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mRNA Therapeutics: Pharmacological Mechanisms and Pharmaceutical Delivery Innovations

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Abstract:

Messenger RNA (mRNA) therapeutics have emerged as a transformative modality for vaccination, protein replacement, and gene therapy. By harnessing the cell's translational machinery, exogenously delivered mRNA can transiently express therapeutic proteins without genomic integration. Recent advances in mRNA chemical modification, lipid nanoparticle (LNP) delivery, and immune evasion strategies have enabled robust pharmacological effects with controllable safety profiles. This review provides a comprehensive overview of mRNA pharmacology, delivery platforms, clinical applications, and the technological innovations driving translation. Emphasis is placed on pharmacokinetics, immunogenicity modulation, and emerging strategies to optimize tissue-specific delivery and therapeutic efficacy.

Keywords: mRNA therapeutics, lipid nanoparticles, immune modulation, gene therapy, vaccines, controlled delivery, translational medicine.

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1. Introduction

Messenger RNA (mRNA) therapeutics leverage the central dogma of molecular biology, instructing cells to produce proteins of interest without integrating into the host genome. Unlike DNA-based therapies, mRNA does not require nuclear entry, thereby minimizing the risk of insertional mutagenesis [1-2]. Its transient expression profile provides temporal control and dose flexibility, making it an attractive platform for diverse therapeutic applications. Historically, mRNA was limited by inherent instability and immunogenicity, which hindered clinical translation. However, recent advancements in nucleotide modification, encapsulation

strategies, and scalable manufacturing technologies have transformed mRNA therapeutics into a mainstream medical modality [3-4]. The rapid development and global deployment of COVID-19 vaccines exemplify the clinical potential of mRNA platforms. Beyond vaccines, mRNA therapies hold promise for protein replacement therapies, oncology, and treatment of rare genetic disorders, highlighting their broad versatility and transformative potential in modern medicine [5-6].

2. Pharmacological Mechanisms of mRNA Therapeutics

The pharmacological efficacy of mRNA therapeutics is underpinned by its structure and cellular processing. Structurally, mRNA contains a 5' cap (m7G) that enhances translation initiation and protects against exonuclease degradation, 5' and 3' untranslated regions (UTRs) that regulate stability and translational efficiency, an open reading frame (ORF) encoding the therapeutic protein, and a poly(A) tail that promotes ribosomal recruitment and stability [7-8]. Upon administration, exogenous mRNA is internalized by cells primarily through endocytosis. Following endosomal escape, cytosolic ribosomes translate the ORF into functional proteins, which are subsequently processed for secretion, intracellular activity, or immune presentation, depending on the therapeutic goal [9-10].

A critical consideration for mRNA therapeutics is immunogenicity. Unmodified mRNA can activate pattern recognition receptors (PRRs) such as TLR3, TLR7, TLR8, and RIG-I, leading to innate immune responses that may limit efficacy or induce adverse effects [11-12]. To mitigate these responses, strategies such as incorporating modified nucleotides (e.g., pseudouridine or 5-methylcytidine), optimizing codon usage, and co-delivering immunomodulatory excipients have been employed, enhancing both stability and tolerability of mRNA formulations [13-14].

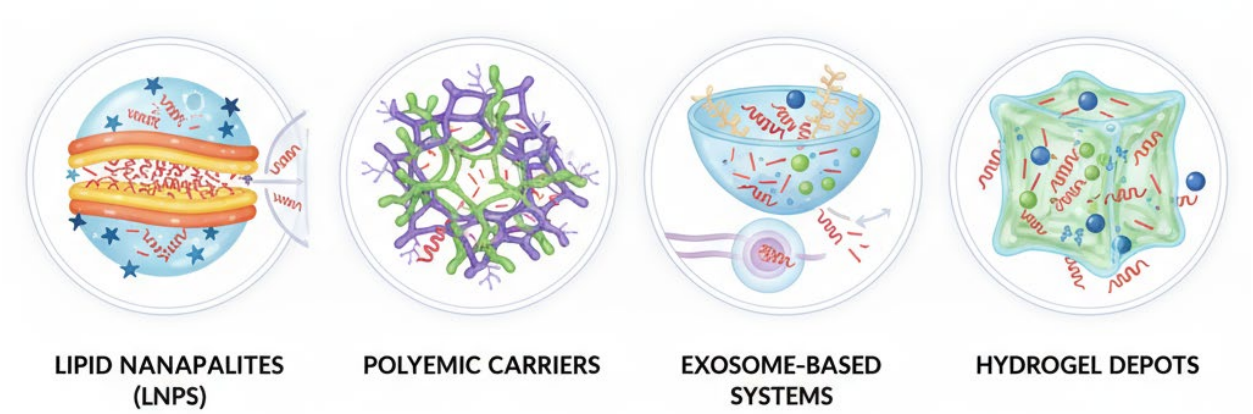
3. mRNA Delivery Platforms

Given the large size and negative charge of mRNA molecules, efficient delivery systems are essential to achieve cellular uptake and therapeutic efficacy. Lipid nanoparticles (LNPs) are the most clinically validated carriers, composed of ionizable lipids, cholesterol, phospholipids, and PEG-lipids. Ionizable lipids facilitate endosomal escape under acidic conditions, ensuring cytosolic release of mRNA [15-16]. LNPs have been successfully implemented in mRNA vaccines against COVID-19, including BNT162b2 and mRNA-1273, demonstrating their safety and effectiveness.

Polymer-based carriers, including polyethylenimine (PEI), poly(lactic-co-glycolic acid) (PLGA), and other cationic polymers, provide additional advantages, such as enhanced endosomal escape, controlled release, and biodegradability, thereby reducing cytotoxicity and enabling sustained protein expression [17-18]. Emerging hybrid and novel delivery systems, including exosomes and cell-derived vesicles, offer tissue-targeted delivery, while stimuli-

responsive nanoparticles allow spatiotemporal control of mRNA translation. Hydrogel-based depots provide localized delivery, enabling precise dosing and extended therapeutic effects. Together, these platforms represent a versatile toolkit that addresses the inherent challenges of mRNA stability, delivery, and immunogenicity, supporting the broad application of mRNA therapeutics across various disease domains [19-20]. (Figure 1)

Figure 1. Major mRNA Delivery Platforms



4. Pharmacokinetics and Pharmacodynamics

The pharmacokinetic and pharmacodynamic profiles of mRNA therapeutics are intricately linked to their delivery platform, chemical modifications, and route of administration. Typically, mRNA therapeutics are administered via intramuscular, intradermal, or intravenous routes, with lipid nanoparticles (LNPs) facilitating efficient cellular uptake [21-22]. LNPs exhibit preferential accumulation in the liver, targeting hepatocytes, and in antigen-presenting cells (APCs), which is particularly advantageous for vaccines and immune-modulating therapies. Biodistribution can be fine-tuned through adjustments in lipid composition, particle size, and surface functionalization with targeting ligands, enabling tissue-specific delivery and improved therapeutic outcomes [23-24].

Once internalized, mRNA is subject to degradation by cytosolic and extracellular RNases. Chemical modifications, such as incorporation of pseudouridine or 5-methylcytidine, along with encapsulation within LNPs, enhance mRNA stability, extending its functional half-life from a few hours to several days [25-26]. Protein expression kinetics depend on both mRNA integrity and carrier design, with translation typically initiating within hours of delivery. The duration of protein expression can last several days, and repeated dosing may be required to maintain therapeutic levels, particularly in chronic conditions or sustained immune activation applications [27-28].

5. Clinical Applications

mRNA therapeutics have rapidly transitioned from experimental concepts to clinically transformative interventions across multiple domains. In vaccines, mRNA platforms have demonstrated exceptional versatility and efficacy. The SARS-CoV-2 mRNA vaccines, for example, showcased rapid design, robust immunogenicity, and scalable production, setting a precedent for future pandemic preparedness. In oncology, neoantigen-based mRNA vaccines are being developed to elicit personalized T-cell responses, offering the promise of highly targeted immunotherapy tailored to individual tumor profiles [29-30].

Beyond vaccines, mRNA therapeutics are being explored for protein replacement therapies. By encoding therapeutic enzymes or hormones such as erythropoietin or VEGF, mRNA can correct deficiencies in genetic disorders or promote tissue regeneration in ischemic conditions. In immuno-oncology, mRNA encoding tumor-associated antigens induces potent cytotoxic T-cell responses, and when combined with checkpoint inhibitors, can significantly enhance anti-tumor efficacy [31-32]. Furthermore, rare genetic disorders, including cystic fibrosis and lysosomal storage diseases, may benefit from in vivo mRNA delivery, restoring deficient protein function and ameliorating disease phenotypes. Collectively, these applications underscore the versatility and transformative potential of mRNA therapeutics across prophylactic, therapeutic, and precision medicine domains [33-34].

Table 1. Representative mRNA Therapeutics in Clinical Development

Therapeutic Area	mRNA Product	Delivery Platform	Clinical Stage	Reference
Infectious Disease	BNT162b2	LNP	FDA-approved	35
Oncology	BioNTech personalized vaccine	LNP	Phase II/III	36
Protein Replacement	mRNA-encoded VEGF	LNP	Phase I	37
Rare Disease	mRNA for the PKU enzyme	Polymer/LNP	Preclinical	38

6. Pharmaceutical Innovations

Significant pharmaceutical innovations have enhanced the stability, efficacy, and targeting potential of mRNA therapeutics. Nucleotide modifications, such as pseudouridine and N1-

methylpseudouridine, have emerged as critical strategies to reduce innate immune recognition while improving translational efficiency [39-40]. These modifications help minimize unintended inflammatory responses and allow higher protein yields from administered mRNA, enhancing therapeutic outcomes [41-42]. Formulation strategies have further optimized mRNA delivery. PEGylation of lipid nanoparticles improves colloidal stability, prolongs circulation time, and reduces aggregation, while the addition of specific surface ligands enables tissue-specific targeting, ensuring that the mRNA reaches its intended cellular destination. Hybrid delivery systems, which combine lipid nanoparticles with hydrogels, microneedles, or other biomaterials, allow localized, sustained release, enhancing therapeutic precision [43-44].

Controlled-release and targeting innovations also play a pivotal role. Stimuli-responsive nanoparticles are engineered to release mRNA in response to specific environmental cues, such as pH changes, enzymatic activity, or temperature variations, which are often present in diseased tissues [45-46]. Additionally, organelle-targeted designs improve intracellular trafficking, ensuring that mRNA efficiently reaches the cytosol for translation, thereby maximizing protein expression and functional impact. Collectively, these innovations underscore the convergence of chemical modification, formulation engineering, and targeted delivery, driving the next generation of mRNA therapeutics [47-48].

7. Challenges and Limitations

Despite remarkable progress, several challenges continue to constrain the broader clinical application of mRNA therapeutics. Stability remains a major concern, as mRNA is inherently labile and sensitive to degradation, necessitating stringent cold-chain logistics for storage and transport [49-50]. Immunogenicity is another limitation; although nucleotide modifications reduce innate immune activation, some degree of immune response may persist, potentially affecting tolerability. Optimizing dosing is complex because achieving sufficient protein expression must be balanced against the risk of toxicity [51-52]. Long-term safety data are limited, particularly for chronic dosing regimens or repeated administration, raising concerns about off-target protein expression and cumulative effects. Manufacturing scalability also poses challenges: producing high-purity, clinical-grade mRNA at large scale is technically demanding and costly, limiting accessibility and widespread adoption [53-54]. Addressing these limitations is essential for translating mRNA therapeutics into diverse clinical settings.

8. Future Directions

The future of mRNA therapeutics is poised for remarkable advancements through innovations in delivery, personalization, and predictive design. Next-generation lipid nanoparticles (LNPs) are being developed to be biodegradable, organ-specific, and minimally immunogenic, improving safety and targeting precision [55-56]. Self-amplifying mRNA (saRNA) platforms offer the potential to achieve high protein expression at lower doses due to intracellular replication,

reducing the amount of administered mRNA required for therapeutic effect. Non-invasive administration routes, including oral and inhaled formulations, are under investigation, promising easier delivery and improved patient compliance [57-58]. Personalized medicine approaches aim to design mRNA therapeutics tailored to individual tumors or genetic mutations, enabling precision therapy for oncology and rare diseases. Integration with artificial intelligence and machine learning is expected to further optimize sequence design, carrier selection, and delivery strategies, enhancing efficacy while minimizing off-target effects. Together, these directions herald a new era of precision mRNA therapeutics, combining safety, efficacy, and patient-centered design [59-60]. (Figure 2)

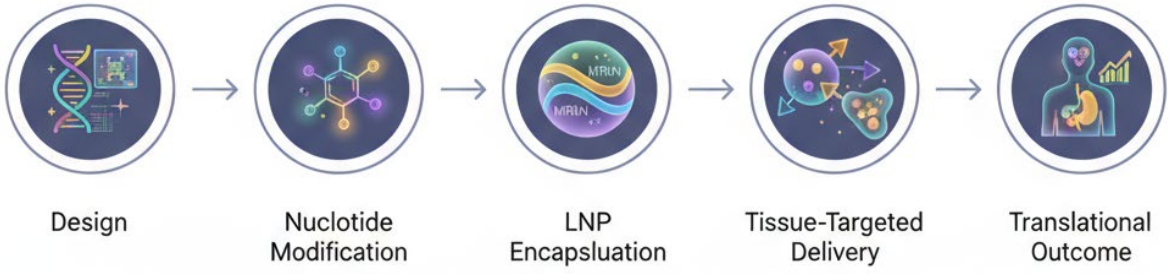


Figure 2. Future mRNA Therapeutics Workflow

9. Conclusion

Messenger RNA therapeutics have fundamentally transformed modern pharmacology, establishing a versatile and safe platform for applications ranging from prophylactic vaccines to protein replacement therapies and gene-based interventions. Through innovations in delivery systems, including lipid nanoparticles, polymer-based carriers, and hybrid formulations, as well as chemical modifications that enhance stability and reduce immunogenicity, many of the historical barriers to clinical translation have been effectively addressed. These advances have enabled the rapid development and deployment of mRNA-based COVID-19 vaccines, highlighting the platform's scalability, speed, and therapeutic potential. Despite ongoing challenges related to long-term stability, tissue-specific targeting, immune modulation, and chronic safety, the field continues to expand at an unprecedented pace. With integration of personalized medicine strategies, AI-driven design, and next-generation delivery technologies, mRNA therapeutics are poised to deliver on the promise of highly precise, patient-specific, and on-demand treatments for a wide spectrum of diseases, marking a new era in precision medicine and translational pharmacology.

References

1. Walsh, G. (2022). Biopharmaceutical benchmarks 2022. *Nature Biotechnology, 40*(12), 1722–1760. https://doi.org/10.1038/s41587-022-01589-3
2. Kaplon, H., & Reichert, J. M. (2023). Antibodies to watch in 2023. *mAbs, 15*(1), 2153410. https://doi.org/10.1080/19420862.2023.2153410
3. Fosgerau, K., & Hoffmann, T. (2015). Peptide therapeutics: Current status and future directions. *Drug Discovery Today, 20*(1), 122–128. https://doi.org/10.1016/j.drudis.2014.10.003
4. Pardi, N., Hogan, M. J., Porter, F. W., & Weissman, D. (2018). mRNA vaccines—a new era in vaccinology. *Nature Reviews Drug Discovery, 17*(4), 261–279. https://doi.org/10.1038/nrd.2017.243
5. Mitragotri, S., Burke, P. A., & Langer, R. (2014). Overcoming the challenges in administering biopharmaceuticals: Formulation and delivery strategies. *Nature Reviews Drug Discovery, 13*(9), 655–672. https://doi.org/10.1038/nrd4363
6. Dowdy, S. F. (2017). Overcoming cellular barriers for RNA therapeutics. *Nature Biotechnology, 35*(3), 222–229. https://doi.org/10.1038/nbt.3821
7. Patton, J. S., Fishburn, C. S., & Weers, J. G. (2004). The lungs as a portal of entry for systemic drug delivery. *Proceedings of the American Thoracic Society, 1*(4), 338–344. https://doi.org/10.1513/pats.2304023
8. Ecker, D. M., Jones, S. D., & Levine, H. L. (2015). The therapeutic monoclonal antibody market. *mAbs, 7*(1), 9–14. https://doi.org/10.4161/19420862.2015.989042
9. Lu, R. M., Hwang, Y. C., Liu, I. J., Lee, C. C., Tsai, H. Z., Li, H. J., et al. (2020). Development of therapeutic antibodies for the treatment of diseases. *Journal of Biomedical Science, 27*(1), 1–30. https://doi.org/10.1186/s12929-019-0592-z
10. Kontermann, R. E. (2009). Strategies to extend plasma half-lives of recombinant antibodies. *BioDrugs, 23*(2), 93–109. https://doi.org/10.2165/00063030-200923020-00001
11. Hamman, J. H., Enslin, G. M., & Kotzé, A. F. (2005). Oral delivery of peptide drugs: Barriers and developments. *BioDrugs, 19*(3), 165–177. https://doi.org/10.2165/00063030-200519030-00003
12. Hansel, T. T., Kropshofer, H., Singer, T., Mitchell, J. A., & George, A. J. T. (2010). The safety and side effects of monoclonal antibodies. *Nature Reviews Drug Discovery, 9*(4), 325–338. https://doi.org/10.1038/nrd3033
13. Jain, R. K., & Stylianopoulos, T. (2010). Delivering nanomedicine to solid tumors. *Nature Reviews Clinical Oncology, 7*(11), 653–664. https://doi.org/10.1038/nrclinonc.2010.139
14. Keizer, R. J., Huitema, A. D. R., Schellens, J. H. M., & Beijnen, J. H. (2010). Clinical pharmacokinetics of therapeutic monoclonal antibodies. *Clinical*

Pharmacokinetics, 49(8), 493–507. https://doi.org/10.2165/11530840-000000000-00000

15. Wang, W., Wang, E. Q., & Balthasar, J. P. (2008). Monoclonal antibody pharmacokinetics and pharmacodynamics. *Clinical Pharmacology & Therapeutics, 84*(5), 548–558. https://doi.org/10.1038/clpt.2008.184
16. Anselmo, A. C., & Mitragotri, S. (2019). Nanoparticles in the clinic: An update. *Bioengineering & Translational Medicine, 4*(3), e10143. https://doi.org/10.1002/btm2.10143
17. Beck, A., Goetsch, L., Dumontet, C., & Corvaïa, N. (2017). Strategies and challenges for the next generation of antibody-drug conjugates. *Nature Reviews Drug Discovery, 16*(5), 315–337. https://doi.org/10.1038/nrd.2016.268
18. Lau, J. L., & Dunn, M. K. (2018). Therapeutic peptides: Historical perspectives, current development trends, and future directions. *Bioorganic & Medicinal Chemistry, 26*(10), 2700–2707. https://doi.org/10.1016/j.bmc.2017.06.052
19. Fosgerau, K., & Hoffmann, T. (2015). Peptide therapeutics: Current status and future directions. *Drug Discovery Today, 20*(1), 122–128. https://doi.org/10.1016/j.drudis.2014.10.003
20. Vlieghe, P., Lisowski, V., Martinez, J., & Khrestchatisky, M. (2010). Synthetic therapeutic peptides: Science and market. *Drug Discovery Today, 15*(1-2), 40–56. https://doi.org/10.1016/j.drudis.2009.10.009
21. Hamman, J. H., Enslin, G. M., & Kotzé, A. F. (2005). Oral delivery of peptide drugs: Barriers and developments. *BioDrugs, 19*(3), 165–177. https://doi.org/10.2165/00063030-200519030-00003
22. Craik, D. J., Fairlie, D. P., Liras, S., & Price, D. (2013). The future of peptide-based drugs. *Chemical Biology & Drug Design, 81*(1), 136–147. https://doi.org/10.1111/cbdd.12055
23. Heitz, F., Morris, M. C., & Divita, G. (2009). Twenty years of cell-penetrating peptides: From molecular mechanisms to therapeutics. *British Journal of Pharmacology, 157*(2), 195–206. https://doi.org/10.1111/j.1476-5381.2009.00148.x
24. Henninot, A., Collins, J. C., & Nuss, J. M. (2018). The current state of peptide drug discovery: Back to the future? *Journal of Medicinal Chemistry, 61*(4), 1382–1414. https://doi.org/10.1021/acs.jmedchem.7b00318
25. Malavolta, L., & Cabral, H. (2021). Peptide-based nanoparticles for systemic therapeutic delivery. *Advanced Therapeutics, 4*(1), 2000123. https://doi.org/10.1002/adtp.202000123
26. Copolovici, D. M., Langel, K., Eriste, E., & Langel, Ü. (2014). Cell-penetrating peptides: Design, synthesis, and applications. *ACS Nano, 8*(3), 1972–1994. https://doi.org/10.1021/nn4061059

27. Mastorakos, P., da Silva, A. L., Chisholm, J., Song, E., Choi, W. K., Boyle, M. P., et al. (2015). Highly compacted biodegradable DNA nanoparticles capable of overcoming the mucus barrier for inhaled lung gene therapy. *Proceedings of the National Academy of Sciences, 112*(28), 8720–8725. https://doi.org/10.1073/pnas.1500983112
28. Patton, J. S., & Byron, P. R. (2007). Inhaling medicines: Delivering drugs to the body through the lungs. *Nature Reviews Drug Discovery, 6*(1), 67–74. https://doi.org/10.1038/nrd2153
29. Sahin, U., Karikó, K., & Türeci, Ö. (2014). mRNA-based therapeutics—Developing a new class of drugs. *Nature Reviews Drug Discovery, 13*(10), 759–780. https://doi.org/10.1038/nrd4278
30. Griesenbach, U., & Alton, E. W. F. W. (2012). Progress in gene and cell therapy for cystic fibrosis lung disease. *Current Pharmaceutical Design, 18*(5), 642–662. https://doi.org/10.2174/138161212799504171
31. Suk, J. S., Xu, Q., Kim, N., Hanes, J., & Ensign, L. M. (2016). PEGylation as a strategy for improving nanoparticle-based drug and gene delivery. *Advanced Drug Delivery Reviews, 99*(Pt A), 28–51. https://doi.org/10.1016/j.addr.2015.09.012
32. Kaczmarek, J. C., Kowalski, P. S., & Anderson, D. G. (2017). Advances in the delivery of RNA therapeutics: From concept to clinical reality. *Genome Medicine, 9*(1), 60. https://doi.org/10.1186/s13073-017-0450-0
33. Yin, H., Kanasty, R. L., Eltoukhy, A. A., Vegas, A. J., Dorkin, J. R., & Anderson, D. G. (2014). Non-viral vectors for gene-based therapy. *Nature Reviews Genetics, 15*(8), 541–555. https://doi.org/10.1038/nrg3763
34. Hou, X., Zaks, T., Langer, R., & Dong, Y. (2021). Lipid nanoparticles for mRNA delivery. *Nature Reviews Materials, 6*(12), 1078–1094. https://doi.org/10.1038/s41578-021-00358-0
35. Pilcer, G., & Amighi, K. (2010). Formulation strategy and use of excipients in pulmonary drug delivery. *International Journal of Pharmaceutics, 392*(1-2), 1–19. https://doi.org/10.1016/j.ijpharm.2010.04.023
36. Ginn, S. L., Amaya, A. K., Alexander, I. E., Edelstein, M., & Abedi, M. R. (2018). Gene therapy clinical trials worldwide to 2017: An update. *Journal of Gene Medicine, 20*(5), e3015. https://doi.org/10.1002/jgm.3015
37. Lostalé-Seijo, I., & Montenegro, J. (2018). Synthetic materials are at the forefront of gene delivery. *Nature Reviews Chemistry, 2*(10), 258–277. https://doi.org/10.1038/s41570-018-0038-0
38. Bray, F., Laversanne, M., Sung, H., Ferlay, J., Siegel, R. L., Soerjomataram, I., & Jemal, A. (2024). Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: A Cancer Journal for Clinicians, 74*(3), 229–263. https://doi.org/10.3322/caac.21708

39. National Cancer Institute. (2025, January 6). Common cancer sites—Cancer stat facts. https://seer.cancer.gov/statfacts/html/common.html
40. Rezaianzadeh, A., Jalali, M., Maghsoudi, A., Mokhtari, A. M., Azgomi, S., & Dehghani, S. L. (2017). The overall 5-year survival rate of breast cancer among Iranian women: A systematic review and meta-analysis of published studies. *Breast Disease, 37*(1), 63–68. https://doi.org/10.3233/BD-170393
41. Debela, D. T., Muzazu, S. G., Heraro, K. D., Ndalama, M. T., Mesele, B. W., Haile, D. C., Kitui, S. K., & Manyazewal, T. (2021). New approaches and procedures for cancer treatment: Current perspectives. *SAGE Open Medicine, 9*, 20503121211034366. https://doi.org/10.1177/20503121211034366
42. Altun, İ., & Sonkaya, A. (2018). The most common side effects experienced by patients receiving the first cycle of chemotherapy. *Iranian Journal of Public Health, 47*(8), 1218–1219. https://pubmed.ncbi.nlm.nih.gov/30495163
43. Danhier, F., Feron, O., & Préat, V. (2010). To exploit the tumor microenvironment: Passive and active tumor targeting of nanocarriers for anti-cancer drug delivery. *Journal of Controlled Release, 148*(2), 135–146. https://doi.org/10.1016/j.jconrel.2010.08.027
44. Zhang, Y., Li, M., Gao, X., Chen, Y., & Liu, T. (2019). Nanotechnology in cancer diagnosis: Progress, challenges and opportunities. *Journal of Hematology & Oncology, 12*, 137. https://doi.org/10.1186/s13045-019-0811-7
45. Zhao, M., Mi, D., Ferdows, B. E., Li, Y., Wang, R., Li, J., Patel, D., Kong, N., Shi, S., & Tao, W. (2022). State-of-the-art nanotechnologies for the detection, recovery, analysis and elimination of liquid biopsy components in cancer. *Nano Today, 42*, 101361. https://doi.org/10.1016/j.nantod.2022.101361
46. Liu, Y., Wang, J., Xiong, Q., Hornburg, D., Tao, W., & Farokhzad, O. C. (2021). Nano-bio interactions in cancer: From therapeutics delivery to early detection. *Accounts of Chemical Research, 54*(2), 291–301. https://doi.org/10.1021/acs.accounts.0c00753
47. Rosenblum, D., Joshi, N., Tao, W., Karp, J. M., & Peer, D. (2018). Progress and challenges towards targeted delivery of cancer therapeutics. *Nature Communications, 9*, 1410. https://doi.org/10.1038/s41467-018-03705-y
48. Islam, M. A., Xu, Y., Tao, W., Ubellacker, J. M., Lim, M., Aum, D., Lee, G. Y., Zhou, K., Zope, H., Yu, M., et al. (2018). Restoration of tumour-growth suppression in vivo via systemic nanoparticle-mediated delivery of PTEN mRNA. *Nature Biomedical Engineering, 2*, 850–864. https://doi.org/10.1038/s41551-018-0302-2
49. Kong, N., Tao, W., Ling, X., Wang, J., Xiao, Y., Shi, S., Ji, X., Shajii, A., Gan, S. T., Kim, N. Y., et al. (2019). Synthetic mRNA nanoparticle-mediated restoration of P53 tumor suppressor sensitizes P53-deficient cancers to mTOR inhibition. *Science Translational Medicine, 11*(489), eaaw1565. https://doi.org/10.1126/scitranslmed.aaw1565

50. Zhang, D., Zhong, D., Ouyang, J., He, J., Qi, Y., Chen, W., Zhang, X., Tao, W., & Zhou, M. (2022). Microalgae-based oral microcarriers for gut microbiota homeostasis and intestinal protection in cancer radiotherapy. *Nature Communications, 13*, 1413. https://doi.org/10.1038/s41467-022-28952-6
51. Xie, A., Hanif, S., Ouyang, J., Tang, Z., Kong, N., Kim, N. Y., Qi, B., Patel, D., Shi, B., & Tao, W. (2020). Stimuli-responsive prodrug-based cancer nanomedicine. *EBioMedicine, 56*, 102821. https://doi.org/10.1016/j.ebiom.2020.102821
52. Yang, J., Zhang, X., Liu, C., Wang, Z., Deng, L., Feng, C., Tao, W., Xu, X., & Cui, W. (2020). Biologically modified nanoparticles as theranostic bionanomaterials. *Progress in Materials Science, 118*, 100768. https://doi.org/10.1016/j.pmatsci.2020.100768
53. Kong, N., Zhang, H., Feng, C., Liu, C., Xiao, Y., Zhang, X., Mei, L., Kim, J. M., Tao, W., & Ji, X. (2021). Arsenene-mediated multiple independently targeted reactive oxygen species burst for cancer therapy. *Nature Communications, 12*, 4777. https://doi.org/10.1038/s41467-021-25087-2
54. Feng, C., Li, Y., Ferdows, B. E., Patel, D. N., Ouyang, J., Tang, Z., Kong, N., Chen, E., & Tao, W. (2022). Emerging vaccine nanotechnology: From defense against infection to sniping cancer. *Acta Pharmaceutica Sinica B, 12*(10), 2206–2223. https://doi.org/10.1016/j.apsb.2022.06.007
55. Patra, J. K., Das, G., Fraceto, L. F., Campos, E. V. R., Rodriguez-Torres, M. D. P., Acosta-Torres, L. S., Diaz-Torres, L. A., Grillo, R., Swamy, M. K., Sharma, S., et al. (2018). Nano-based drug delivery systems: Recent developments and future prospects. *Journal of Nanobiotechnology, 16*, 71. https://doi.org/10.1186/s12951-018-0392-8
56. Bregoli, L., Movia, D., Gavigan-Imedio, J. D., Lysaght, J., Reynolds, J., & Prina-Mello, A. (2016). Nanomedicine applied to translational oncology: A future perspective on cancer treatment. *Nanomedicine: Nanotechnology, Biology, and Medicine, 12*(1), 81–103. https://doi.org/10.1016/j.nano.2015.09.003
57. Huayamares, S. G., Loughrey, D., Kim, H., Dahlman, J. E., & Sorscher, E. J. (2024). Nucleic acid-based drugs for patients with solid tumours. *Nature Reviews Clinical Oncology, 21*(6), 407–427. https://doi.org/10.1038/s41571-024-00788-7
58. Kommineni, N., Butreddy, A., Jyothi, V. G. S., & Angsantikul, P. (2022). Freeze-drying for the preservation of immunoengineering products. *iScience, 25*, 105127. https://doi.org/10.1016/j.isci.2022.105127
59. Ray, P., Ferraro, M., Haag, R., & Quadir, M. (2019). Dendritic polyglycerol-derived nano-architectures as delivery platforms of gemcitabine for pancreatic cancer. *Macromolecular Bioscience, 19*(9), 1900073. https://doi.org/10.1002/mabi.201900073