Chapter 33

Nanotechnological Approaches to Immune Enhancement: A Novel Strategy

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ABSTRACT

The immune system is the body's defense system that protects it from any foreign pathogen. This defense system has two main components; the innate immunity which is the first line of defense and the adaptive immunity which retains the memory of all the past infections. With time and evolving microbes, the immune system has also developed mechanisms to control and combat a wide array of pathogens using body's both lines of defenses. Many people believe in using traditional immune boosting methods by consuming herbs and spices that include garlic, mushroom, ginger etc. but all of these methods are not really backed by strong scientific evidence. Nanotechnology is a promising new approach for targeted and enhanced immune responses. It has introduced improved and better ways to make immune system stronger. Use of nanotechnology in improved vaccine delivery and efficacy can be seen through the example of nano vaccine created by Novavax®. On the other hand, nanotechnology in cancer immunotherapy is also being recognized as a valuable tool for drug delivery in cancer treatments. Moreover, use of nanomaterials have also given hope to the researchers as a promising tool for managing various autoimmune diseases and allergic reactions as well.

KEYWORDS
Nanotechnology, Nanocarriers, Targeted drug delivery, Immune enhancement, Immunomodulation

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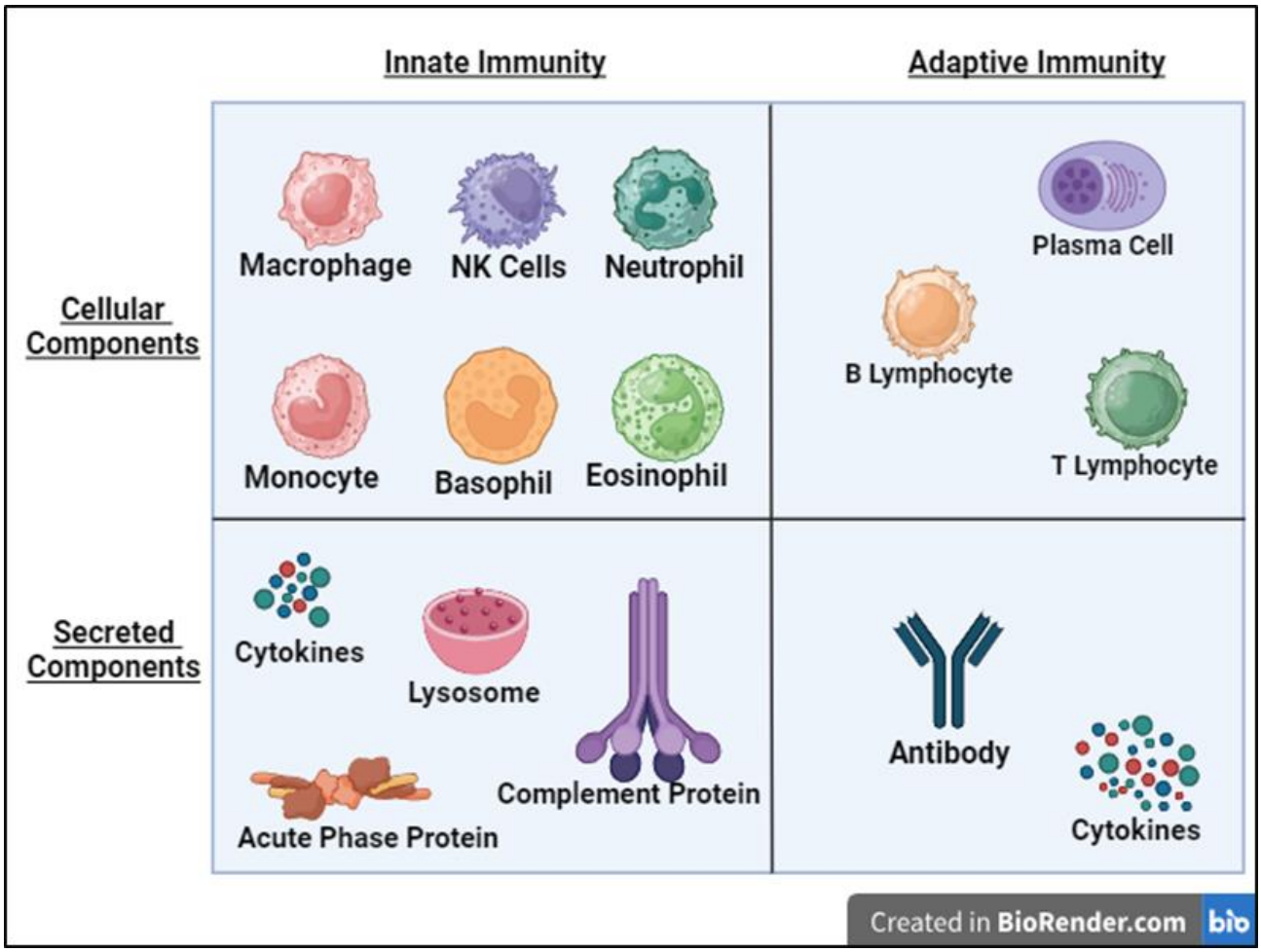
INTRODUCTION

The body has its unique and specialized system through which it protects itself against the harmful invaders. This is known as immune system of the body. It can be thought as a team made up of different components which includes organs, specialized cells, proteins and even chemicals, all of which work together to protect the body. This defense team has two main components that unite against the invaders to protect the body: Innate immunity and adaptive immunity. Innate immunity is body's first line of defense and guards the body against all the pathogens without remembering the specific threats and responds right away. On the other hand, the adaptive immunity is like body's special force which takes some time to respond but since remembers the past encounters, the response by adaptive immunity is more precise and targeted (Marshal et al., 2018). The immune system provides the body the necessary protection against a lot of dangers that range from harmful substances to all those microorganisms that may cause a disease. One of the main job is to protect the body against germs and foreign invaders, and prevent from the illness that they might bring. Moreover, the immune system monitors the body constantly for any changes inside the cells that could lead to illness. When and if something goes wrong and the body gets sick, the immune system steps in to helps the body heal and feel better (Marshal et al., 2018). The immune system has some special cells that include white blood cells, antibodies, complement proteins, and interferon etc. that act as frontline soldiers and play an important role in the body's defense and in maintaining the overall health by fighting any infections away.

Recognition and Response to Pathogens

When a pathogen invades the body, the immune system starts the response by first identifying the pathogen and

then it initiates a response against the invaders by initiating a complex set of actions to neutralize them. One of the important role of the immune system is its ability to differentiate and distinguish between body's own self and foreign/ non-self-entities in order to start a targeted defense mechanism against allergens, or any infectious agent. This ability to differentiate between self and non-self-entities is important for the immune system to ensure that it provides an accurate, efficient, and timely defense against foreign threats. The cells, proteins and chemicals in innate immunity and adaptive immunity work together as a team to detect and remove the infections. Antibodies also have an important role in finding and labeling the antigens by identifying and recognizing the microbes, hence making it easier for the immune system to destroy them (Chaplin, 2010).



On the other hand, pathogens have evolved and have developed various strategies to bypass the body's defense responses, including techniques that allow them to evade detection and elimination by the body. *Mycobacterium tuberculosis* is an example where we see that the bacteria have developed a complex cell wall resistance for the digestive enzymes of macrophages, which makes its eradication challenging for the immune system (Betts et al., 2013). The immune system has developed mechanisms to control and combat a wide array of pathogens using the body's both line of defenses, innate and adaptive, to detect and eliminate pathogenic threats effectively. (Betts et al, 2013 and Chaplin 2010).

Moreover, the immune system has a significant feature to retain the memory of past infections which, upon reinfection, enables it to generate a targeted response. This immune memory, along with the vaccination process, plays a vital role in providing a long-term protection and helps strengthen the ability of the immune system's to prevent pathogens without causing harm to self-tissues (Nicholson, 2016).

Common Traditionally Used Immune - Boosting Methods and Their Effectiveness

Many people are interested in traditional immune-boosting techniques that improve the immune system's memory-based reaction to antigens. Consumption of herbs such as garlic, mushrooms, ginger, soups, etc. that are traditionally thought to have immune-boosting qualities, is one of the popular strategies. But it should be kept in mind that the effectiveness of all these herbs and spices etc. is only backed by low quality evidence and traditional medicine, and not primarily based on medical advice (Cassa et al., 2019 and Wagner et al., 2020). Vitamin C is another traditional and common method which is used and believed to enhance one's immunity and prevent the body from infections. Vaccination, on the other hand, is one of the most effective methods and which is scientifically proven to develop antibodies against specific pathogens boosting up the immunity (Cassa et al., 2019 and Wagner et al., 2020). Scientific

evidence favors and supports vaccination, unlike traditional methods, and is considered a gold standard to prevent infections and enhance immunity in the long run (Wagner et al., 2020 and Cassa et al., 2019).

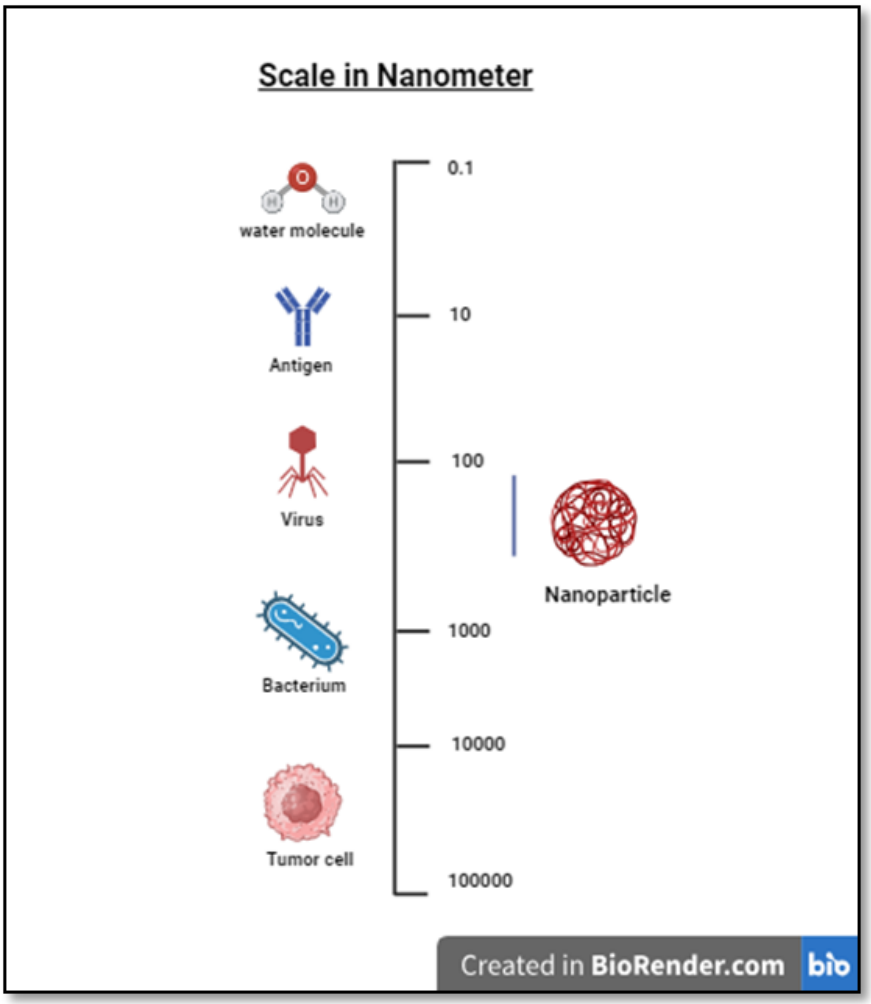
Multiple strategies and dietary modifications, including lifestyle improvements, are generally included in traditional treatments for boosting immunity and have even shown effectiveness in strengthening of the immune responses. It is important to establish an antioxidant balance in the immune cells to help them remain functional and protect them from oxidative stress, also making it sure that they receive enough nutrients for their sustenance (Mitra et al., 2022).

It has been proved through studies that when nutritional deficiencies are rectified through dietary adjustments and supplementations, the immune system might get the required strength to help the body fight off the disease. Moreover, vitamin like substances like coenzyme Q, choline, carnitine and inositol have been proved to play a huge role in regulating immune responses resulting in enhanced immunity. Additionally, experimental studies provide evidence that favors the effectiveness of vitamins and minerals in boosting immune functions and strengthening of the immune system (Mitra et al., 2022). Furthermore, immunity is significantly enhanced by physical activity. Exercise on a daily basis improves circulation and increases immune cell mobility, which allows them to actively reach for dangers and develop more robust and effective defenses (the guardian, 2016).

Introduction to Nanotechnology as a Promising New Approach for Targeted and Enhanced Immune Responses

Nanotechnology and its Scope in Immunology

Nanotechnology has expanded and opened new paths in the field of immunology. It has introduced improved and better ways to make our immune system stronger and create treatments that are specific to the problem. These nanoparticles filled with the right blend of cytokines and antigens not just give the body a quick boost against the diseases but also help it fight off the illness. Nanotechnology, through passive immunity, delivers immunoglobulin genes through nanoparticles which strengthen the immune system by making target specific antibodies without the body having to do much. These nanoparticles have different shapes, sizes, charge and other properties, and can be used to generate customized immune responses in unprecedented ways. This could not only help the body to prevent infections but also helps the body to fight off the disease before it occurs (Smith et al., 2013). Moreover, the science of nanotechnology helps the scientists to design and make synthetic materials that are proficient in delivering the drugs and biological treatments to the targeted immune cells, enhancing the effectiveness of gene and drug delivery, making the treatment work better. (Chuang et al., 2022)



Nanotechnology and Improved Targeted Immune Responses

Emergence of nanotechnology has revolutionized the field of immunology in multiple ways by offering creative approaches to strengthen the immune system. Nanogels, cationic liposomes and other nanoparticles act as carriers for the antigens and a guide for innate and adaptive immune responses to fight off the illness. (Smith et al., 2013 and Chehelgerdi et al., 2023). These nanoparticles, when acting as carriers, have the special ability to affect the immune responses, in a dose-dependent way, to activate the complement system, enhance antigen presentation and stimulate the toll-like receptor (Chehelgerdi et al., 2023). Moreover, the arrangement of antigens on the nanoparticle's surface can also encourage B-cell activation leading to efficient antibody production. (Smith et al., 2013 and Chehelgerdi et al., 2023). Additionally, these nanoparticles, by antigen cross presentation and signaling toll-like receptors, can also boost and influence the innate immune system positively. Nanoparticles also have the ability to release mediating substances like cytokines and chemokines and other immunomodulation substances to enhance the cytotoxic activity of T lymphocytes (Smith et al., 2013).

Nanotechnology, through these methods show a significant potential in areas like cancer immunotherapy, vaccine design, targeted drug delivery etc. opening new opportunities for fine-tuning the immune system and developing effective treatment plans (Chehelgerdi et al., 2023).

Nano Immunology - Interaction between Nanomaterials and Immune System

The interaction between nanoparticles and our immune cells depends highly upon their physicochemical properties like size, shape, charge, hydrophobicity etc. These factors play a pivotal role in deciding how nanoparticles will interact with different immune cells. This interaction sometimes may lead to immune toxicity which makes it important for the researchers to study how exactly these nanoparticles work in the body. This understanding will make sure they are safe for medical use minimizing the undesirable reactions. Moreover, nanoparticles can also interact with the immune system's soluble components like complement components further emphasize the complex relationship between nanoparticles and immune responses. Engineered nanoparticles have the ability to interact with different types of immune cells like monocytes/macrophages, neutrophils, granulocytes, dendritic cells etc. which sometimes may result into direct cytotoxicity or modulation of immune responses (Boraschi et al., 2017). Moreover, nanoparticles can also sometimes suppress some of the immune effector cells while activating the immune regulatory cells highlighting their effects on immune system. This might prove to be useful for vaccine delivery and increasing the efficacies of anti-inflammatory, antiviral and anticancer treatments (Dobrovolskaia et al., 2016).

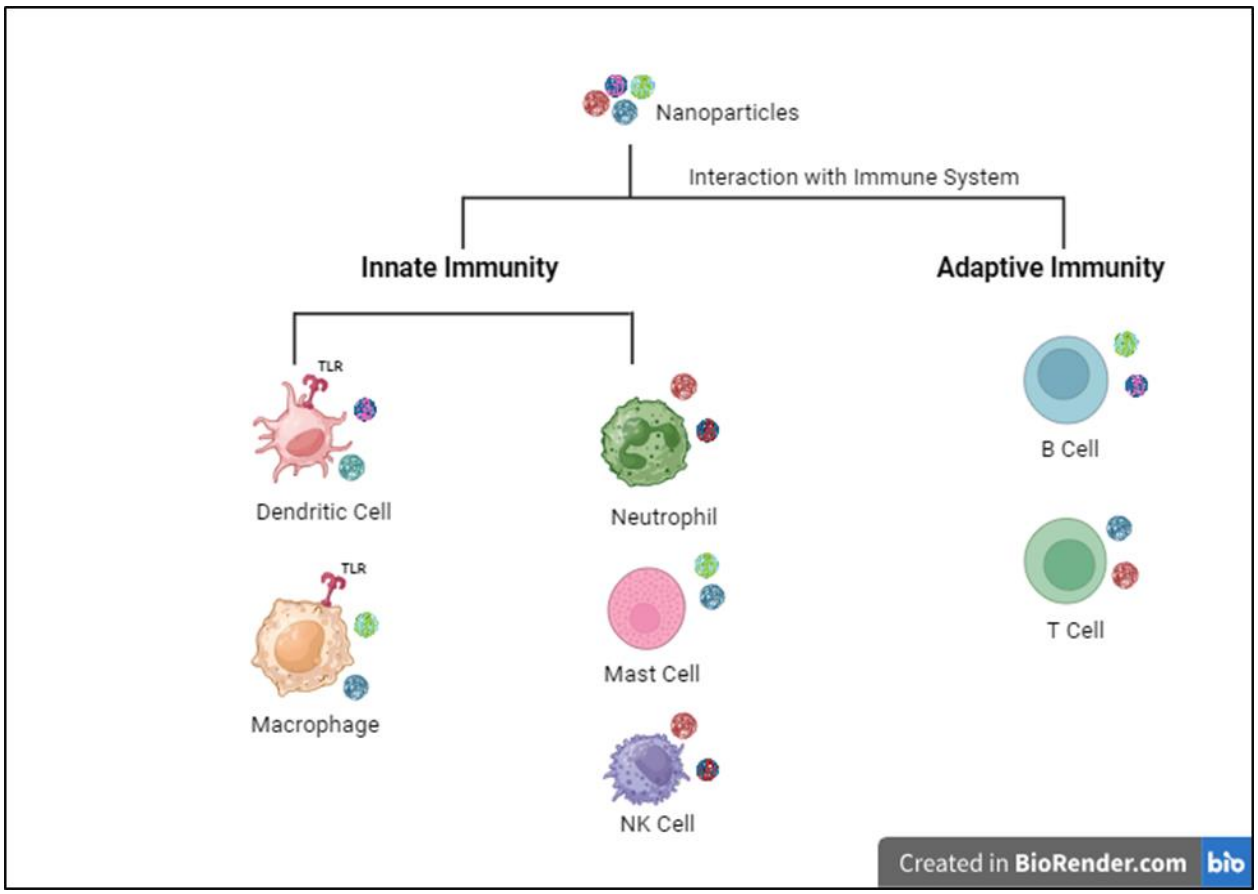


Fig. 1: Generic illustration of Nanomaterials multicolored circles, depicting their interaction with different cells in the Immune system. The image was generated by BioRender.

Nanotechnology and Immune Boosting Methods

Vaccine Development

Nanoparticles and Improved Vaccine Delivery

Nanoparticles are tiny but mighty tools that have distinct properties and capabilities, and bring opportunities for improving the vaccination process. They are custom-made miniature delivery vehicles specifically designed to carry the vaccine, so small and mirroring the structure of the pathogen, without causing any harm to the body. The nanoparticles can be tweaked to include the adjuvants that make the vaccines more effective resulting in better immunity. This customization allows controlled delivery and release of antigens, helping the immune system do its job in a better fashion. Nanoparticles also have the special ability to enter the cell and deliver the antigens to APCs which results in enhanced insusceptibility to disease (Panda, 2012).

Role of Nanomaterials in Vaccine Efficacy

Scientists and researchers use nanoparticles as special tools to make the vaccines work more effectively and efficiently. Researchers, with the help of nanotechnology, are learning more and more about the immune system and the way it responds to vaccines, making innovations for prevention and treatment of diseases. This is not only focused on just creating and developing new vaccines but also about making those vaccines that we already have, much better and effective. Nanoparticles like virus-like particles and protein nano-cages etc. mimic the look and apparent functioning of the pathogens, efficiently delivering the vaccine without causing any harm to the body. These nanoparticles also interact closely with the body's defense system helping it build a stronger immunity against diseases (Smith et al., 2013). Taking the example of nano vaccine created by Novavax®, it uses the spike protein of SARS-Cov-2. This vaccine has demonstrated effectiveness in triggering a strong immune response, showing the potential of nano vaccines in strengthening the body's ability to build immunity.

Nanotechnology and Cancer Immunotherapy

Utilization of Nanoparticles in Cancer Immunotherapy

Nanoparticles are now being recognized as valuable tools in cancer treatments. These tiny particles act as superheroes with special abilities and features that could bring about a significant change in ways cancer is treated. These super small materials are designed in a way that makes cancer treatment more effective along with reduction in side effects (Shams et al., 2022 and Dang et al., 2024). Nanoparticles play a very important role in cancer therapy by transporting the therapeutic agents directly to the targeted cells. This target delivery helps in the distribution and release of immune components at tumor location, eventually enhancing the effectiveness of treatment while reinforcing the immune system to fight off the cancer (Dang et al., 2024 and Shams et al., 2022). Besides all that, the transport of adjuvants and antigens to the antigen presenting cells is greatly enhanced by the nanoparticles, which in turn induce the specific immune response that is needed to fight off cancer (Shams et al., 2022). In this regard, cancer immunotherapy that is based on nanotechnology, not only just increases the treatment efficacy but also makes it more effectiveness (Dang et al., 2024). Furthermore, these nanoparticles can also pass through the body's natural defense barriers and get into the tumor environment, thus helping and allowing the treatment to go directly right where it is needed without being accumulated in any other parts of the body (Dang et al., 2024). Thus, nanoparticles can be considered as a multifunctional tool in cancer immunotherapy which includes their ability to transport the immunotherapeutic agents, act as immune-modulators and even help the vaccines to strengthen up the body's immune system against cancer etc, ultimately making them extremely useful in increasing the treatment efficacy in cancer (Debele et al., 2020).

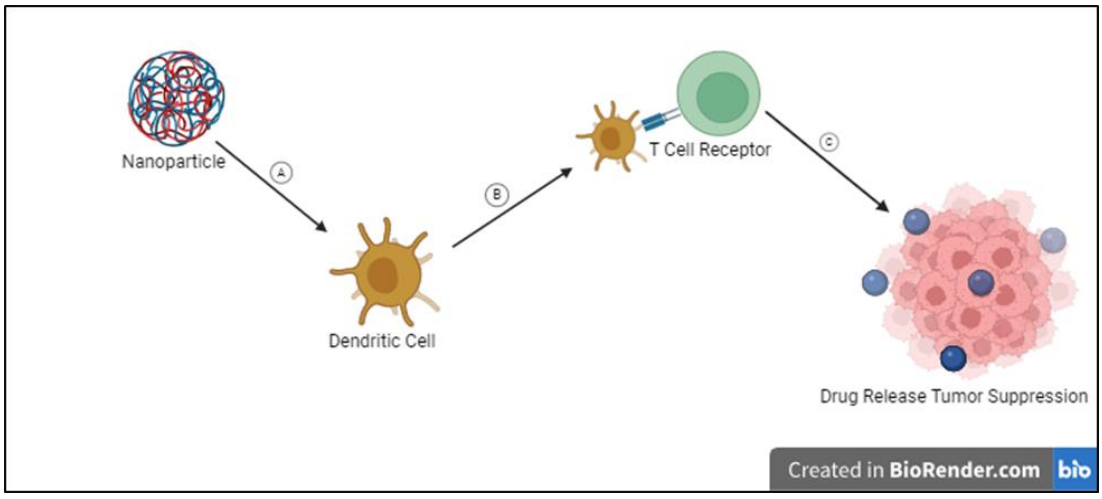


Fig. 2: Schematic illustration of nanoparticles interacting with Immune system A) Immunostimulation of dendritic cells through nanoparticles B) Priming of T cells by dendritic cells C) Release of drug into the tumor cells

Nanotechnology based Drug Delivery System and Immunotherapy

Nanoparticles and Delivery of Immunotherapeutic agents

Nanoparticles are emerging as an important and popular tool for delivering immunotherapeutic treatments and offer ways to make the treatments work better. These nanoparticles, after radiation or chemotherapy, grab the antigens shed by tumors and carry molecules, either immune stimulant or immune modulant in nature, to enhance the immune response. Moreover, vaccines that are based on nanoparticles are crafted in a way to trigger a strong response from T cells by delivering the adjuvants and antigens together, activating the dendritic cells and ensure that antigens are released constantly (NCI, 2023). Another method is the combined treatment of immunotherapy and phototherapy, done by putting the photo-dermal substances and immunotherapy drugs together inside the nanoparticle (Zhao et al., 2022). Furthermore, nanoparticles can be customized to target the specific cells and molecules within the tumor, bringing change in immunosuppressive conditions, to improve the treatment outcomes. The abilities of nanoparticles have a huge potential to make cancer treatment better by efficient drug delivery and enhanced immune responses. However, further studies are still needed necessarily to completely understand the actual effectiveness of using such method for the transportation and delivery of immunotherapeutic agents could be (Wu et al., 2022).

Targeted Drug Delivery and Advantages of using Nanocarriers in Immunotherapy

Nanocarriers serve as delivery vehicles that carry the drugs to the diseased cells with fewer side effects and offer a lot of advantages and effectiveness in drug delivery in immunotherapy (Kumbhar et al., 2023):

1. Nanocarriers can be custom designed to respond to the specific conditions of tumors, making sure that the drugs delivered are right where they are needed and enhancing the treatment efficacy at shrinking the tumor.
2. The encapsulation of antigens and adjuvants together inside the nanocarriers helps to create a long lasting immune response by activating the antigen presenting cells (APCs) effectively.
3. Specific cells like dendritic cells (DCs) etc. can be targeted by using customized nanocarriers resulting in enhanced antigen presentation and improved immune response (Kumbhar et al., 2023).
4. These nanocarriers, through special pH sensitive methods, can even cause lysosomes to rupture and trigger the production of reactive oxygen species (ROS) in dendritic cells. This results in boosting proteasome activity, making the immune system stronger.
5. Nanocarriers that are loaded with CD80 antibodies, bind to receptors on dendritic cells which further enhance the immune response (Kumbhar et al., 2023).
6. The use of nanocarriers in immunotherapy not only just delivers the drugs but also helps to target the blood vessels that are present around the tumor. This plays a role to overcome the resistance to the treatment. (NCI, 2023 and Wu et al., 2022).
7. Nanocarriers can even possess the ability to shift the cell-behavior in tumor from supporting the tumor growth to fighting against it (from pro-tumor to anti-tumor) (Kumbhar et al., 2023).

Nanotechnology and Autoimmune Diseases

Nanotechnology and Modulation of Immune Responses in Autoimmune Diseases

Researchers are hopeful that using nanotechnology they could be able to change or modulate how our immune system behaves in diseases like autoimmune disorders. The special abilities and features of nanotherapeutics, scientists can aim and stop the harmful immune reactions that occur in autoimmune diseases, leading to new and creative ways to deal and treat these conditions. Nanotechnology also helps us understand more about the working of the immune system in such diseases which is essential to find ways from their prevention and treatment (Smith et al., 2013). Also, nanomaterials have shown that they have the ability to either boost up or calm down the body's defense system which could be highly helpful for treating the diseases in which the immune system mistakenly attacks healthy tissues. Additionally, these particles can also serve as delivery vehicles and effectively carry the medicines directly to the problem causing cells that are involved in autoimmunity, thus, making the treatment more effective. Gold nanoparticles especially, have given hope to the researchers as a promising tool for managing various diseases like joint inflammation and nerve damage, indicating that this technology could be a huge help in treating such conditions (Chountoulesi and Demetzos, 2020). Furthermore, the intricate relations of the characteristics of nanoparticles, for example their size, shape, composition, surface properties etc, is what determines how they influence the immune system in autoimmune diseases. This also shows how essential it is to know what these factors are in order to effectively control the immune response (Mitarotonda et al., 2022).

Nanoscale Strategies to Target Autoimmune Cells and Induction of Immune Tolerance

In today's time and age, where autoimmune diseases are on rise, the use of nanotechnology has been a source of hope to many. Through the development of smart nano devices, researchers could be able to attain targeted drug delivery to those specific cells that cause the autoimmune inflammation, through which a more personalized treatment approach will be possible. Nanotechnology hold the potential to change the way how autoimmune diseases are managed by introducing new and improved therapeutic methods that are not only effective but also less invasive at the same time (Zhu et al., 2022).

The ability of nanoparticles to act as helpers by protecting, stabilizing and displaying antigens to APCs is significant for

inducing immune tolerance. The release of antigens into the bloodstream and surrounding tissues in a regulated manner, these nanoparticles can organize a targeted and effective immune response making them valuable in autoimmune treatments. However, it should also be kept in mind that these nanoparticles having all these unique properties to stimulate immunity could also, possibly, lead to their elimination or rejection by the body's defenses (Mobeen et al., 2022).

Nanotechnology and Allergic Diseases

Nanotechnology and Diagnosis and Treatment of Allergic Diseases

Nanotechnology has a great potential to change the ways practitioners deal with allergies. Scientists are now using nanoparticles to aim at the cells causing allergic reactions. This could mean there can be more accurate ways through which we can now figure out the allergies and treat them effectively (Paris et al., 2021). For example, nanoparticles made up of polymers when combined with CpG ODNs show that they can help in treating allergic reactions that are triggered by house dust mites. This is done by bringing and activating more dendritic cells to the airways resulting in a helpful and positive response to fight off the allergies (Johnson et al., 2020). Moreover, nanoparticles that contain protein or peptide antigens are more likely to stop and counteract the harmful immune reactions in allergies, which might be considered a new way to treat allergies. One of the major advantages of using nanotechnology in the management of allergic diseases is their ability to create immune tolerance that is antigen specific. This means it can help and control the way our immune system reacts and responds to the unwanted reactions that are commonly noticed in current treatments (Johnson et al., 2020). Also, when we use delivery systems based on nanotechnology, it helps make food allergens more available in the body and delivers them right where they're needed. This makes allergy diagnosis and treatment more effective because it targets the delivery exactly where it's needed (Rai et al., 2023).

Nanoparticles and Prevention from Allergic Reactions through Immunomodulation

Nanoparticles possess the ability to prevent allergies by changing how the immune system works through immunomodulation. The size of these antigen loaded nanoparticles, being so small and minute, helps to increase their permeability hence they are able to enter the tissue, facilitating the delivery to the target areas like blood vessels and lymph nodes. Some nanoparticles made up of amorphous silica have been noted to be even more efficient at penetration through skin and localized lymph nodes. Research has also shown that nanoparticles can boost up the potential of immunomodulation. For example, amorphous silicon dioxide nanoparticles when delivered through the skin in an allergy model help control the immune system way better. Hence, we can easily say that they are effective in preventing allergic reactions through immunomodulation. The physicochemical properties of nanoparticles, including their composition, size, charge etc. actually makes them useful for treating the allergies. They have the ability to activate and differentiate T-cells which makes them better to fight off the allergies. Nanoparticles also strengthen the immune system for the allergen uptake of allergens responsible to trigger allergies.

Conclusion

Incorporating the traditional immune-boosting methods with the improvements in nanotechnology presents a new approach to enhancing immune responses and effective management of immune-related diseases. The target specific abilities of nanotechnology, mostly in drug delivery and immune modulation is a huge step in the field of medical science. These improvements are impactful mainly in the fields of cancer immunotherapy and management of autoimmune and allergic conditions. These are the areas where targeted treatments can improve outcomes to a great extent and where precise modulation of the immune system is important. As nanotechnology makes progress, deep understanding of the complex interactions between nanomaterials and the immune system is necessary. This understanding of interactions will allow us to use this technology to great extent while also ensure that it remains safe and effective. Combining these advanced technologies with traditional methods may transform the approaches for addressing immune-related health challenges, laying foundations for more effective and personalized treatments in the future.

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