REVIEW ARTICLE

RFP Indian Journal of Hospital Infection
Volume 1 Number 1, January - June 2024

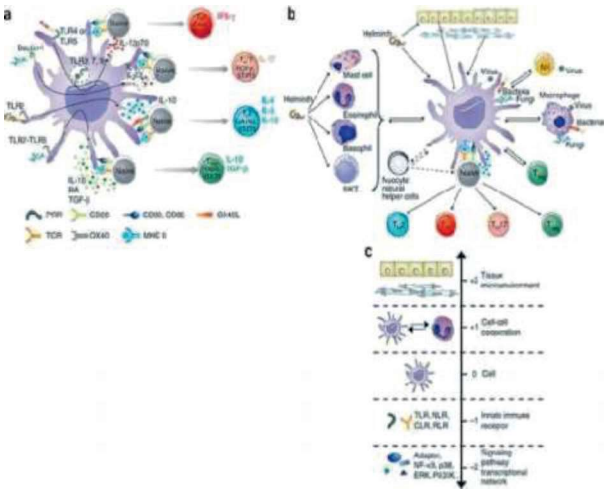
Nanomedicine and Immune Response

Ramendra Pati Pandey[1], Suresh Kumar[2]

Abstract

Nanoparticles are promising area of research in the area of drug delivery system. Immunostimulation or Immunosuppression properties are imporatnt to taking into consideration during the preparation of nanoparticles. Nanoparticles drug delivery system mediated immunostimulation and immunosuppression is crucial to make effective delivery systems. Nanomedicine is promising to use for diagnosis and relatively new therapeutics of infectious diseases.

Nanoparticles have unique physicochemical properties which make them promising platforms for drug delivery. However, immune cells in the bloodstream (such as monocytes, platelets, leukocytes, and dendritic cells) and in tissues (such as resident phagocytes) have a propensity to engulf and eliminate certain nanoparticles. (opsonins) and blood components (via hemolysis, thrombogenicity and complement activation) may influence uptake and clearance and hence potentially affect distribution and delivery to the intended target sites. Nanoparticle uptake by the immune cells is influenced by many factors. Different nanoparticles have been shown to act on different pathways, while various characteristics/ properties also affect which pathway is employed for particle internalization. Nanoparticle protein binding occurs almost instantaneously once the particle enters biological medium, and the physical properties of such a particle-protein complex are often different than those of the formulated particle. These new properties can contribute to different biological responses and change nanoparticle biodistribution. Therefore, in the situation when specific delivery to immune cells is not desired, the ideal nanoparticle platform is the one whose integrity is not disturbed in the complex biological environment, which provides extended circulation in the blood to maximize delivery to the target site, is not toxic to blood cellular components, and is "invisible" to the immune cells which can rem most recent data on nanoparticle interactions with blood components and how particle size and surface charge define their hematocompatibility. This includes properties which determine particle interaction with plasma proteins and uptake by macrophages.



Ref. Programming dendritic cells to induce TH2 and tolerogenic responses Bali Pulendran, Hua Tang & Santhakumar Manicassamy Nature Immunology, 11,

AUTHOR'S AFFILIATION:

[1]University of Sao Paulo, Brazil, [2]National Institute of Biologicals, Noida, India.

CORRESPONDENCE AND REPRINT REQUESTS:

Ramendra Pati Pandey, University of Sao Paulo, Brazil.

E-mail: bhavinhetal@yahoo.co.in

Received on: 12.01.2024 **Accepted on:** 20.03.2024

647–655 (2010)

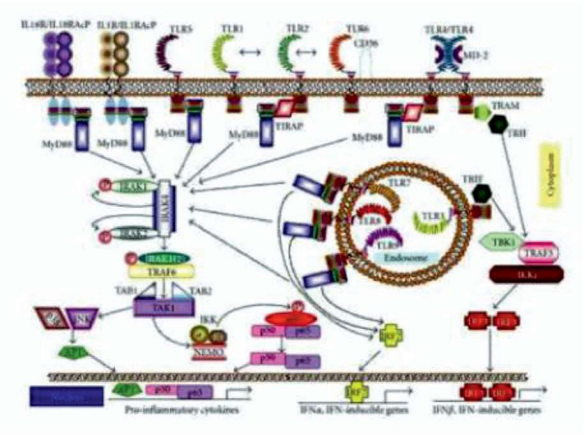


Figure: *TLR/IL-1R signalling pathways. Once activated by their respective ligands, IL-1R, IL-18R, and TLRs engage with one or more adaptor proteins. These adaptors, namely, MyD88, MAL/TIRAP, TRIF, and TRAM are recruited, in various combinations, to the cytoplasmic domains of the receptors through homophilic interactions between Toll/IL-1 receptor (TIR) domains present in each receptor and each adaptor. TIRAP is required to act as a bridge for MyD88 in TLR2 and TLR4 signalling, while TRIF is used in TLR3 signalling and, in association with TRAM, in TLR4 signalling. In the MyD88-dependent pathway, MyD88 associates with IRAK4, IRAK1 and/or IRAK2. IRAK4 in turn phosphorylates IRAK1 and IRAK2 and promotes their association with TRAF6, which serves as a platform to recruit the kinase TAK1. Once activated, TAK1 activates the IKK complex, composed of K± nIKNM, whichIK)catalyzes phopoyainadsbeun e NF-B(.. 5/6)fe otasoae-B-dependentrmgenes. Theh yo transcription factor IRF7 is also activated downstream of TLRs 7, 8, and 9, leading to its translocation into the ulu n oatvto-inducibleg enes.TLR3fand TLR4F±both signaln through Ftheadaptor TRIF, hc neat ihTA3t ciaetennaoiaactivto fIF,wihte rnlcts and IFNno-inducibleh ul genes.*

Activation of the innate immune system is mediated by pattern recognition receptors (PRRs) on particular immunocompetent cells that recognize pathogen-associated molecular patterns. The best characterized signaling PRRs to date are the Toll-like receptors (TLRs) present in plants, invertebrates and vertebrates that represent a primitive host defense mechanism against bacteria, fungi and viruses. Toll-like receptors (TLRs) play an important role in innate immunity. Individual TLRs recognise microbial components that are conserved among pathogens, such recognition initiates necessary inflammatory immune responses and induces subsequent activation of adaptive immunity (Uematsu & Akira, 2006). TLRS are like the sixth sense in our bodies, because they have an exquisite capacity to sense viruses and bacteria, and convey this information to stimulate the immune response. To achieve the best immune response, you need to hit more than one kind of Toll-like receptor. In conclusion TLRs are a type of pattern recognition receptors (PRRs) which recognize molecules broadly shared by pathogens but distinguishable from host molecules. TLRs can be divided into two groups according to their cellular localization: TLRs 1, 2, 4, 5 and 6 are mainly located on the cell surface and primarily recognize bacterial components, while TLRs 3, 7, 8 and 9 are mostly found in the endocytic compartments and mainly recognize viral products (Akira et al., 2006).

Toll-like receptors (TLR) and their ligands are one of the main players in the initiation of innate immunity which precedes, and is required, for the establishment of adaptive immunity. Manipulating the immune response by using TLR agonists or antagonists might be of therapeutic and/or prophylactic value (Makkouk & Abdelnoor, 2009). Exogenous signals are provided by TLRs mechanisms which affect the initiation, maintenance and progression of inflammatory diseases. Moreover, reagents that enhance TLR signaling pathways can be powerful adjuvants for fighting pathogens or cancer.

Role of Dendritic cells (DCs) in Immune Response

Dendritic cells (DCs) are potent antigen-presenting cells capable of initiating a primary immune response and possess the ability to activate T cells and stimulate the growth and differentiation of B cells. DCs provide a direct connection between innate and adaptive immune response, and arise from bone marrow precursors that are present in immature forms in peripheral tissues, where they are prepared to capture antigens. DCs migrate from the peripheral tissues to the closest lymph nodes through afferent lymphatic vessels to present the foreign antigens, stimulating T-cell activation and initiating a cellular immune response. Moreover, it is known that DCs have an important role in various diseases and conditions involving the immune system, particularly in cancer and autoimmune disorders. For these reasons, targeting nanoparticles (NPs) to DCs provides a promising strategy for developing an efficient balanced and protective immune response. NPs can modulate the immune response and might be potentially useful as effective vaccine adjuvants for infectious disease and cancer therapy.

References

1. Pulendran B, Tang H, Manicassamy S. Programming dendritic cells to induce T(H)2 and tolerogenic responses. Nat Immunol. 2010 Aug; 11(8):647-55. doi: 10.1038/ni.1894. Review. PubMed PMID: 20644570.
2. Ishii KJ, Uematsu S, Akira S. 'Toll' gates for future immunotherapy. Curr Pharm Des. 2006; 12(32):4135-42. Review. PubMed PMID: 17100616.

3. Makkouk A, Abdelnoor AM. The potential use of Toll-like receptor (TLR) agonists and antagonists as prophylactic and/or therapeutic agents. Immunopharmacol Immunotoxicol. 2009; 31(3):331-8. doi: 10.1080/08923970902802926. Review.

4. Chanchal, Abhishek; Vohra, Richa; Elesela, Srikanth; Bhushan, Lokesh; Kumar, Santosh; Kumar, Suresh; Ahmad, Saheem; Pandey, Ramendra Pati. Gelatin Biopolymer: A Journey from Micro to Nano. Journal of Pharmacy Research 2014; 8(10).

5. Ramendra Pati Pandey, Abhishek Chanchal, Richa Vohra, Md. Najmul Islam, Santosh Kumar, Lokesh Bhushan, Suresh Kumar, Pawan Sharma. Immune Response of Biopolymeric nanoparticulate systems. Journal of Pharma Research 2015; 4(8).