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Special issue: Recent advances in immunotherapy and immunoengineering

Recent advances in immunotherapy, such as immune checkpoint inhibitors and chimeric antigen receptor (CAR) T-cell therapy, have transformed the landscape of cancer treatment. By leveraging the body's own immune system, immunotherapy has expanded beyond cancer to address autoimmunity, fibrosis, and senescence. Nonetheless, there are still obstacles to overcome to further improve the efficacy of current immunotherapies. To that end, efforts have been made to elucidate the underlying mechanisms behind resistance to current immunotherapy regimens, alongside the exploration of novel therapeutic approaches to target and manipulate components of the immune system. In this special issue on *"Recent Advances in Immunotherapy and Immunoengineering"* of Bioactive Materials, we introduce cutting-edge biomedical and bioengineering technologies to boost the efficacy of immunotherapies and overcome current challenges in the field. Selected research and review articles from multiple disciplines, including biology, immunology, synthetic biology, material science, and biomedical engineering, showcase examples of these interdisciplinary approaches and their target areas.

While CAR T-cell therapy has demonstrated remarkable success in treating B cell malignancies, it has encountered several challenges in solid cancers, including limited tumor infiltration and safety concerns. Zhu et al. highlight the importance of optimizing CAR T-cell designs, tumor modulation, and delivery strategies to enhance efficacy and safety in solid tumor treatment [1]. The immunosuppressive tumor microenvironment (TME) weakens current cancer immunotherapies, but advanced nanocomposites with synergistic functions have the potential to boost immune responses against cancer. The review by Sharma and Otto [2] explores recent advancements in nanomedicine, emphasizing the potential of TME-modulating nanocomposites in cancer immunotherapy, with candidates at the clinical-stage.

In addition to T cells, other cell types are engineered for application in immunotherapy:

- The integration of neutrophils with nanotechnology has opened new avenues in drug delivery, as reviewed by Yuan and Hu [3]. Neutrophil-based nano-drug delivery systems demonstrate enhanced biocompatibility and targeting abilities, offering potential applications in disease treatment. Despite challenges, these innovative approaches offer hope for more effective and targeted therapies in the future.
- Regulatory T cells (Tregs) are pivotal for immune tolerance, showing promise in treating organ transplants and autoimmune diseases. Recent advances in Treg biology have led to clinical trials confirming their safety and efficacy. Biomaterial-assisted Treg immunotherapy, as discussed by the Kim group, holds significant potential to tackle challenges like cell migration and stability, offering hope for enhanced transplant medicine and autoimmune treatments [4].
- Lin et al. utilized synthetic biology to engineer tumor-targeting bacteria, offering a promising approach to produce therapeutics such as granulocyte-macrophage colony-stimulating factor (GM-CSF) and IL-7, within tumors [5]. Engineered Salmonella typhimurium VNP20009, producing GM-CSF and IL-7, preferentially colonize tumors, inhibit tumor growth by enhancing immune cell infiltration, and when combined with PD-1 antibody, synergistically impede tumor progression and metastasis.
- Lee's group emphasizes the significance of targeting chronic systemic inflammation, which ultimately leads to type 2 diabetes, coronary heart disease, and breast cancer, at its source in the microenvironment of obese white adipose tissue [6]. They suggest immunotherapy as a promising therapeutic approach for obesity-induced non-communicable diseases, while also addressing associated challenges and perspectives.
- Mesenchymal stromal cells (MSCs) show promise for treating neuroinflammation in neurodegenerative diseases through their immunomodulatory function mediated by secreted extracellular vesicles (EVs). Larey et al. investigate the potential of 'priming' MSCs with inflammatory signals to enhance their function and the manufacturing of MSC-EV in bioreactors, offering insights into improving large-scale MSC-EV manufacturing and therapeutic efficacy [7].

Various cellular components have been engineered using biomaterials to address different aspects of the immune system:

- Exosomes, highlighted by Essola et al., have garnered substantial scientific interest for their ability to facilitate inter-tissue communication and their easily absorbable size range [8]. Originating from diverse cells, these vesicles can transport specific biomolecular cargoes, either enhancing immune responses or facilitating immune suppression, thereby advancing immunotherapy research across molecular biology, nanomedicine, and nanotechnology.
- Since the approval of lipid nanoparticle (LNP)-mRNA vaccines for SARS-CoV-2, there has been an increased interest in mRNA delivery via LNPs. However, current LNP formulations containing PEG lipids may trigger anti-PEG antibodies, potentially causing adverse reactions and reducing therapeutic efficacy. Given the widespread use of COVID-19 vaccines, the Dong group evaluated alternative LNP

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formulations such as a series of polysarcosine (pSar) lipids without PEG components [9].
- Singh et al. emphasized smart nanomaterial-based delivery systems for therapeutics utilizing non-coding RNAs (ncRNAs), including miRNAs, lncRNAs, and circRNAs, in the treatment of glioblastoma (GBM) [10]. This approach aims to address challenges associated with delivering therapeutics to GBM, such as overcoming the blood-brain barrier and RNA fragility.

Finally, critical advances have been made in the development of drug delivery systems for the effective delivery of therapeutics to target organs, with the goal of reversing immunoediting or regulating the homeostasis repair of lymphocytes [11].

We hope that this special issue highlights the rapid progress of multidisciplinary research within immunotherapy and immunoengineering. Looking forward, the prospects of immunoengineering appear promising, with further advancements in disease prevention, diagnostics, and treatment on the horizon. Essential to this progress are collaborative efforts among immunologists, material scientists, engineers, and clinicians, to enable the bench-to-bedside translation of innovative research.

It has been a pleasure to organize this special issue on *"Recent Advances in Immunotherapy and Immunoengineering"* for Bioactive Materials. We would like to thank all the contributing authors and extend our deepest gratitude to the Editors-in-Chief, Dr. Yufeng Zheng and Dr. Jian Yang, for giving us the opportunity to spearhead this project. We also would like to give our special thanks to Publishing Director Jessica Wang and Journal Manager Arjun Narayanna for their extensive support.

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