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Drug/gene delivery and theranostics FREE

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INTRODUCTION

Delivery strategies have significantly contributed to the conversion of potential therapeutics into effective pharmaceutical formulations.[1] By improving the delivery of therapeutic agents to disease sites and reducing the off-target deposition, delivery technologies have greatly improved drug properties and patient compliance.[2,3] Small-molecule drugs have dominated the therapeutic landscape over the past few decades.[4] Since the bioavailability and therapeutic efficacy of these molecules are dramatically affected by their physicochemical properties, delivery strategies have been utilized to increase their solubility, control their release, expand their efficacy, and improve their pharmacokinetics.[5] Over time, new types of therapeutics, such as gene editing, have emerged. The delivery of genes into cells can be challenging due to their instabilities and immune responses.[6] However, dedicated delivery techniques can help genes resist nuclease degradation, decrease immunogenicity, and enhance intracellular delivery.[7] The development of delivery systems has enabled the clinical approval of some gene therapeutics, including Onpattro,[8] Givlaari,[9] and COVID-19 vaccines.[10] With the development of therapeutic drugs, delivery technologies had to evolve to meet delivery requirements and tackle emerging challenges.[11]

Theranostics, which combines therapy and diagnosis in a single formulation, plays a crucial role in propelling the biomedical industry toward personalized medicine.[12,13] In this context, various therapeutic approaches, including chemotherapy, photothermal therapy, photodynamic therapy, gene therapy, etc., are integrated with diagnosis with various diagnostic reagents such as fluorescent markers, magnetic resonance imaging contrast agents, nuclear imaging agents, and so on.[12] Different imaging probes can be conjugated onto therapeutic drugs and delivery carriers or be encapsulated into delivery systems to track drug distribution and monitor treatment outcomes (Fig. 1).[14] Theranostics has the potential for industrial production and clinical translation, which pave the way for achieving precision medicine and personalized prescription.

The Drug/Gene Delivery and Theranostics Special Topic in *APL Bioengineering* is therefore intended to highlight the advanced drug/gene delivery technologies and the development of theranostics. This collection sheds light on their breakthroughs, challenges, and future perspectives, featuring 12 articles in total, as detailed here.

SUMMARY OF AREAS COVERED

When it comes to disease treatment, the superiorities of advanced drug delivery systems for drug administration are undeniable. Specifically, developing multi-agent delivery systems for combination therapy or engineering stimuli-responsive delivery systems for precise regulation of drug releases at specific sites can significantly enhance the efficacy of various therapeutics while minimizing their adverse effects. Along this line, Chen *et al.* summarized the recent advances of various nanosized chemotherapeutic drug delivery systems for the treatment of osteosarcoma.[15] In addition, Cao *et al.* uncovered the crucial role of microRNA-99b (miR-99b) in governing the mechanotransduction and differentiation of bone marrow mesenchymal stem cells (BMSCs), revealing its immense promise in MSC-based tissue engineering. Therefore, they transfected BMSCs with Ad-miR-99b-sponge for miR-99b overexpression and encapsulated these BMSCs in 3D hydrogels to promote bone regeneration.[16] Specific applications of delivery systems for combination therapy and stimuli-responsive drug release were further demonstrated by the following research groups.

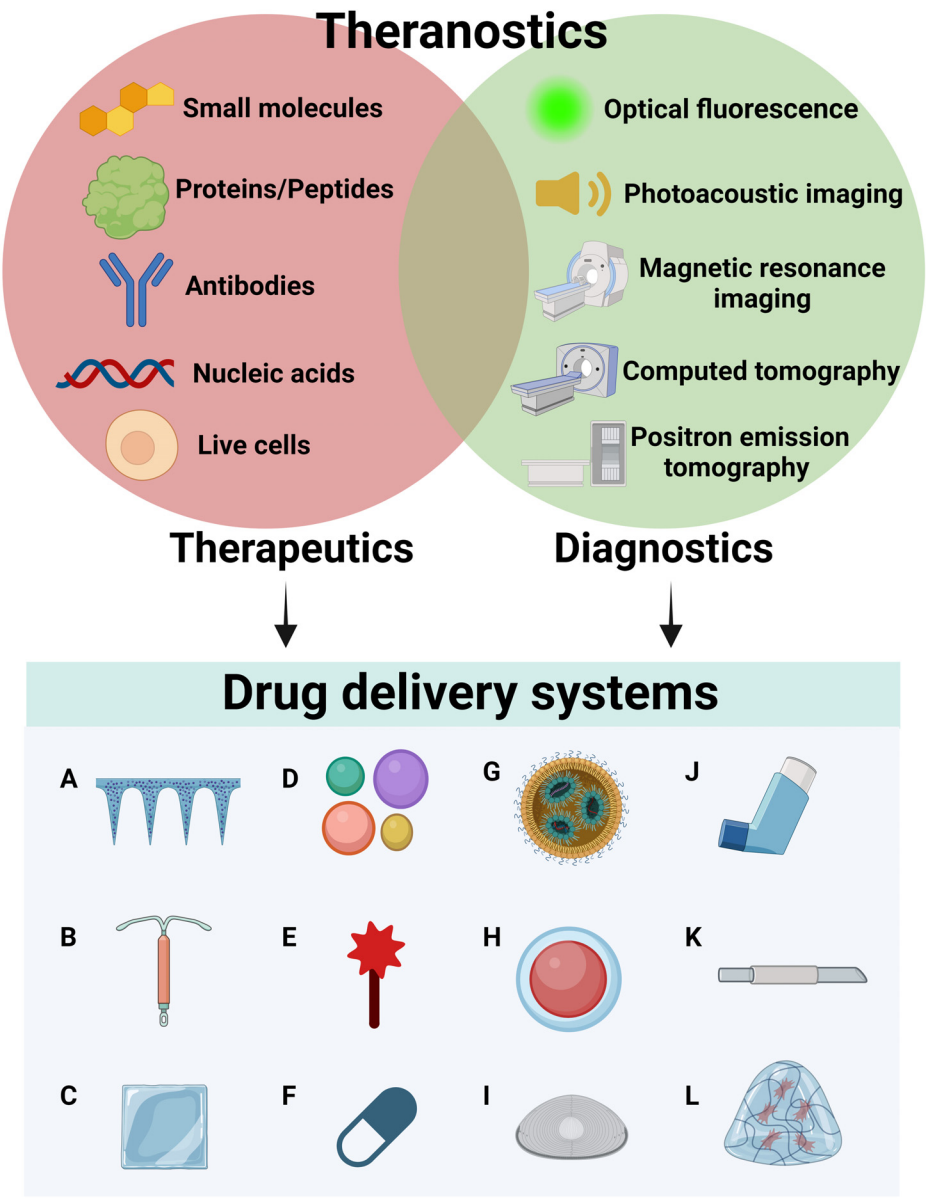

FIG. 1. Various therapeutic agents, diagnostic methods, and types of delivery systems. The term theranostics refers to the combination of diagnostics and therapeutics. A wide range of drug delivery systems has been developed for both therapeutic and diagnostic agents to meet delivery requirements and tackle emerging challenges. A, Microneedle patch; B, intrauterine device; C, polymer film; D, multiparticulate system; E, antibody-drug conjugate; F, pH-responsive capsule; G, nanoparticle; H, microencapsulation; I, drug-loaded contact lens; J, inhalable device; K, controlled-release implant; and L, swellable hydrogel.

To be specific, Zhao and colleagues developed a black phosphorus-enhanced injectable hydrogel for effective synergistic antibacterial therapy against soft tissue infections.[17] Ghosh *et al.* reported an efficient combination therapy approach that involves immunotherapy, chemotherapy, and photodynamic therapy in a pancreatic tumor model. Administration of immune checkpoint inhibitors combined with irinotecan-loaded porphyrin–phospholipid liposomes successfully ablated pancreatic tumors and induced memory immune responses.[18] Peng and colleagues also demonstrated the efficacy of a therapeutic combination of chemotherapy and immunotherapy for treating prostate cancer. They co-encapsulated the chemotherapeutic drug cisplatin and checkpoint kinase 1 inhibitor AZD7762 in glutathione-sensitive nanoparticles, highlighting their promise as a new treatment strategy.[19]

In addition, Cai *et al.* prepared acid-sensitive ketal-linked dexamethasone microcrystals for the treatment of autoimmune uveitis.[20] The biosafety evaluation of drug delivery systems is indispensable for both preclinical and clinical research. Zhu and colleagues studied the biodistribution and biotoxicity of gold and aluminum nanoparticles in tumor-bearing mice, which provided ideas for designing anti-tumor drug delivery systems.[21]

The latest advancements in drug delivery systems have also created opportunities for combining diagnostic strategies in various biomedical applications. For example, Wang and colleagues developed a multifunctional drug delivery system that is responsive to both pH and thermal changes and utilized it to achieve efficient photoacoustic imaging-guided therapy against breast cancer.[22] The dual-modal

bioprobes, which were composed of gold nanorods and ultrasmall iron oxide nanoparticles, were developed by Pan *et al.* for surface-enhanced Raman spectroscopy and magnetic resonance imaging to detect programmed cell death ligand-1 (PD-L1) expression in triple-negative breast cancer.[23] Tu *et al.* comprehensively reviewed the recent progress of organic nanoparticles for the diagnosis and treatment of atherosclerosis.[24] The intricate designs and unpredictable structures created by nature consistently inspire scientists in the drug delivery field. In nature, membraneless organelles are formed by the liquid-liquid phase separation (LLPS) process. The insights acquired from the LLPS process can inspire researchers to engineer novel drug/gene delivery strategies. Zhang *et al.* introduced the molecular mechanism of LLPS process and summarized the imaging tools employed in LLPS studies, which may provide some inspiration for designing drug delivery systems.[25] Sun *et al.* provided a systematic review on the clinical applications of platelet concentrates and platelet-derived extracellular vesicles for implant surgery and periodontal tissue regeneration.[26]

CONCLUSIONS

In summary, the Special Topic on Drug/Gene Delivery and Theranostics collects a broad range of articles that offer a glimpse into the latest advancements in multifunctional delivery systems for therapeutic and theranostic applications. We believe this collection will help readers gain a deeper understanding of delivery systems and inspire them to conduct further research in the development of novel therapeutic and theranostic modalities.

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AUTHOR DECLARATIONS

Conflict of Interest

The authors have no conflicts to disclose.

Ethics Approval

Ethics approval is not required.

DATA AVAILABILITY

The data that support the findings of this study are available from the corresponding authors upon reasonable request.

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