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PREFACE

Relationship between Tissue Regeneration and Immune Modulation

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The immune system is a sophisticated network of tissues, cells, and immune proteins that guards the body of the host against harmful materials like infection. I am sure everybody is thrilled to usher in a new era for precision and personalized medicine thanks to the development of technologies such as genome editing tools like the RNA-guided CRISPR (clustered regularly interspaced short palindromic repeats)-Cas (CRISPR-associated) nucleases system, miniaturized self-organized three-dimensional tissue units known as organoid, and chimeric antigen receptor (CAR) therapy. When these technologies are paired with nanotechnology to modify amenities like modification of physicochemical characteristics or targeted gene delivery, it becomes a formidable tactic. In fact, to increase the effectiveness of gene delivery, Mohammad Ariful Islam et al. [1] recently addressed key cues on how to manage the cellular absorption paths of polymeric carriers and their endocytic trafficking.

I would like to introduce five articles to discuss tissue regeneration and damage control through immune modulation. The article titled "Remodeling and Restraining Lung Tissue Damage Through the Regulation of Respiratory Immune Responses" by Pyung et al. [2] covers how immunological reactions can be triggered by a variety of stimuli, and how controlling these reactions is essential for manage organ and tissue damage. The role of the innate and adaptive immune systems in modifying and designing lung tissue is the core part of the discussion. While adaptive immune cells, such as resident memory T cells in the lung, stop chronic illness that leads to tissue destruction, innate immune cells, such as macrophages and type 2 innate lymphoid cells (ILC2s), are engaged in tissue damage and remodeling. In accordance with biological and environmental signals, authors provided an overview of pulmonary innate and adaptive immune responses in association with damage control and remodeling of lung tissue.

The article, entitled "Intestinal Peyer's patches: structure, function, and in vitro modeling" by Park et al. [3] discusses the importance of understanding the mechanisms that control and regulate antigens in Peyer's patches (PPs) in developing immune therapeutic strategies against gut inflammatory diseases. The article provides an overview of the unique structure and function of PPs and current technologies used to establish in vitro PP system. The article highlights the shortcomings of the current in vitro PP models, which are not sufficient to recapitulate how the mucosal immune system works in vivo, and thus proposes the use of advanced three-dimensional cell culture technologies to bridge the gap between animal models and human conditions.

The article, entitled "Enhancement of Immune Responses Elicited by Nanovaccines through a Cross-Presentation Pathway" by Kim et al. [4] discusses the need for advanced vaccine delivery system in order to overcome the limitations of traditional vaccines in preventing emerging viral and bacterial infections. To note that for the induction of $CD8^+$ T cell responses, cross-presentation of foreign

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antigens on major compatibility complex class I molecules is crucial, particularly when it comes to vaccination against intracellular infection, and anti-tumor therapy. Therefore, nanovaccines, which can induce exogenous antigens in $CD8^+$ T cells through the cross-presentation pathway, are a promising option for protection against intracellular infections. The article discusses the advantages, preparation, and requirements of nanovaccines, as well as the various factors that affect cross-presentation. In addition, future perspectives on the use of nanovaccines are described.

The article entitled "Nanoparticle-Based Chimeric Antigen Receptor Therapy for Cancer Immunotherapy" by Shin et al. [5] highlights the drawbacks of conventional chimeric antigen receptor (CAR)-engineered T cell therapy for solid tumors and how nanoparticle-based CAR therapy might be able to address these limitations. Nanoparticles could offer an alternative to traditional CAR-T therapy, since they can serve as a delivery platform for not only drugs but also targeting specific cells. Nanoparticle-based CAR therapy can be applied to CAR-natural killer cell and CAR-macrophage, compensating for some limitations of conventional CAR-T therapy. The article describes future perspectives on immune cell reprogramming and introduces nanoparticle-based enhanced CAR immune cell treatment. While further research is needed to optimize this approach, with continued advancement in nanotechnology and immunotherapy, nanoparticle-based CAR immune cell therapy is likely to become an important tool in the fight against cancer.

The last but not least, the article entitled "Immunomodulation for Tissue Repair and Regeneration" by Moon et al. [6] examined how the immune system may regulate inflammation, cell proliferation, and tissue remodeling to promote tissue repair and regeneration. Various immune cell subtypes, such as macrophages, neutrophils, T cells and B cells, have distinct roles to play. While they are not without drawbacks like the possibility of immunological rejection and adverse immune reactions, regulatory T (Treg) cell-based and biomaterial-based immunotherapy techniques seem promising for tissue repair and regeneration. It comes beyond saying that in order to address the difficulties associated with immunotherapy techniques, we need a greater comprehension of the specific role of host immune regulation. The article discusses recent technological advancements with a specific focus on the role of Tregs for cell- and biomaterial-based modulation of the immune system.

It has been my immense pleasure to invite review articles focusing immune modulatory activities that could be utilized in number of different areas including remodeling of mucosal damages, three-dimensional cell culture techniques, induction of specific immune memory cell activation by using nanomaterials and CAR immune cell therapy. With series of articles in the special issue, we might be able to explore the mucosal innate and adaptive immune systems for the regulation of respiratory immune responses to control lung tissue damage and remodeling. The intestinal PPs are another mucosal immune organ that could benefit from the application of cutting-edge three-dimensional cell culture techniques to improve the model system for studies closely connected to the human intestinal mucosa [7]. Since mucosal sites are the major portal to infectious pathogens it could be important to adapt the potential of nanovaccines to overcome limitations of traditional vaccines in preventing intracellular infections with a focus on inducing $CD8^+$ T cell responses through cross-presentation [8]. Furthermore, we should understand how the immune system regulates inflammation, cell proliferation, and tissue remodeling for tissue repair and regeneration, with a focus on the role of ICL2 or Tregs for cell- and biomaterial-based modulation of the immune system. There are recent technological advancements of nanoparticle-based CAR immune cell therapy as an alternative to traditional CAR-T therapy for the treatment of solid tumors. Collectively, I am confident that big data-related approaches leveraging AI and machine learning will swiftly combine and use all of these technology platforms.

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