27

Plasma Membrane Camouflaged Nanoparticles: An Emerging Antibacterial Approach

AUTHORS DETAIL

Sidra Altaf, Tasawar Iqbal, Wafa Majeed, Muhammad Akmal Farooq, Dawood Naseer, Muhammad Saleem, Saif-ur-Rehman Babar, Mamoona Ikram

[1]Department of Pharmacy, University of Agriculture, Faisalabad
[2]Institute of Physiology and Pharmacology, University of Agriculture, Faisalabad
*Corresponding author: sidra.altaf@uaf.edu.pk

Received: Oct 23, 2022 Accepted: Dec 27, 2022

INTRODUCTION

Diseases caused by bacterial infections pose a major impact on both human and animal health and this threat is continuously increasing by enhanced antibiotic resistance (Carly et al. 2021). These bacterial infections may result in high rates of morbidity and mortality. Hence, emphasizing the urgent need to treat life threatening bacterial infections effectively. Recent developments in antibacterial treatment have mainly focused on targeted and responsive approaches for antibiotics and antibiotic alternatives (Wu et al. 2021).

Currently, new innovative approaches in nanomedicine hold promise for the treatment of bacterial infections, as the application of metal, metal oxide and polymeric nanoparticles dramatically promotes the therapeutic efficacy during infection (Baptista et al. 2018) as mentioned in Table 1.

A nanoparticle that has been administered into the body is destined to face a highly complex environment that is naturally capable of identify and eliminate foreign substances. For instance, the bloodstream contains various cellular and protein-based components, which may quickly impair the subscribed function of the nanoparticle (Haroon et al. 2022).

Furthermore, destruction by the reticuloendothelial system is one of the significant obstacles that almost all platforms must overcome before a nanoparticle can reach its target (Caliskan et al. 2019).

However, the difficulties associated with the application of synthetic nanoparticles divert the researcher's attention towards bioinspired nanotechnology which obtains its design cues from nature (Jiang et al. 2019).

Cell membrane coated nanoparticle based solutions are becoming increasingly popular in medical research, as they may offer significant benefits in terms of both efficacy and safety over current therapies and diagnostics (Islam et al. 2018).

Researchers are now working to exploit naturally-derived cell membranes as a way to deliver nanoparticles with enhanced bio interference capabilities, rather than attempting to replicate these biocompatible functions via synthetic techniques. This top-down approach is simple, versatile and has the potential to increase therapeutic efficacy as compared to existing nanocarriers significantly. Furthermore, introducing a natural membrane substrate on the surface of the nanoparticles has allowed additional applications beyond those traditionally associated with nano-medicine. Overall, there is still a considerable slot for improvement and development of new coated nanodrug moieties as researchers continue to improve existing workflows and discover new and exciting applications of this emerging nanotechnology (Fang et al. 2018). Ultimately, the goal is to create nanoparticles with surfaces that help them ignore everything but their targets, which is extremely difficult. Therefore, the addition of specific targeting mechanisms during the formulation of nanoparticles can improve efficacy by promoting preferential accumulation at the site of interest by reducing nonspecific targeting (Panda et al. 2020). The cell membranes coated nanoparticles.

Cell Membrane-coating Techniques

Membrane Extrusion

To produce a cell membrane-coated nanoparticle, the specific cell membrane must be coated over the nanoparticles core. The most frequently mentioned technique for cell membrane coating is membrane extrusion. It is one of the primary cell membrane-coating techniques. Biological membrane extrusion is performed so that the cell membranes and nanoparticles may move through membranes of various pore sizes concurrently, leading to the wrapping of the membranes over the nanoparticles. This method is beneficial; however, mechanical forces may affect the structure of the membrane (Hu et al. 2011).

Citation: Altaf S, Iqbal T, Majeed W, Farooq MA, Naseer D, Saleem M, Babar SUR and Ikram M, 2023. Plasma membrane camouflaged nanoparticles: an emerging antibacterial approach. In: Abbas RZ, Saeed NM, Younus M, Aguilar-Marcelino L and Khan A (eds), One Health Triad, Unique Scientific Publishers, Faisalabad, Pakistan, Vol. 2, pp: 193-200. https://doi.org/10.47278/book.oht/2023.60

Table 1: Summary of potential antibacterial nanoparticles against specific species of bacteria

Nanoparticles	Antibacterial Mechanism	Characterization	Targeted Species	References
Silver nanoparticles	Damage cell wall structure	19 nm	E. coli	Bruna et al. 2021
PEGylated Liposomes	Accumulate Selectively Soft tissues infections	90-100 nm	*Staphylluscoccus aureus*	Laverman et al. 2001
Superparaegnative Iron Oxide Nanoparticles (SPIONPs)	Accumulate Selectively Soft tissues infections (lungs)	35nm	*Staphylluscoccus aureus*	(Kaim et al. 2002)
Cationic Peptide Nanoparticles	increase the local charge and mass densities of the bactericidal components (Electrostatic Interactions)	177±6 nm, 152±8 nm	Broad spectrum gram positive Bacteria, MRSA, yeast and *C. albicans*	(Liu et al. 2009)
polycarbonate-based block copolymer nanoparticles	Disintegration of cell membrane	0.2 um	Broad spectrum gram positive Bacteria, MRSA and fungi	(Nederberg et al. 2011)

Ultrasound

Consistent and stable cell membrane-coated nanoparticles (CMCNPs) can be obtained by ultrasound technique. This technique also encourages the membrane and nanoparticles to naturally form a core shell structure with a little loss of substantial material. However, it may destroy the nanoparticles (Copp et al. 2014).

Electroporation

In this technique, nanoparticles and cell membrane vesicles are first mixed in the microfluidic system with the S and Y-shaped channels. Then instantaneous pores are created on the vesicles by using electrical pulses at the exit of the channels and thus allowing nanoparticles to penetrate the vesicles (Rao et al. 2017).

Co-incubation

Another technique involves co-incubation of nanoparticles and live cells followed by the addition of serum-free media for secretion and production of exosomes. While wrapping the cell membrane over nanoparticles, it is vital to keep in mind that the coating process makes stable homogenous nanoparticles that do not interfere with the function of the nanoparticles or the cellular membrane (Silva et al. 2013).

Improving the Approaches of Membrane Extraction and Coating

Complete elimination of harmful intracellular proteins or organelles is necessary to obtain high purity and quality membranes; however, it is challenging to do so with the present methods of membrane extraction and wrapping over nanoparticles, which mainly include gradient centrifugation, sonication and mechanical extrusion. These might significantly restrict application; thus a new technique or technology must be created. For instance, microfluidic sonication and microfluidic viscoelastic flow technologies have demonstrated their unique ability to sort extracellular vesicles of high purity according to their size. Additionally, rapid and large -scale synthesis of functional membranes following standardized operation techniques is required to address clinical translational needs. Similar to earlier research, current technology cannot accomplish it well. The development of good manufacturing practice (GMP) standards for the clinical use of dendritic cells, stem cells and T cells has aided in the production of high-quality cell membrane-coated nanoparticles (Gurunathan et al. 2021).

Cell Membrane Protein Displaying Multifunctional

Membrane proteins are vital in maintaining cell signaling adhesion and mediating the effectiveness of medication administration and targeting for bioinspired membrane-coated nanoparticles. However, the cell lysis caused by extrusion, sonication, and centrifugation operations may disrupt specific critical proteins or membrane uniformity. Functional proteins may assist in improving targeting capacity and enhancing treatment efficacy. However, surface engineering or changing cell membrane is essential for better targeting the disease-related sites. Both chemical modification and gene synthesis are widely used techniques, but they frequently include unknown dangers or clinical application concerns. It makes sense to learn how to develop and maintain repeatable, affordable, and controllable quality. The development of improved and effective immunotherapies, such as CAR-T cells and dendritic cells-based vaccines, may provide us with a suggestion to enhance or create new modification approaches for meeting clinical requirements (Zhang et al. 2021).

Bioinspired Membrane Coated Nanoplatform for Treatment of Bacterial Infections

Nanodecoy-immunotherapy

Bacterial infection is becoming significant health concern for people worldwide and is intimately correlated with the host immune system. The bacteria are adapted to their host by dodging the immune system which contributes to antibiotic resistance. Most bacteria initially attach to the cells and tissues of the host, increasing their infectious rate and facilitating immune evasion (Palmela et al. 2018).

Therefore, exploiting the underlying mechanism of infection and coming up with new innovative ways to overcome it might aid in preventing bacterial infection. Nanotherapeutics based on cell membranes have recently demonstrated their unique benefits as anti-bacterial. One of the most serious infectious diseases, sepsis is brought on by bacteria involving systemic inflammatory reactions. If patients with sepsis are not given the right care, they may develop organ dysfunctioning or failure. Recently, red blood cell membranes-coated cores were synthesized for detoxication purposes. These nanosponges can neutralize bacterial toxins and pesticides that may cause the death in humans as well as animals (Chen et al. 2019).

These nanosponges may also considerably detoxify staphylococcal alpha-toxin, particularly in toxin-challenged mouse models increasing survival rates. Furthermore, using of the nanosponges in methicillin-resistant *Staphylococcus aureus* infection showed therapeutic efficacy. The red blood cell membrane-based nanosponges provide considerable survival benefits in MRSA-challenged mice model. Furthermore, the red blood cell nanosponges reduce lung damage and inhibit nuclear factor kappa B activation in the spleen in MRSA sub lethal dose mouse models. The findings showed that RBC-NS was a viable therapy for severe MRSA infectious diseases. Furthermore, the RBC-NS reduced lung damage and inhibited nuclear factor kappa B activation in the spleen in MRSA sub lethal dose mouse models. Furthermore, immune cells (monocytes and macrophages) can capture or trap endotoxins by binding to the membrane-inherited receptors or proteins of immune cells using the lipoplysacchrides endotoxins which are released from lytic or dead bacteria in the form of the pathogen-associated molecular pattern (PAMP) (David et al. 2020).

Neutralization of Bacterial Toxins

Pathogenic bacteria can produce toxins which cause lethal diseases. Endotoxins and exotoxins, two types of bacterial toxins, are the main culprits behind cytokine release brought on by bacterial infections. Both types of toxins are destructive and involved in several crucial pathogenic pathways. So, these must be neutralized to disarm microorganisms and directly treat infection-related symptoms (Rasko and Sperandio 2010).

Toxins must somehow interact with biological membranes depending on the cell membrane function. Cell membrane-coated nanoparticles may take advantage of high affinity receptors on several of these interactions to increase their potency. The cell membrane-coated nanoparticles have been classified on the basis of poisons against which they showed therapeutic efficacy (Fang et al. 2015).

Exotoxins

Exotoxins are chemically protein-based poisons that are so toxic that even a minute dosage may lead to organism death (Stevens et al. 2007). Gram-positive bacteria are predominantly responsible for secreting bacterial exotoxins. Traditional detoxification techniques for exotoxins depend upon the specific binding of a single antigen with an antibody. These techniques require complete knowledge of the structure of the toxin and the kind of pathogenic bacteria presenting several difficulties for clinical application. By covering the polymeric nanoparticle cores with the red blood cell membrane, a biomimetic nanoformulation system known as nano sponge was introduced to get over the therapeutic barriers (Hu et al. 2013).

The nanosponge was developed to prevent the hemolytic effect of the lethal toxin on erythrocytes. The ability of nanosponges to neutralize bacterial exotoxins was observed in vivo. The injection of alpha-hemolysin alone significantly injured mice's skin and underlying muscular tissue; however, when the toxin was combined with nanoparticles the mice's mutilation was restricted (Hu et al. 2013).

According to natural cell membranes, a monoclonal antibody plasmid against α-hemolysin was produced by genetic engineering and then transfected into cells to form an efficient antibody on the cellular membrane. The sensosenitizer Meso-tetrakis chromic was then enclosed inside these antibody membrane vesicles which were removed from the antibody modified cell membranes. The genetically produced ANVs were more effective in capturing exotoxins than passive harmful absorption through natural red blood cell membranes because of the strong interaction between the highly active antibodies and the toxin. When activated by ultrasound, the ultrasonic sensitizer nanoparticle core may efficiently produce reactive oxygen species, facilitating antibodies in removing the toxin and eliminating microorganisms. Because of the extremely particular interactions between monoclonal antibodies and the son sensosnitizer intrinsic luminous features, these monoclonal antibodies assisted nanoparticles also enabled accurate optical detection of MRSA infections (Pang et al. 2019).

The ANVs-mediated antimicrobial sonication and antitoxin therapy were shown to entirely eradicate muscle abscesses in mice when used in combination, according to in vivo research (Guerrant et al. 1999). The antitoxin treatment approaches do not target specific bacteria and prevent the natural selection of antibiotics against drug-resistant bacteria. So, these are a viable alternative to conventional antimicrobial therapy (Mellbye and Schuster 2011).

Endotoxins

Endotoxins also known as lipopolysaccharides (LPS) are components of gram-negative bacteria's cell walls produced by the inner membrane upon death, division or after receiving antibiotic drugs (Shen et al. 2019). Immune cells including neutrophils, dendritic cells, and macrophages can identify these endotoxins as pathogen-associated molecular patterns (Akira et al. 2001).

The systemic inflammatory response syndrome which includes sepsis, multi-organ failure, shock and intravascular coagulation, can be brought on by the increasing activity of the mammalian immune system caused by lipopolysaccharides (Yuk et al. 2021). Therefore, the important treating disorders is the efficient elimination of LPS. LPS can be trapped by macrophage membrane-coated nanoparticles which can also suppress the immune response. Macrophage membrane TLR-4 and CD-4 receptors are linked to LPS binding and the release of downstream inflammatory components. Utilized the LPS-binding properties of macrophage membrane-coated PLGA nanoparticles to reduce the level of pro-inflammatory factors (Thamphiwatana et al. 2017).

Vaccine-immunotherapy

A crucial defense against bacterial illnesses is vaccination. Due to the distinctive properties of nanoparticles and cell membranes certain cell membrane coated nanoparticle oriented vaccines have been investigated to prevent several lethal infections. Generally, nanoparticles are readily absorbed by cells enabling the antigen associated with nanoparticles to be rapidly ingested and processed by antigen-presenting cells. The antigen bridging on the nanoparticle surface perfectly mirror the natural appearance and presentation of pathogenic antigens. Nanoparticles and plasma membranes can be made with various infectious pathogens to serve as vaccine delivery systems.

Based on their antimicrobial action these antimicrobial vaccines can be divided into two primary categories: antibacterial vaccines and antitoxin vaccinations (Angsantikul et al. 2018).

Antibacterial Vaccines

Inactivated bacteria, attenuated bacteria, bacterial component antigens, or inactivated bacterial toxins make up the majority of traditional antibacterial vaccinations. Each year, these vaccines successfully prevent millions of deaths worldwide (Plotkin 2003).

The live attenuated vaccines have high immunogenicity, but they also come with safety hazards, especially for people with impaired immune systems. Compared to this inactivated bacterium are less immunogenic than living bacteria, which means that they are less effective at producing the immune system's defence against infection. Proteins and polysaccharides present in bacterial outer membrane vesicles have the same bacterial natural immunostimulatory effects (Gerritzen et al. 2017).

Some of these vesicles have been used in clinical bacteria pathogen protection such as a meningococcal vaccination where it has been shown to boost the host immune response (Holst et al. 2013). In particular, the outer membranes of bacteria are promising antigen-derived materials because they have enriched immunogenicity and distinctive adjuvant qualities that can activate innate immunity and trigger adaptive immune responses (Irene et al. 2019).

The outer membranes of bacteria were gathered and coated onto gold nanoparticles to create an antibacterial vaccination (Gao and Zhang 2015). The study involved the extraction of *E. coli* outer membrane vesicles and their unique wrapping onto tiny gold nanoparticles of diameter 30 -50 nm. This is due to the gold nanoparticles (AuNPs) distinctive size and form, which would be specifically tuned to increase the rate of an immune response. In addition to their high stability, the subsequent subcutaneously administered bacterial membrane-coated AuNPs may quickly activate and mature dendritic cells in vivo. Additionally, the BM-AuNPs stimulate the increased production of IFN-g and IL-17 in vivo but not IFN-g or IL-4, indicating that they can specifically target and induce Th1 and Th17 preferred cell responses to destroy the pathogenic bacteria. The research demonstrated a significant promise for antibacterial vaccinations by using bacterial outer membranes to surround synthetic inner cores. Similar to earlier research, bacteria-related antigens integrated into cell membrane-coated nanoparticles were utilized as a vaccine to prevent lethal infection by stimulating the immune system of the body against pathogen-associated antigens. Recently, multiple cytolysins or proteins released by gram-negative bacteria attached to the macrophage membrane and were covered on PLGA nanoparticle as a multiantigen nanotoxoid vaccine to strengthen the immunity against bacteria resistant to antibiotics (Wei et al. 2019).

Antitoxin Vaccine

Vaccines which are effective against toxins, are usually made from toxoids that have undergone chemical and thermal treatment for safety reasons still these inactivation techniques can degrade proteins tertiary structure, reduce immunogenicity and alter antigenic epitopes (Qin and Sun 2020).

The characteristics of cell membrane coated nanoparticles such as antigen distribution over membrane and toxin adsorption, are considered helpful in creating antitoxin vaccines. A new method for creating multiantigen vaccines utilized red blood cell-coated nanoparticles that can absorb toxins to generate high immunogenicity without adjuvants (Wei et al. 2017).

Chemo-immunotherapy

Antibiotics have been extensively developed and used in modern medicine, but still a big challenge of active targeting of antibacterial drugs particularly for bacterial infections. Antibiotics are frequently given systemically to ensure that they kill or at least inhibit the growth of harmful bacteria, however doing so increases the risk of

antibiotic resistance and toxicity. The synthesis of CMCNPs that may actively target diseased microenvironments and pathogen may provide an efficient therapeutic approach against microbial infections in recent decades (Lobanovska and Pilla 2017).

The bacteria has the tendency to attach themselves to the surface of platelets and then produce several virulent toxins that ultimately damage the platelets and increase the severity of bacterial infection (Theodora et al. 2018). One of these bacteria is MRSA, which potentially releases α-toxin leading to the aggression of platelet and inflammation, making the pathogen too strong to be cleared by the immune system. Keeping the pathogenic mechanism in mind, scientists successfully developed platelet membrane-coated therapeutics. The platelet membrane was shawled onto the nanoparticles loaded with vancomycin and administered to target MRSA (Hu et al. 2015). Platelet membrane-coated nanocores evaluated to have greater binding power with MRSA than the bare nanoparticles or red blood cell membrane-wrapped nanoparticles. Moreover, vancomycin-loaded platelet membrane coated nanoparticles showed more potent bacterial inhibition than bare vancomycin-loaded nanoparticles. Ultimately, the bio interfacing antibacterial strategy enhance antibiotic potency (Yesi et al. 2022).

Additionally, the bacteria interact with platelets, such as direct bridging with surface proteins or connecting with plasma molecules, among other mechanisms. For instance, by adhering to platelet membranes, MRSA can evade the immune system's clearance. Researchers discovered that vancomycin-loaded platelet membrane-coated nanoparticles (PNPs) showed a 12 times higher capability to bind with MRSA than bare nanoparticles. In a mouse model of MRSA attack, this potent combination significantly increased the bactericidal efficiency and was six- folds more effective than a free antibiotic (vancomycin) (Hu et al. 2015).

Sono-immunotherapy

Sono-immunotherapy may be a viable option for treating bacterial infections. Antibiotic-free protocols may provide a promising role in preventing and controlling resistance against bacterial infection through eradicating of pathogenic bacteria and pathogenic virulence. A bioinspired method was considered for combining antibacterial sonodynamic therapy with the antivirulence immunotherapy. The technique involved genetic engineering of the surface of plasma membrane nanovesicles via an antibody which aids in neutralizing the toxin of methicillin-resistant *Staphylococcus aureus* (MRSA) through son sensitizer encapsulation. Compared with the old conventional passive virulence absorption technique, the sono-immunotherapy provides strong junction between antibody and alpha-toxin enabling the nanovesicles to absorb pathogenic virulence more effectively in the lab. The underlying principle is that, the sonosensitizers effectively produce reactive oxygen species to kill the pathogen and enhance the clearance of virulence. In vivo testing through optical imaging indicated that the antibody decorated nanovesicles successfully targeted MRSA infection and accurately identified the foci from sterile inflammation. So, these antibiotic decorated nanocaptures may robustly fight against resistant bacterial infections (Pang et al. 2019). Fig. 1 and Table 2 summarizes the different therapeutic approaches of biomimetic nanoparticles for treating the bacterial infections.

Perspectives and Challenges

The membrane components, including membrane polysaccharides, proteins and lipids have been moved to the surface of the nanoparticles. CMCNPs naturally possess the functions and characteristics of derived cells. By taking advantage of interactions between pathogenic bacteria or the contaminated microenvironment and the cell membrane coating, these CMCNPs can be employed for various therapeutic objectives. This approach is adaptable and permits the fusion of various nanoparticles and plasma membranes depending on the therapeutic goal. Additionally, genetically modified plasma membranes of various cells can be employed to provide capabilities that donor cells lack (Ren et al. 2021).

Using these methods as inspiration it will be possible to express many antimicrobial components on cell membranes at once to create a multifunctional cell membrane that can treat bacterial infections. For example, antimicrobial peptides might be genetically designed on cell membranes to kill bacteria. The pathogen recognition receptors might be expressed on plasma membranes to improve the capacity of the membranes to target specific pathogenic bacteria. However, some bacterial species remain in the host for a long time and have a higher ability for attaching to the host cells to maintain their growth and pathogenic activity leading to long-lasting and chronic infections. Extracting cell membranes from host cells via in vitro culture could decrease inflammatory reactions and provide more precisely targeted antimicrobial medication. Such host-derived cell membranes have lower immunogenicity and are better able to target pathogenic germs (Yu et al. 2021).

Conclusion

One of the major threats to human life comes from bacterial infections, and traditional antimicrobial strategies such as vaccination, antibiotic resistance, and drug delivery are ineffective. Due to the use of NPs and cell membranes, cell membrane coated nanoparticles (CMCNPs) have a distinct advantage in treating of bacterial infections. It is anticipated that CMCNPs would be developed into a very effective antibacterial and antitoxin vaccine. It can give more targeted delivery of antibacterial medications and efficiently eliminate the bacterial toxins. CMCNPs can offer a new

Table 2: Cell membrane coated nanoparticles used for the treatment of bacterial infections

Types of Cell Membrane	Methods of preparation	Characteristics of Membrane	Material used for Nanoparticles	Antibacterial Mechanism of action	Limitations	References
Red Blood Cell Membrane	Repeated freezing and thawing under isotonic conditions	Long-term systemic circulation of toxins and immune evasion	Gold PLGA	Antitoxin vaccination that neutralizes exotoxins over a broad spectrum	Prolong storage and lack of cell sources	Gao et al. 2015: Hu et al. 2013
Neutrophil Membrane	Sonication	Enlarge at inflammatory sites and have a prolonged pulmonary circulation	Ceftazidime, RvD1, and PCL pefloxacin and PEG	Targeting the microenvironment of microbe's infection	Limitations of cell sources and long storage	Gao et al. 2021: Wang et al. 2020
Bacterial vesicles with a cell wall	Ultrafiltration and ultra-high speed centrifugation	Homologous, natural immunostimulatory targeting	Mesoporous silica, rifampicin, and gold	Medication delivery and vaccination against microorganisms	low density of cell membranes, immunogenicity	Gao et al. 2015: Wu et al. 2021
Platelet Membrane	Isotonic therapy and repeated process of freeze and thaw	Specific bacterial binding protein and cell signaling	PLGA,	Emphasis on harmful microorganisms	Absence of cell sources and prolonged storage	Hu et al. 2015
Dendritic Membrane	Sonication	Immune escape, CD14, and strain receptors are present on the surface	CuFeSe2	Destroy Endotoxins while emphasizing on pathogenic microbes	Describe pro-inflammatory factors	Hou et al. 2021
Macrophase Membrane	Sonication	Immune evade, CD14, and toll-like receptors are expressed on the surface	Gold nanocage, PLGA, and Fe_3O_4	Eliminate endotoxins while relying on harmful bacteria	Discuss pro-inflammatory substances	Thamphiwatana et al. 2017: Wang et al. 2018: Shen et al. 2018
Genetically Engineered Membrane	Sonication	Elevated antigen and antibody sensitivities	Sonosensitizer	emphasizing on bacterial infections, neutralizing exotoxin, and diagnosing infection with pathogenic bacterial exotoxin	Extreme technical demand	Pang et al. 2019
Hybridoma Membrane	Depend upon the type of cell membrane used	Integrate many cells membrane processes	PLGA	Eliminate both endo and exotoxins, concentrating on harmful microorganisms	Control of hybrid mitogenic quality	Dehaini et al. 2017: Jiang et al. 2021
Gastric Epithelial Cell Membrane	Sonication	An assortment of receptors that are developed bind to Helicobacter pylori	Clarithromycin and PLGA	Emphasis on pathogenic organisms	Inadequate cell sources	Angsantikul et al. 2018

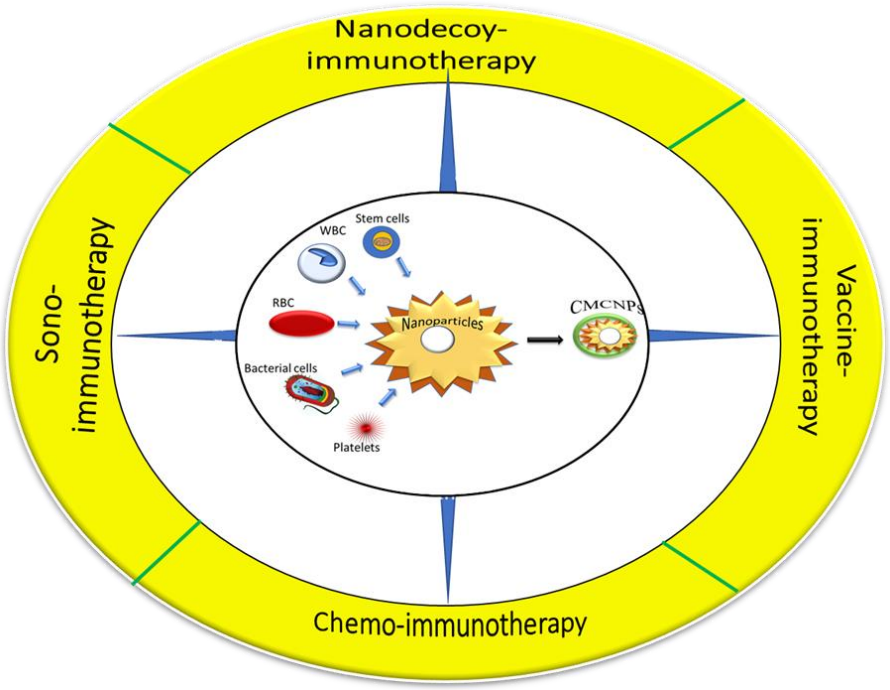

Fig. 1: Antibacterial therapeutic strategies of cell membrane coated nanoparticles

approach to successfully reduce bacterial drug resistance when combined with photodynamic and sonodynamic therapy. Even though a large portion of the research is still in the laboratory, future developments in this area are anticipated to benefit human health.

REFERENCES

Akira S et al., 2001. Toll-like receptors: Critical proteins linking innate and acquired immunity. Nature Immunology 2(8): 675–680.

Angsantikul P et al., 2018. Coating nanoparticles with gastric epithelial cell membrane for targeted antibiotic delivery against Helicobacter pylori infection. Advanced Therapeutics 1(2): 1800016.

Baptisa PV et al.,2018. Nanostrategies to fight multidrug resistant bacteria –" A battle of the titans". Front 90: 69-80.

Bruna OC et al., 2021. Optimization of technetium-99m-labeled PEG liposomes to image focal infection: effects of particle size and circulation time. Journal of Nuclear Medicine 38: 3489-3493.

Caliskan Y et al., 2019. A new therapeutic combination for osteosarcoma: Gemcitabine and Clofazimine co-loaded liposomal formulation. International Journal of Pharmaceutics 557: 97-104.

Carly D et al., 2021. Recent Innovations in Bacterial Infection Detection and Treatment. Infectious Diseases 10 (10): 21-890.

Chen Y et al., 2019. Biomimetic nanosponges suppress in vivo lethality induced by the whole secreted proteins of pathogenic bacteria. Small 15(6): 1804994.

Copp JA et al., 2014. Clearance of pathological antibodies using biomimetic nanoparticles. Proceedings of the National Academy of Sciences of the United States of America 111(37): 13481–13486.

David MZ et al., 2020. Community-associated methicillin-resistant Staphylococcus aureus: epidemiology and clinical consequences of an emerging epidemic. Clinical Microbiology Reviews 23(3): 616-687.

Dehaini D et al., 2017. Erythrocyte–platelet hybrid membrane coating for enhanced nanoparticle functionalization. Advanced Materials 29(16): 1606209.

Fang RH et al., 2015. Engineered nanoparticles mimicking cell membranes for toxin neutralization. Advanced Drug Delivery Review 90: 69–80.

Fang RH et al., 2018. Cell membrane coating nanotechnology. Advanced Materials 30(23): 1706759.

Gao J et al., 2021. Human neutrophil membrane-derived nanovesicles as a drug delivery platform for improved therapy of infectious diseases. Acta Biomaterialia 123: 354-363.

Gao W et al., 2015. Modulating antibacterial immunity via bacterial membrane-coated nanoparticles. Nano Letters 15(2): 1403–1409.

Gao W and Zhang L, 2015. Coating nanoparticles with cell membranes for targeted drug delivery. Journal of Drug Targeting 23(7-8): 619-626.

Gerritzen MJ et al., 2017. Bioengineering bacterial outer membrane vesicles as vaccine platform. Biotechnology Advances 35(5): 565–574.

Guerrant RL et al., 1999. What an intestinal bacteria cause disease. Journal of Infectious Diseases 179: 331–337.

Gurunathan S et al., 2021. A comprehensive review on factors influences biogenesis, functions, therapeutic and clinical implications of exosomes. International Journal of Nanomedicine 16: 1281.

Haroon HB et al., 2022. A brief history of long circulating nanoparticles. Advanced Drug Delivery Reviews 11: 43-96.

Hu CM et al., 2011. Erythrocyte membrane-camouflaged polymeric nanoparticles as a biomimetic delivery platform. Proceedings of the National Academy of Sciences of the United States of America 108(27): 10980–10985.

Holst J et al., 2013. Vaccines against meningococcal serogroup B disease containing outer membrane vesicles (OMV): Lessons from past programs and implications for the future. Human Vaccines and Immunotherapeutics 9(6): 1241–1253.

Hou X et al., 2021. Pathogen receptor membrane-coating facet structures boost nanomaterial immune escape and antibacterial performance. Nano Letters 21(23): 9966–9975.

Hou XH et al., 2021. Pathogen Receptor Membrane-Coating Facet Structures Boost Nanomaterial Immune Escape and Antibacterial Performance. Nano Letters 21: 9966–9975.

Hu CM et al., 2013. A biomimetic nano sponge that absorbs pore-forming toxins. Nature Nanotechnology 8(5): 336–340.

Hu CM et al., 2015. Nanoparticle biointerfacing by platelet membrane cloaking. Nature 526: 118–121.

Irene C et al., 2019. Bacterial outer membrane vesicles engineered with lapidated antigens as a platform for Staphylococcus aureus vaccine. Proceedings of the National Academy of Sciences 116(43): 21780-21788.

Islam MA et al., 2018. Restoration of tumor-growth suppression in vivo via systemic nanoparticle-mediated delivery of PTEN mRNA. Nature Biomedical Engineering 2: 850-864.

Jiang L et al., 2021. Bacteria-anchoring hybrid liposome capable of absorbing multiple toxins for antivirulence therapy of escherichia coli infection. ACS Nano 15(3): 4173-4185.

Jiang Y et al., 2019. Engineering biological interactions on the nanoscale. Current Opinion in Biotechnology 58: 1-8.

Kaim AH et al., 2002. Imaging with ultrasmall superparamagnetic iron oxide particles in experimental soft-tissue infections in rats. Radiology 225: 808–814.

Laverman P et al., 2001. Microscopic localization of peg-liposomes in a rat model of focal infection. Journal of Controlled Release 75: 347–355.

Liu L et al., 2009. Self-assembled cationic peptide nanoparticles as an efficient antimicrobial agent. Nature Nanotechnology 4: 457–463.

Lobanovska M and Pilla G, 2017. Focus: drug development: Penicillin's discovery and antibiotic resistance: lessons for the future? The Yale journal of biology and medicine 90(1): 135.

Mellbye B and Schuster M, 2011. The sociomicrobiology of ant virulence drug resistance: A proof of concept. mBio 2(5): 131.

Nederberg F et al., 2011. Biodegradable nanostructures with selective lysis of microbial membranes. Nature Chemistry 3: 409–414.

Palmela C et al., 2018. Adherent-invasive Escherichia coli in inflammatory bowel disease. Gut 67(3): 574-587.

Panda M et al., 2020. Role of nanoparticles and nanomaterials in drug delivery: an overview. Advances in Pharmaceutical Biotechnology 2020: 247-265.

Pang X et al., 2019. Sono-immunotherapeutic Nanocapturer to combat multidrug-resistant bacterial infections. Advanced Materials 31(35):1902530.

Plotkin SA, 2003. Vaccines, vaccination, and vaccinology. The Journal of Infectious Diseases 187(9): 1349–1359.

Qin M and Sun X, 2020. Biomimetic cell-derived nanocarriers for modulating immune responses. Biomaterials Science 8(2): 530– 543.

Rao L et al., 2017. Microfluidic electroporation-facilitated synthesis of erythrocyte membrane-coated magnetic nanoparticles for enhanced imaging-guided cancer therapy. ACS Nano 11(4): 3496–3505.

Rasko DA and Sperandio V, 2010. Anti-virulence strategies to combat bacteria-mediated disease. Nature Reviews Drug Discovery 9(2): 117–128.

Ren E et al., 2021. Genetically engineered cellular membrane vesicles as tailorable shells for therapeutics. Advanced Science 8(21): 2100460.

Shen SF et al., 2018. Engineered nanoparticles disguised as macrophages for trapping lipopolysaccharide and preventing endotoxemia. Biomaterials 10: 10-29.

Shen S et al., 2019. Engineered nanoparticles disguised as macrophages for trapping lipopolysaccharide and preventing endotoxemia. Biomaterials 189: 60–68.

Silva AK et al., 2013. Cell-derived vesicles as a bio platform for the encapsulation of theragnostic nanomaterials. Nanoscale 5(23): 11374–11384.

Stevens DL et al., 2007. Impact of antibiotics on expression of virulence associated exotoxin genes in methicillin-sensitive and methicillin-resistant Staphylococcus aureus. The Journal of Infectious Diseases 195(2): 202–211.

Thamphiwatana S et al., 2017. Macrophage-like nanoparticles concurrently absorbing endotoxins and proinflammatory cytokines for sepsis management. Proceedings of the National Academy of Sciences of the United States of America 114(43): 11488–11493.

Theodora AM et al., 2018. Platelet glycoprotein VI aids in local immunity during pneumonia-derived sepsis caused by gram-negative bacteria. Blood 131: 8864-8876.

Wang C et al., 2018. Pretreated macrophage-membrane-coated gold nanocages for precise drug delivery for treatment of bacterial infections. Advanced Materials 30(46): 1804023.

Wang KY et al., 2020. Colloids and Surfaces B: Biointerfaces Neutrophil membranes coated , antibiotic agent loaded nanoparticles targeting to the lung in fl ammation. Colloids Surfaces B: Biointerfaces 188: 110755.

Wei X et al., 2019. Multiantigen nanotoxoids for ant virulence vaccination against antibiotic-resistant gram-negative bacteria. Nano Letters 19(7): 4760-4769.

Wei X et al., 2017. In situ capture of bacterial toxins for anti-virulence vaccination. Advanced Materials 29(33): 1701644.

Wu S et al., 2021. Bacterial outer membrane-coated mesoporous silica nanoparticles for targeted delivery of antibiotic rifampicin against Gram-negative bacterial infection in vivo. Advanced Functional Materials 31(35): 2103442.

Yesi S et al., 2022. Bioinspired membrane-based nanomodulators for immunotherapy of autoimmune and infectious diseases. Acta Pharmaceutica Sinica 12: 31126-31147.

Yu Y et al., 2021. Single-atom catalysis for efficient sonodynamic therapy of methicillin-resistant Staphylococcus aureus-infected osteomyelitis. ACS Nano 15(6): 10628–10639.

Yuk SA et al., 2021. Nano capsules modify membrane interaction of polymyxin B to enable safe systemic therapy of Gram-negative sepsis. Science Advances 7(32): 1577.

Zhang B et al., 2021. In vitro elimination of autoreactive B cells from rheumatoid arthritis patients by universal chimeric antigen receptor T cells. Annals of the Rheumatic Diseases 80: 2176-2184.