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EDITORIAL

Nanomedicine for Cancer

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Over the past decades, oncology has occupied the lion's share of all nanomedical applications [1-3]. In 2020, up to 65% of the clinical trials involving nanomaterials were attending to cancer therapeutics and diagnostics [4]. The focus of most trials is not limited to enhancing the efficacy of available therapeutics or the accuracy and precision of existing diagnostic tools but rather directed to improving the quality of life of cancer patients. Indeed, one approach to overcoming drug resistance can be achieved *via* modulating the pharmacological characteristics of these therapies [4, 5]. This, in turn, permits their passive and selective delivery to the targeted tumorigenic sites. Furthermore, the use of biocompatible drug delivery systems embracing cancer-specific antibodies facilitates the active delivery of these therapeutics to cancer cells [6].

A breakthrough application of nanotechnology was the modification of key chemotherapeutics such as cisplatin, doxorubicin, and paclitaxel [6]. These highly efficacious drugs are used to combat a variety of cancers. For instance, cisplatin is currently sought as a treatment for breast, bladder, genital, gastrointestinal, lung, and prostate cancers among others [7]. Although it is still considered a first-line therapy for a battery of tumors, its application is limited due to its deleterious side effects. The pleiotropic effects of cisplatin were reflected by (1) preventing DNA replication and arresting cellular proliferation, (2) generating reactive oxygen species, and (3) affecting the homeostasis of the mitochondria and the endoplasmic reticulum, have rendered cisplatin a nonspecific chemotherapeutic agent that affects almost tissues with high proliferative index. This explains the many undesired side effects that include nephrotoxicity, neurotoxicity, and ototoxicity among others [7]. The morbid outcomes implied by these toxic effects cannot be disregarded. Unfortunately, even after years of treatment, cisplatin-treated patients may suffer from permanent irreversible outcomes such as hearing loss and kidney failure. The same applies to paclitaxel, which is often associated with peripheral neuropathy in up to ~ 70% of patients. Indeed, this neurotoxicity is irreversible in some of these patients [8]. Modalities and approaches that reduce these side effects would significantly enhance the quality of life of treated patients and boost their momentum against cancer. Accumulating evidence clearly shows the promising future that nanoformulations are well-suited to assume.

The life-changing side effects associated with several essential therapeutics have fueled both the discovery and the evaluation of nanoformulations in pre-clinical studies and multi-phase clinical trials. Interestingly, two and five different nanoformulations of doxorubicin and paclitaxel, respectively, are currently approved and available in the market, and dozens of new formulations are being investigated in ongoing clinical trials [6]. These new formulations are posed to not only reduce the toxicity of their precursors but also to improve their delivery to targeted tumor cells while sparing healthy cells. Second-generation nanomedicines are likely more capable of delivering more than one therapeutic at a time and releasing their cargo in response to extrinsic (*i.e.* heat, light, magnetic field) or intrinsic stimuli (*i.e.* pH or redox changes, enzymatic cleavage) [6, 9].

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More recently, nanomedicine has emerged as an attractive tool for delivering gene therapies. The value of these innovative modalities and the efficacy of nanomaterials in ensuring delivery and physiologic stability have been lately enforced during the pandemic of COVID-19. Interestingly, the most successful mRNA-based COVID-19 vaccines were coupled with liposomal carriers to prevent the premature degradation of mRNA and enhance its physiologic stability [6]. In oncology, this novel therapy is likely gaining more attention as a compelling tactic for suppressing tumorigenesis at the genetic level. Impressively, although few gene therapies are currently approved for use in clinics, hundreds are being assessed in ongoing clinical trials [6]. Coupling these therapies with biocompatible nanocarriers is crucial as it can drastically improve their delivery to the tumor site while minimizing their degradation.

The therapeutic value of nanotechnologies is also portrayed in the development of immunotherapies geared toward inhibiting tumor progression. Immunotherapies, which include two rising entities, namely cancer vaccines, and chimeric antigen receptor T cell therapies, in addition to the well-established subset of the immune checkpoint inhibitors can significantly benefit from nanotechnology [6]. This growing technology can optimize the delivery of these therapies as well as their cellular uptake while allowing the exclusive targeting of cancer cells. This is particularly achievable as nanocarriers can be easily modified to incorporate tumor-specific antigens, permitting targeted delivery [6].

Together, nanotechnology is a low-hanging fruit capable of improving both the treatment and the diagnosis of hard-to-treat cancers. It opens new avenues to personalized medicine as it can account for the heterogenous nature of almost all cancers [10-12]. Nonetheless, the high cost of generating effective nanomedicines along with the lengthy course needed to transfer these medicines from wet bench to clinical practice remains the key hurdle to success. Hence, it is very important to approach these much-needed inventions from a cost-effective perspective.

CONCLUSION

Nanomedicine is proving to be a rather attractive modality in the management of several diseases including cancer. However, it is of paramount importance to consider the various hurdles that have so far prevented many nanocarriers from attaining the ultimate phase of clinical trials. Moreover, to reduce the failure rate and the cost of fostered nanocarriers, one should first address the bottleneck limitations facing the therapeutic success of nanomedicine. These include (1) suboptimal permeability and retention of these vehicles at the tumor site, (2) limited capacity to couple nanocarriers simultaneously with multiple therapeutics, and (3) scarcity of pre-clinical studies involving humanized animal models that are more comparable to the human physiology.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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REFERENCES

[1] Younis, N.K.; Roumieh, R.; Bassil, E.P.; Ghoubaira, J.A.; Kobeissy, F.; Eid, A.H. Nanoparticles: Attractive tools to treat colorectal cancer. *Semin. Cancer Biol.,* **2022**, *86*(Pt 2), 1-13. http://dx.doi.org/10.1016/j.semcancer.2022.08.006 PMID: 36028154

[2] Younis, N.K.; Ghoubaira, J.A.; Bassil, E.P.; Tantawi, H.N.; Eid, A.H. Metal-based nanoparticles: Promising tools for the management of cardiovascular diseases. *Nanomedicine,* **2021**, *36*, 102433. http://dx.doi.org/10.1016/j.nano.2021.102433 PMID: 34171467

[3] Gholami, L.; Ivari, J.R.; Nasab, N.K.; Oskuee, R.K.; Sathyapalan, T.; Sahebkar, A. Recent advances in lung cancer therapy based on nanomaterials: A review. *Curr. Med. Chem.,* **2021**, *28* [Epub ahead of print] http://dx.doi.org/10.2174/0929867328666210810160901 PMID: 34375182

[4] Germain, M.; Caputo, F.; Metcalfe, S.; Tosi, G.; Spring, K.; Åslund, A.K.O.; Pottier, A.; Schiffelers, R.; Ceccaldi, A.; Schmid, R. Delivering the power of nanomedicine to patients today. *J. Control. Release,* **2020**, *326*, 164-171. http://dx.doi.org/10.1016/j.jconrel.2020.07.007 PMID: 32681950

[5] Akter, Z.; Khan, F.Z.; Khan, M.A. Gold nanoparticles in triple-negative breast cancer therapeutics. *Curr. Med. Chem.,* **2023**, *30*(3), 316-334. http://dx.doi.org/10.2174/0929867328666210902141257 PMID: 34477507

[6] Kemp, J.A.; Kwon, Y.J. Cancer nanotechnology: current status and perspectives. *Nano Converg.,* **2021**, *8*(1), 34. http://dx.doi.org/10.1186/s40580-021-00282-7 PMID: 34727233

[7] Manohar, S.; Leung, N. Cisplatin nephrotoxicity: A review of the literature. *J. Nephrol.,* **2018**, *31*(1), 15-25. http://dx.doi.org/10.1007/s40620-017-0392-z PMID: 28382507

[8] Staff, N.P.; Fehrenbacher, J.C.; Caillaud, M.; Damaj, M.I.; Segal, R.A.; Rieger, S. Pathogenesis of paclitaxel-induced peripheral neuropathy: A current review of *in vitro* and *in vivo* findings using rodent and human model systems. *Exp. Neurol.,* **2020**, *324*, 113121. http://dx.doi.org/10.1016/j.expneurol.2019.113121 PMID: 31758983

[9] Mirhadi, E.; Majeed, M.; Kesharwani, P.; Sahebkar, A. Reactive oxygen species-responsive drug delivery systems: A new approach in nanomedicine. *Curr. Med. Chem.,* **2022**, *29*(25), 4320-4323. http://dx.doi.org/10.2174/0929867329666220127110654 PMID: 35086442

[10] Khan, F.; Akhtar, S.; Kamal, M.A. Nanoinformatics and personalized medicine: An advanced cumulative approach for cancer management. *Curr. Med. Chem.,* **2022**, *29*. http://dx.doi.org/10.2174/0929867329666220610090405 PMID: 35692148

[11] Wei, G.; Wang, Y.; Yang, G.; Wang, Y.; Ju, R. Recent progress in nanomedicine for enhanced cancer chemotherapy. *Theranostics,* **2021**, *11*(13), 6370-6392. http://dx.doi.org/10.7150/thno.57828 PMID: 33995663

[12] Hamze, K.; Abdallah, R.H.; Younis, N.K.; Fardoun, M.; Darwiche, N.; Kobeissy, F.; Iratni, R.; Bouhadir, K.; Eid, A.H. 2-Nucleobase-substituted 4,6-diaminotriazine analogs: synthesis and anti-cancer activity in 5-fluorouracil-sensitive and resistant colorectal cancer cells. *Curr. Med. Chem.,* **2022**. PMID: 36111761