly inhibited DAD1 expression in bladder cancer cells and induced apoptosis through the MAPK signaling pathway. Intravesical administration of these nanoparticles resulted in significant therapeutic outcomes without systemic toxicity, presenting a new strategy for targeted intravesical therapy for bladder cancer with high clinical potential. However, the path to clinical translation often faces hurdles related to scalability, reproducibility, and regulatory approval. Addressing these challenges will be crucial for the widespread adoption of nanoparticle-based therapies in the treatment of bladder cancer.

The article offers a comprehensive analysis of the present status of nanoparticle-based therapies for bladder cancer; however, several research gaps remain. One notable gap is the requirement for a more profound understanding of the



long-term safety and efficacy of these nanoparticles in clinical environments. To fully evaluate their potential toxicity, biodistribution, and clearance, as well as their long-term impact on human health, additional research is essential. Moreover, further investigation is necessary to tackle the existing challenges and facilitate the translation of these therapies into clinical practice.

Disclosure

The author declares no conflicts of interest in this communication.

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