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EDITORIAL

Overcoming transport barrier to immunotherapies

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The number of immunotherapies has rapidly grown in the last decades, ranging from new cancer immunotherapies to better treatments for chronic ailments like inflammatory bowel disease, asthma, and arthritis. Currently, the global immunotherapy market is expected to reach a market growth of $275 billion by 2025 from $163 billion in 2020 [1], highlighting the rapid advancements in this field. Despite these advances, effective delivery of immunotherapies to their site of action—whether tissues or cells—poses a significant obstacle to maximizing immunotherapeutic efficacies. As part of the Immuno Delivery Focus Group's effort, we have compiled a special issue focusing on overcoming transport barriers to immunotherapeutic treatments.

We first introduce the topic of the special issue via a perspective from our distinguished colleagues Drs. Shann Yu, Melody Swartz, and Jeffrey Hubbell [2]. The special issue includes articles highlighting design of new drug delivery vehicles to improve therapeutic targeting as well as mechanisms and in vitro model systems to study transport barriers to immunotherapy that can inform the development of future drug delivery platforms. Several of the articles focus on challenges relating to cancer immunotherapy. Ukidve et al. describe the current tumor-associated barriers, in vitro model systems to study these barriers, and drug delivery strategies to overcome these barriers [3]. Carney et al. describe current strategies explored for treating breast cancer brain metastases using nanotherapeutics, ranging from targeting the blood–brain/tumor barrier to the tumor cells directly [4]. Ramesh et al. used a self-assembled lipid nanoparticle system containing anti-PDL1 antibodies and CSF1R inhibitors to effectively treat melanoma [5]. Rui et al. highlight physiological, immunological, and drug delivery barriers to enhance glioblastoma immunotherapies [6]. Turk et al. describe different cell-based therapies for treating brain disorders including cancer and neurodegeneration [7]. Another group of articles highlight the extracellular matrix (ECM) and stroma as barrier to immunotherapies. Chung et al. describe different strategies that have been developed to overcome stromal barriers to cancer immunotherapy [8]. Aghlara-Fotovat et al. describe drug and cellular therapeutic delivery strategies to target ECM in diseased microenvironments to restore tissue homeostasis [9]. Several articles describe design of therapeutics for treating inflammatory conditions like arthritis and type 1 diabetes, as well as targeting lymph node–resident leukocytes for various immune applications. Tu et al. describe current biomaterial-based strategies for targeting immunity in rheumatoid arthritis [10]. Li et al. designed a dexamethasone and MCL-1 siRNA containing nanoparticle system to reduce the inflammatory response in rheumatoid arthritis [11]. Zewail et al. describe a new smart hydrogel system that can be injected intra-articularly to reduce inflammation in arthritic joints [12]. Carey et al. used microparticles loaded with rapamycin and type 1 diabetes–relevant antigens to induce regulatory T cell differentiation and reduce proinflammatory cytokines against diabetes [13]. Archer et al. quantitatively assess uptake of different macromolecules and drug delivery systems by lymph node–resident leukocytes within the lymph node parenchyma [14]. And lastly, several articles highlight existing model systems of immune tissues or immunological components of larger tissues as well as the immune-vascular niche. Ramirez et al. describe microfluidic systems designed to study lymphoid tissues such as lymph nodes and bone marrow, to assess immune involvement in diseases like cancer, and screening tools to better design immunotherapies [15]. Finally, Silberman et al. describe in vitro model systems to investigate endothelial cell—immune cell interactions, particularly in the context of cancer and other diseases [16].

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