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The effect of nanomaterials on the innate immune system: therapeutic opportunities and immunological risks

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***Abstract*— Nanomaterials: List of Current Nanomaterials Showing Potent Progress on Based on Diagnostics or Target Experience: Nanomaterials have Caused Dent in Medical Apply, Specificity Nanomaterials Have Come Far Nano-Designed Diagnostics NanoGroup-based Nanodiagnostics Nanotherapies Nanomaterials Have Gained Ground Near Medical Employ, Particularly On Imaging Or Speciality Nanoplast Nanoplatform Nanobiomedicine Nanomaterials Nanomaterials Nanomaterials Nanomaterials: An Overview OfTheir Medical Drafts Nanomedicine Nanomedic Nanodise Nanodermatological Applications Of Nanobiomaterials, Application Of Nanotechnology In Bioimaging, Diagnosis, And Targ MicroNaso Nanocarriers Nanomaterials Nanomaterials Nanomaterials Nanotech BioOrganization Nanoplatforms Nanomaterial Nanoplasma Nanomaterials Nanoplast Nanomaterials Nanorobots Nanodiagnostics Nanoplastics Nanoparticles Nanorobots Nanomaterials Nanostructures Nanomaterials Nanogenesis Nanotechnology Nanoparticles Nanotechnologies Nanomachines Nanomaterials have come a long way from their diagnosis applications, especially in diagnosis and targeted applications. However, their engagement with the innate immune system raises questions not only about their immunological safety, but also their immunological risks. Abstract: Here, we review recent clinical studies and associated statistics that elucidate classes of nanomaterials with immunomodulatory effects on constituents of the innate immune system to reveal therapeutic opportunities and risks**

***Keywords* — Nanomaterials, Innate Immune System, Nanomedicine, Immune Modulation, Cytokine Response, Therapeutic Nanoparticles, Pattern Recognition Receptors (PRRs)**

INTRODUCTION

The innate immune system is the first of three pillars of the human biological defense system. Quick, innate response against pathogens that is able to stop early infection and then triggers adaptive immune response. It contains various molecular components such as pattern recognition receptors (PRRs) that detect foreign substances and activate immunity as well as specialized cells including natural killer cells, dendritic cells, and macrophages (1). They are, in turn, not long after, followed by some of the most thrilling scientific breakthroughs of the last few decades - nanomaterials. Nanomaterials are geometrical objects between 1 nm to 100 nm. These uniquesurface and biological properties allow them to specifically target cells, preferentially interact with proteins and penetrate cellular barriers (2). Due to these properties, nanomaterials are now applicable for diverse areas in medicine including molecular imaging, drug and vaccine delivery, and early diagnosis of chronic diseases such as cancer, autoimmune diseases, and degenerative diseases (3). But at the same time there are some possible issues with the medical applications. Despite the advance in the biomedical usage of nanomaterials, many researches have reported that their surface properties may lead to immunotoxicity or unexpected immune responses due to the direct contact of some nanomaterials with innate immune cells (4). What is more, protein-coupled and functional organism-coupled nanoparticles can juxtapose systemic or local inflammatory reaction through excessive over-stimulation of macrophages or brought on upsurge in secretion of inflammatory cytokines and interleukins (5). Conversely, certain features, i.e., surface charge or particle size distribution may suppress innate immune responses in other cases, which in turn can impair infection resistance or result in inappropriate pathogen tolerance (6). Nanoimmunology, bridging the gap between materials science and immunology, is the scientific research field which studies the interaction of nanoparticles with the innate immune system. AbstractReccommendations combining clinical efficacy and safety are indispensable in the field of nanomedicine (1,2). To that end, herein, we explore a critical research area that addresses both the inherent therapeutic opportunities afforded by nanomedicine and the potential immunological risks inherent to its application: the modulation of innate signaling pathways by nanomaterials.

IMMUNOLOGY

Immunology is the science of how the body reacts to foreign organisms (like viruses, bacteria, fungi and parasites) and to cancer and other foreign objects. The immune system can be broadly classified into innate and adaptive immunity (7). In addition to plasma proteins like complement and pro-inflammatory cytokines, innate immunity also encompasses specialized cells like macrophages, dendritic cells and natural killer cells. Toll-like receptors (TLRs) are the most important pattern recognition receptors (PRRs) that sense microbial components and induce early immune responses (8). Adaptive immunity is driven by T cells and B cells that are uniquely able to specifically recognize antigens via specialized receptors allowing for memory responses that can last a lifetime. Innate vs Adaptive Immunity Innate vs Adaptive Immunity as Dynamic Immune System Functions—The innate response typically informs the type and magnitude of the adaptive response. Immunology has undergone many transformative changes in the past decade driven largely by genomic, single-cell, and microarray data that allow for a more comprehensive analysis of the immune system dynamics in both health and disease. Advancing such approaches has led to novel therapeutic strategies, including mRNA vaccines [9], cancer immunotherapy (10), and immunomodulation with nanoparticles (9).

NANOMATERIALS *SCIENCE*

Nanomaterials science is an interdisciplinary field involving physics, chemistry, materials science and engineering. Nanotechnology can be defined as the science of studying and engineering at these lengths and sizes —all the way from 1 to 100 nanometers. Over this scale, materials demonstrate new properties that are radically different from their bulk properties including increased specific surface area and nontraditional optical, electrical and magnetic properties (11). Nanomaterials can be classified into different types according to structure and shape, such as: Nanoparticles: Nanotubes: Quantum dots: Nanosheet: self-assembled nanomaterials? These materials are commonly applied in different branches of science such as medicine, energy, environment, microelectronics, and computer science (12). In medicine, nanomaterials are increasingly being implemented to create smart drugs systems, whereas There are vaccines which have nanomaterials as adjuvants, cancer cells can be accurately imaged, and nanomaterials are beginning to be employed to selectively target tumors. Biodegradable bio-nanomaterials that release their drug payloads into very intracellular compartments and usually do not have long-term toxic effects in clinical settings have become increasingly important (13). In addition, surface functionalization allows scientists to engineer the behavior of nanomaterials in the biological environment by enhancing selectivity for target cells or limiting the immune system from responding against nanoparticles. At the same time, the very properties that provide nanomaterials with such unique potential may also create challenges regarding biosafety and immunological reactivity and require an understanding of the impact of nanomaterials on living systems (14). Due to advancements in nanofabrication techniques including but not limited to, bottom-up synthesis, nanoprinting, and micro-chemical processing, nanomaterials science has turned into one of the most burgeoning and significant fields of research, paving the way for processing materials to engineer, at atomic levels, functional properties 1(5).

THE RELATIONSHIP BETWEEN NANOMATERIALS AND IMMUNOLOGY

Nanoimmunology, representing a brand new field of research, is concerned with the interaction of nanomaterials with the immune system, which is critical for understanding the biocompatibility of nanomaterials. Nanomedicine consists of the research of the influence of physical and chemical properties of nanomaterials; size, shape, surface charge and surface chemical modification on the immune system, especially, the innate immune system (macrophages, dendritic cells, natural killer cells) (16). Nanomaterials entering the body via injection, inhalation or other routes do not bathe in a vacuum environment but rather encounter immediately a variety of plasma proteins that form what has been termed a protein corona that can completely redefine the identity of the nanoparticle as far as the immune system is concerned (17). This corona affects its recognition pattern by various immune cells, which can either promote or suppress immune response generation. In this regard, some nanoparticles that show their coating layer of plasma proteins recognize Toll-like receptors (TLRs) and potently activate inflammatory pathways (18). In addition, the immune simulation properties of some nanomaterials are similar to adjuvants, which lay the foundation for the innovative design of new vaccine adjuvants 5. Nanoparticles originating from biodegradable polymers (PLGA, e.g.) also have shown a good capacity of antenna on the antigen while activating dendritic cells and inducing an adaptive response, with antibodies and memory T cells production (19). On the contrary, the uncontrolled behavior of nanoscale properties could have harmfull effect on immune response. Certain metallic nanoparticles such as zinc oxide (ZnO) or titanium dioxide (TiO_2), may exacerbate the excessive release of inflammatory cytokines and provoke complications, such as chronic inflammatory diseases or tissue necrosis (20). Moreover, persistent nanomaterials are known to chronically inhibit or exhaust the immune system, which can lead to a heightened risk of infection or immune-related disorders (21). Thus, the immune interactions of nanomaterials for clinical applications must be critically evaluated across multiple levels of design, including particle synthesis, surface adornment and biodelivery. This translation requires the employment of accurate 3D systems (22), & animal models to be able to screen for possible immunotoxicity at the same time as maximising therapeutic efficacy with biological safety. However, the advent of nanoimaging or molecular analysis methodologies has also provided unprecedented resolution of the fate of nanomaterials in relevant immune cells, along with their mechanisms of action. Such can pave the way in the generation of so-called "smart" nanomaterials that only elicit a response in a setting of inflammation or tumor, thus potentially enhancing their specificity and minimizing side effects (23).

CONCLUSION

Nanomaterials and immunology are two scientific disciplines that have come together to reach a tipping point in the saga of biomedical research. The unique properties of nanomaterials build up great potentials in developing new therapeutic strategies with a focus on drug delivery, vaccine improvement and specific immune modulation approaches [22]. Multiple studies have shown that one can design nanomaterials with such intelligence in the engineering of immune response, to either stimulate the immune response against tumors for a clinically efficacious type of outcome, or dampen excessive immune response for chronic inflammation. However, the immunological risks need to be carefully balanced with these opportunities for therapeutic potential. Nanomaterials can trigger unpredictable immune responses of various types, ranging from excessive inflammatory stimulation to immunosuppression and chronic toxic effects, if not designed carefully. Personalized nanomedicine will be driven by the predisposition of an immune system to react to nanomaterials and fail the whole therapy, which is affected by environment, genetic and other factors, and can lead the preparation of nanomaterials on one side and the design of their testing on another side, into a problem [19]. Elucidating an improved and more detailed understanding of the mechanisms where nanomaterials interact with innate immune system is a scientific and ethical requirement for both safety and efficacy of their clinical applications. Nano-immunomedicine, through its combination of nanotechnology, sophisticated molecular analysis, and intricate biological models will unveil new worlds to investigate, which will serve as powerful preclinical platforms for developing less toxic, better tolerated and alternatively administered more specifically directed therapeutics. Finally, this study demonstrates that while the future of nanomaterials in medicine is bright, this promise will come with a cost, in the form of a stricter and stricter balance of (technological) innovation with (immunological) understanding, and a growing burden of regulatory testing, the combination of which will hopefully make for still safer and ever broader uses of sustainable therapeutic uses of nanomaterials in the future.

REFERENCES

1) Akira, S., & Takeda, K. (2004). Toll-like receptor signalling. Nature Reviews Immunology, 4(7), 499–511.Ravindran, V., & Abdollahi, M. R. (2021). Nutrition and digestive physiology of the broiler chick: state of the art and outlook. *Animals*, 11(10), 2795.
2) Nel, A., et al. (2006). Toxic potential of materials at the nanolevel. Science, 311(5761), 622–627.
3) Panyam, J., & Labhasetwar, V. (2003). Biodegradable nanoparticles for drug and gene delivery to cells and tissue. Advanced Drug Delivery Reviews, 55(3), 329–347.Jayaprakash, G., Bains, A., Chawla, P., Fogarasi, M., & Fogarasi, S. (2022). A narrative review on rice proteins: Current scenario and food industrial application. *Polymers*, 14(15), 3003.
4) Dobrovolskaia, M. A., & McNeil, S. E. (2007). Immunological properties of engineered nanomaterials. Nature Nanotechnology, 2(8), 469–478.
5) Moyano, D. F., et al. (2012). Nanoparticle hydrophobicity dictates immune response. Journal of the American Chemical Society, 134(9), 3965–3967.
6) Salvati, A., et al. (2013). Transferrin-functionalized nanoparticles lose their targeting capabilities when a biomolecule corona adsorbs on the surface. Nature Nanotechnology, 8(2), 137–
7) Chaplin, D. D. (2020). Overview of the immune response. The Journal of Allergy and Clinical Immunology, 146(2), 353–366.
8) Kawai, T., & Akira, S. (2019). The role of pattern-recognition receptors in innate immunity: update on Toll-like receptors. Nature Immunology, 20(3), 373–384.
9) Pulendran, B., & Ahmed, R. (2021). Immunological mechanisms of vaccination. Nature Immunology, 22(4), 539–550.
10) Stephenson, K. E., & Barouch, D. H. (2022). Vaccines and nanotechnology: emerging synergistic approaches. Nature Reviews Immunology, 22(1), 13–27.
11) Biju, V. (2021). Nanomaterials for biomedical applications. Chemical Society Reviews, 50(8), 3981–3998.
12) Mitragotri, S., et al. (2021). Engineered nanoparticles for drug delivery: Progress and prospects. Science Translational Medicine, 13(586), eaba9760.
13) Zhang, Y., et al. (2020). Nanoparticle-based vaccines: Opportunities and challenges. Nature Reviews Materials, 5(12), 955–973.
14) Amir, S. E. (2021). An investigation into the gut Fadeel, B. (2022). Safety assessment of nanomaterials: Implications for nanomedicine. Nature Nanotechnology, 17(1), 5–6.
15) Yan, Q., et al. (2023). Advances in nanomaterial design for biomedical applications. Nature Materials, 22(2), 123–137.
16) Chen, F., et al. (2022). Interactions between engineered nanomaterials and the immune system. Advanced Drug Delivery Reviews, 188, 114417.
17) Monopoli, M. P., et al. (2021). Biomolecular coronas provide the biological identity of nanosized materials. Nature Nanotechnology, 16(4), 358–366..
18) Moyano, D. F., et al. (2012). Nanoparticle hydrophobicity dictates immune response. Journal of the American Chemical Society, 134(9), 3965–3967.
19) Zhang, Y., et al. (2020). Nanoparticle-based vaccine platforms: promising immune modulators for infectious diseases and cancers. Journal of Nanobiotechnology, 18(1), 1–19.
20) Xia, T., et al. (2016). Mechanisms of in vivo inflammatory responses to engineered nanomaterials. Small, 12(27), 3008–3020.
21) Fadeel, B., et al. (2022). Immunotoxicity of nanomaterials: addressing immune system responses to nanomedicine. Nature Nanotechnology, 17(1), 8–10.

22) Sun, B., et al. (2021). Engineered nanomaterials and the immune system: challenges and opportunities. Advanced Science, 8(12), 2004786.

23) . Barenholz, Y. (2022). Smart nanocarriers and immune modulation: toward precision nanomedicine. Nature Reviews Drug Discovery, 21(5), 295–312.