



# Emerging immunotherapeutics for immune activation and tolerance

Ryan M. Pearson<sup>1,2,3</sup> · Abhinav P. Acharya<sup>4,5,6,7,8</sup> · James J. Moon<sup>9,10,11,12</sup>

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Immunotherapy has risen as a powerful and effective approach to treat a variety of diseases including cancer, infection, autoimmune disease, and several others. Numerous breakthroughs in recent years have garnered intense excitement, including monoclonal antibodies, checkpoint inhibitors, and adoptive cell therapies. Despite the current success of immunotherapies in the clinic, numerous opportunities are available to improve therapeutic responses. In particular, the ability to controllably modulate innate and adaptive immune responses by employing novel approaches in drug delivery and immune engineering holds significant promise for the future, where achieving the appropriate balance between immunostimulatory and immunosuppressive responses is required. The Immuno Delivery Focus Group of the Controlled Release Society (CRS) has therefore assembled this special issue of Drug Delivery and Translational Research (DDTR). This issue aims to provide the latest scientific and technological advances in the development of

immunotherapeutics for immune activation and tolerance focusing on the use of biomaterials- and nanotechnology-based approaches. Six original research articles as well as six reviews from leading research groups and institutions globally were contributed from the UK, Spain, Jordan, Iran, South Korea, and the USA. Together, this group of contributors has expertise in cancer immunotherapy, autoimmune disease, antigen-specific immune tolerance, protein engineering, regenerative medicine, innate and adaptive cell immunomodulation, cell transplantation, targeted drug delivery, natural product drug discovery, and cancer immunotherapy.

Modulation of innate immune and adaptive immune cells holds great promise to positively affect clinical outcomes. Dr. Abhinav P. Acharya (Arizona State University) describes the development of microparticle-based vaccines for the metabolic reprogramming of immune cells to prevent the reintroduction of rheumatoid arthritis symptoms [1]. In an

✉ Ryan M. Pearson  
rpearson@rx.umaryland.edu

Abhinav P. Acharya  
apachary@asu.edu

James J. Moon  
moonjj@med.umich.edu

<sup>1</sup> Department of Pharmaceutical Sciences, University of Maryland School of Pharmacy, 20 N. Pine Street, Baltimore, MD 21201, USA

<sup>2</sup> Department of Microbiology and Immunology, University of Maryland School of Medicine, 685 W. Baltimore Street, Baltimore, MD 21201, USA

<sup>3</sup> Marlene and Stewart Greenebaum Comprehensive Cancer Center, University of Maryland School of Medicine, 22 S. Greene Street, Baltimore, MD 21201, USA

<sup>4</sup> Chemical Engineering, School for the Engineering of Matter, Transport, and Energy, Arizona State University, Tempe, AZ 85281, USA

<sup>5</sup> Biological Design, School for the Engineering of Matter, Transport, and Energy, Arizona State University, Tempe, AZ 85281, USA

<sup>6</sup> Biomedical Engineering, School of Biological and Health Systems Engineering, Arizona State University, Tempe, AZ 85281, USA

<sup>7</sup> Materials Science and Engineering, School for the Engineering of Matter, Transport, and Energy, Arizona State University, Tempe, AZ 85281, USA

<sup>8</sup> Biodesign Center for Immunotherapy, Vaccines and Virotherapy, Arizona State University, Tempe, AZ 85281, USA

<sup>9</sup> Department of Pharmaceutical Sciences, University of Michigan, Ann Arbor, MI 48109, USA

<sup>10</sup> Department of Biomedical Engineering, University of Michigan, Ann Arbor, MI 48109, USA

<sup>11</sup> Department of Chemical Engineering, University of Michigan, Ann Arbor, MI 48109, USA

<sup>12</sup> Biointerfaces Institute, University of Michigan, Ann Arbor, MI 48109, USA

approach associated with cell transplantation, Dr. Catherine A. Fromen (University of Delaware) describes the use of nanoparticles as a pre-treatment strategy to improve the survival and activation of pulmonary macrophage transplants [2]. Drs. Eduardo Fernández-Megía, María José Alonso, and Fernando Torres Andón (Universidade de Santiago de Compostela) report on the development of mannose-modified nanocapsules to improve targeting tumor-associated macrophages in fibrosarcoma [3]. Dr. Nisarg J. Shah (University of California, San Diego) reports on the use of short-chain fatty acids and liposomal carriers for the epigenetic modulation of inflammatory T cells [4]. Dr. Khuloud T. Al-Jamal (King's College London) studied the effects of in situ vaccination of tumors using immunoadjuvants on the anti-tumor antibody response [5]. Finally, Dr. Suhair Sunoqrot (Al-Zaytoonah University) presents research on anti-oxidant nanoassemblies from the extract of roasted coffee beans and their behavioral and molecular effects on smoking withdrawal-induced anxiety [6].

Additionally, the assembled review papers demonstrate the breadth of research ongoing for immunotherapies and immune engineering. Dr. Yu-Kyoung Oh (Seoul National University) reviews nanomaterial-based strategies to induce antigen-specific immune tolerance for the treatment of autoimmune and allergic diseases, including current challenges and perspectives for the induction of antigen-specific immune tolerance [7]. Dr. Leila Arabi (Mashhad University) summarizes the potential for targeting fibroblast activation protein to improve cancer immunotherapy [8]. Dr. Yong Taik Lim (Sungkyunkwan University) reviews how nanoengineered delivery strategies are being developed to overcome the immunosuppressive tumor microenvironment [9]. Dr. James J. Moon (University of Michigan) highlights the roles of neutrophils and neutrophil extracellular traps (NETs) in cancer progression and metastasis and how new drug delivery approaches can be leveraged to improve cancer therapeutics [10]. Dr. Jutaeck Nam (Chonnam National University) discusses the potential of nanocarriers for cancer nano-immunotherapy, preclinical studies designed to improve clinical cancer immunotherapy modalities, and how nanocarriers possess the opportunity to address challenges faced by immune-oncology and clinical translation [11]. Finally, Dr. Christopher B. Rodell (Drexel University) presents biotherapeutic and biomaterial-based approaches to control the post-infarct immune microenvironment [12].

On behalf of the leadership of the CRS Immuno Delivery Focus Group, we are immensely grateful to the authors for contributing their excellent submissions and insights to this special issue of DDTR. We believe that the diverse range of research and perspectives highlighted can serve as a catalyst to spur new insights and innovations in the rapidly evolving immunotherapy development field. Through the

collaborative efforts of researchers in this highly multidisciplinary field, we hope that the full potential of immunotherapy can be uncovered to yield revolutionary approaches to the treatment of immune-mediated diseases to improve human health.

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