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Editorial of Special Column on Delivery Nanotechnologies to Modulate the Immune System and Combat Inflammation and Infection

Our immune system has a vital role, and any variation because of either heritable or non-heritable stimuli might cause health disorders such as cancer, diabetes, and cardiovascular diseases[1]. In addition, the complexity of the anatomical barriers, such as the blood–brain barrier, challenges the therapy of central nervous system (CNS) diseases. The goal of nano-dimensional drugs (nanomedicines) is to improve the efficacy of treatments while minimizing systemic toxicity and side effects. The clinical translation of nanomedicine has made significant progress in the past ten years, and there are already over 85 approved nanomedicines on the market for clinical use[2]. For example, several siRNA/mRNA-carrying lipid nanoparticles have been approved to treat hereditary transthyretin amyloidosis (hATTR) polyneuropathy and combat the COVID-19 pandemic. This special issue provides a quick and broad snapshot of nanomedicine applications in treating immune disorders, related symptoms (inflammation and infection), and CNS disorders. The special issue is a compendium of eight reviews and three original research articles. It includes nanoparticulate technologies such as cell-derived nanovesicles[3,4], metal[5,6] and polymeric nanoparticles[7], nanocrystals[8], nanovaccines[9,10], wearable patches[11], and functional nanomaterials[12,13].

Zhao et al.[3] comprehensively reviewed the principles for the design of engineered cellular nanovesicles with tailored immunomodulatory activities and discussed their new advances as immunotherapies for treating major diseases, such as cancer, infectious diseases, hyperinflammation, acute respiratory distress syndrome and pulmonary hypertension (PH). Then, Huang et al.[10] summarized the inhaled delivery strategies, such as pulmonary and intranasal administration, and discussed the benefits of inhaled nanomedicines for preventing and treating the COVID-19 pandemic. Also, they reviewed the inhaled antibodies and nanobodies for combating lung infection and inflammation. He et al.[8] provide a case of nanocrystal co-delivery to combat a severe lung inflammation disease, PH. The co-delivery system was prepared by loading the active caspase three on paclitaxel-crystal nanoparticles, followed by a glucuronic acid coating to target the glucose transporter-1 on the pulmonary artery smooth muscle cells. Their results indicated that PH could be alleviated significantly by regressing the remodeling of pulmonary arteries and improving hemodynamics.

To inspire increasing drug delivery against increasing inflammation, Han et al.[6] outlined the common inflammatory diseases and pathways and reviewed the emerging applications of self-therapeutic metal-based nanoparticles for managing inflammatory diseases in animals, focusing on therapeutic outcomes and anti-inflammatory mechanisms. Then, they addressed the biodistribution, long-term toxicity, and clinical translation of these nanomedicines. CNS disorder is attracting increasing attention worldwide and is closely related to inflammation [14]. Consequently, Awad et al.[7] described the challenges faced in treating neurodegenerative and neurodevelopmental conditions, the nasal mucosa's molecular and cellular features, and the contribution of intranasal nano-drug delivery to overcome them. Then, a comprehensive overview of polymeric nanocarriers investigated to increase drug bioavailability in the brain is presented. Periodontitis is an inflammatory disease caused by bacterial infection directly, and the dysregulation of the host immune-inflammatory response finally destroys periodontal tissues. Ding et al.[13] summarized the role of various nanomaterials in periodontitis treatment, i.e., nanofibers and metal nanoparticles. They also introduced the nanoparticles utilized for antibacterial therapy, host modulatory therapy, and periodontal regeneration. Du et al.[9] reviewed several nanotechnology strategies for enhancing mucosal immune responses, including designing nano-vaccines with superior mucoadhesion and mucus penetration capacity for better targeting efficiency to M or antigen-presenting cells and co-delivering adjuvants. In addition, they briefly discuss applications of mucosal nanovaccines, including the prevention of infectious diseases and the treatment of tumors and autoimmune diseases. Wang et al.[12] provided an overview of the most widely used types of cancer immunotherapy, their mechanisms, and their clinical status. Furthermore, they summarized and discussed light-controlled nanoplatforms for improving the efficacy of

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immunotherapeutics and PDT/PTT-related immunotherapy. Lastly, two specific nanomedicines are present to manage wound healing and cancer. A report by Pastorin et al.[4] developed cell-derived nanovesicles generated from mesenchymal stem cells (MSC-CDNs) by shearing MSCs through membranes with different pore sizes. Their results demonstrated that MSC-CDNs could mimic naturally cell-secreted extracellular vesicles and improve angiogenesis in human dermal microvascular endothelial cells in a 3D PEG-fibrin scaffold and animal model, accelerating wound healing *in vitro* and *in vivo*. Later, Choi et al.[5] reported a hollow gold-iron oxide nanoparticle modified with the sialic acid-binding lectin. Lectin-coated nanoparticles induced a blockade of the terminal sialic acid of CD24, leading to the inhibition of the interaction between CD24 and Siglec-10 that activated the macrophages. The particulate system is also responsive to NIR irradiation, which synergistically induces the progression of apoptosis in tumor cells and augments the phagocytic effect of macrophages. Last but not least, nanomaterials can also be integrated with the latest wearable technologies to improve patient comfort and compliance. Xu et al.[11] outlooked the use of wearable technologies in transdermally delivering drugs for immune disorders and related symptoms (inflammation and infection).

In sum, the research and development of nanomedicine have gained significant momentum in the past ten years and have been accelerating during this pandemic. We hope this issue points out some potential future direction of nanomedicine to integrate with electronics and communication engineering.

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