Editorial: Recent advances in the design of novel polymer nanoagents for cancer theranostics

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Editorial on the Research Topic
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theranostics

The significance of early and precise cancer theranostics in reducing patient mortality
has been well established (Tringale et al., 2018; Crosby et al., 2022). In recent years,
nanoagents have emerged as a promising tool for cancer theranostics, owing to their
passive and active targeting effects on cancerous tissues (Torchilin, 2011). Among the
various types of nanoagents, polymer nanoagents have gained increasing attention due to
their excellent biocompatibility, ease of processability, and flexible surface functionalization
(Ou et al., 2019). In this Research Topic, 9 published articles focus on the design of novel
polymer nanoagents for cancer theranostics, providing valuable insights into the
development of effective and precise cancer therapies using polymer nanoagents.

One review in this Research Topic, Zhang et al. summarized the recent progress of
chemiluminescent polymer nanoagents based on various chromophore substrates, including
luminol, peroxyoxalates, 1,2-dioxetanes and their derivatives, for cancer detection. The
authors emphasized the design strategies, mechanisms, and diagnostic applications of
representative chemiluminescent polymer nanoagents. Huang et al. reviewed the general
advances of polymer nanoagents and presented their applications in cancer diagnosis,
treatment, and theranostics, respectively. The authors also proposed the challenges and
prospects of polymer nanoagents in the cancer theranostics field. As the human tongue can
extend out of the mouth and is approximately 1 cm thick, the utilization of polymer
nanoagents in oral cancer theranostics is less restricted by tissue depth and is easier to apply
in clinical practice. Zhang et al. focused on the application of polymer nanoagents in the
diagnosis and treatment of oral cancer. As one of the most frequently used clinically

approved biodegradable polymers, poly (lactic-co-glycolic acid) (PLGA)-based nanoagents have been extensively applied in the field of cancer theranostics, including emerging cancer immunotherapy (Koerner et al., 2021). Gao et al. reviewed the advances of PLGA-based nanoagents in cancer immunotherapy, focusing on cancer vaccines and tumor microenvironment modulation.

In recent years, peptide-based nanoagents have gained extensive attention from researchers due to their high specificity and low systemic toxicity (Habibi et al., 2016). Focusing on peptide-based nanoagents, Zeng et al. summarized the applications of peptide-based nanoagents in the diagnosis and treatment of bladder cancer. As a class of lipid membrane-bound vesicles released by various cells, extracellular vesicles (EVs) with high physiochemical stability and biocompatibility have emerged as a new kind of drug delivery system for cancer theranostics (Bose et al., 2018). Nan et al. reviewed the direct modification of EVs and their application for cancer theranostics. The authors highlighted the prevailing approaches for direct modification of EVs, including cargo loading strategy for EVs modification and modification approaches of the EVs membrane. For conventional chemotherapy drugs, their poor tumor targeting effect is a key factor limiting their effectiveness in cancer treatment (Zeng et al., 2021). To address this issue, Rana et al. outlined the design of Smart Drug Delivery Systems (SDDSs) and their application in the cancer theranostics field. SDDSs that respond to redox, enzyme, light, ultrasound, and magnetic stimuli are highlighted. The authors proposed that SDDSs could become the future of Translational Medicine.

In an original research article in this Research Topic, Sun et al. prepared ROS-responsive Amplex® Red (ADHP) nanoprobes and studied their application in image-guided tumor resection, which has not been explored much. ADHP probes can rapidly oxidize in response to ROS in the tumor microenvironment to form resorufin, which significantly reduces the background fluorescence signal compared to the single resorufin probe. With the fluorescence guidance of ADHP nanoprobes, the authors successfully carried out image-guided surgery of 4T1 abdominal tumors. In addition, in response to the severe toxicity and gastrointestinal side effects of colchicine that limit its application in cancer treatment, Li et al. designed and synthesized a novel colchicine-magnolol hybrid (CMH) by splicing colchicine and magnolol, a multifunctional polyphenol showing favorable gastrointestinal protection. The antitumor results showed that CMH inhibited the growth of Lewis lung carcinoma (LLC) cells 100 times more potently than cisplatin, while the cytotoxicity of CMH was 10-fold lower than that of colchicine in normal human lung cells. Western blot results revealed that CMH dose-dependently suppressed the protein expression of phosphorylated ERK.

In conclusion, the rational design of polymer nanoagents, including inner probes/small molecule drugs and the outer polymer matrix (synthetic polymers, peptides, exosomes), plays a significant role in the cancer theranostics effect of polymer nanoagents. To further improve the effectiveness of polymer nanoagents in cancer theranostics, follow-up research could focus on developing smart probes/small molecule drugs with higher sensitivity and tumor responsiveness, and polymeric matrices with enhanced biodegradability and tumor targeting effects. In addition, the biosafety and ease of preparation of polymer nanoagents also need to be considered to make them clinically applicable, which needs to be balanced with the intelligence of polymer nanoagents. We expect that this Research Topic will inspire the design and synthesis of more advanced polymer nanoagents and promote their widespread application in cancer diagnosis and treatment.

Author contributions

HO wrote the editorial which was revised, proofread, and accepted by all authors. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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References

Bose, R. J. C., Kumar, S. U., Zeng, Y., Afjei, R., Robinson, E., Lau, K., et al. (2018). Tumor cell-derived extracellular vesicle-coated nanocarriers: an efficient theranostic platform for the cancer-specific delivery of anti-miR-21 and imaging agents. *ACS Nano* 12 (11), 10817–10832. doi:10.1021/acsnano.8b02587

Crosby, D., Bhatia, S., Brindle, K. M., Coussens, L. M., Dive, C., Emberton, M., et al. (2022). Early detection of cancer. *Science* 375 (6586), eaay9040. doi:10.1126/science.aay9040

Habibi, N., Kamaly, N., Memic, A., and Shafiee, H. (2016). Self-assembled peptide-based nanostructures: smart nanomaterials toward targeted drug delivery. *Nano Today* 11 (1), 41–60. doi:10.1016/j.nantod.2016.02.004

Koerner, J., Horvath, D., Herrmann, V. L., MacKerracher, A., Gander, B., Yagita, H., et al. (2021). PLGA-particle vaccine carrying TLR3/RIG-I ligand Riboxxim synergizes with immune checkpoint blockade for effective anti-cancer immunotherapy. *Nat. Commun.* 12 (1). doi:10.1038/s41467-021-23244-3

Ou, H., Li, J., Chen, C., Gao, H., Xue, X., and Ding, D. (2019). Organic/polymer photothermal nanoagents for photoacoustic imaging and photothermal therapy *in vivo*. *Sci. China Mater.* 62 (11), 1740–1758. doi:10.1007/s40843-019-9470-3

Torchilin, V. (2011). Tumor delivery of macromolecular drugs based on the EPR effect. *Adv. Drug Deliv. Rev.* 63 (3), 131–135. doi:10.1016/j.addr.2010.03.011

Tringale, K. R., Pang, J., and Nguyen, Q. T. (2018). Image-guided surgery in cancer: A strategy to reduce incidence of positive surgical margins. *WIREs Syst. Biol. Med.* 10 (3), e1412. doi:10.1002/wsbm.1412

Zeng, S., Ou, H., Gao, Z., Zhang, J., Li, C., Liu, Q., et al. (2021). HCPT-peptide prodrug with tumor microenvironment -responsive morphology transformable characteristic for boosted bladder tumor chemotherapy. *J. Control. Release.* 330, 715–725. doi:10.1016/j.jconrel.2020.12.042