Review Article

Nanotechnology-enabled Responses against COVID-19 Pandemic

Govind P. Chate, Shashwat S. Banerjee

Central Research Laboratory, MIMER Medical College, Talegaon Dabhade, Maharashtra, India

ABSTRACT

The severity of coronavirus disease 2019 (COVID-19) pandemic has made us aware of the inadequacies in our fight against respiratory viral diseases. It has triggered researchers and medical doctors into acting quickly against COVID-19 using a large variety of tools based on nanoscience and nanotechnology. In this review, we outline how nanotechnology-based strategies have helped the medical and scientific communities combat the pandemic, emphasizing the role of nanomaterials in detection, sanitation, therapies, and vaccines.

Key words: Covid-19, nanotechnology, SARS-CoV-2

INTRODUCTION

The coronavirus disease 2019 (COVID-19) outbreak has fueled a global demand for effective diagnosis and treatment as well as mitigation tools to contain the impact on global health.[1,2] At this time of writing, more than 79,673,754 patients have been affected with over 1,761,381 deaths due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), according to the World Health Organization.[3] This global emergency can be responded successfully with science and technology, wherein nanotechnology approaches may assist with advanced solutions to this crisis.[4] Nanotechnology comes into play when keeping in mind that SARS-CoV-2 has nanometric dimensions with a core–shell nanostructure and, therefore, could be regarded as a functional nanomaterial.[4]

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Nanoparticles, due to their size similarity with viruses, enter cells to assist expression of antigens from nucleic acids to be delivered (mRNA and DNA vaccines) and/or directly target immune cells to achieve delivery of antigens (subunit vaccines). Many vaccine technologies have recently utilized these advantages by encapsulating genomic material, protein/peptide antigens, or adenoviral vectors in carriers like lipid nanoparticles (LNPs). The University of Oxford/Astrazeneca and CanSino vaccines incorporate antigen-encoding sequences within the DNA carried by adenoviral vectors. BioNTech/Pfizer and Moderna encapsulate their mRNA vaccines within LNPs and they would be the first messenger RNA (mRNA)-based vaccines hitting clinical use.[5-7] mRNA-based therapies have several advantages as compared to other methods. Compared to whole virus or DNA delivery, mRNA delivery is safer as mRNA is not infectious and cannot be combined into the host genome; while DNA is required to reach the nucleus to be decoded. mRNA is more stable and resistant to RNase-mediated degradation when complexed with positively charged lipids. Furthermore, the self-assembled virus sized particles are suitable for administration through different routes. However, a major drawback of these formulations is that they require low temperatures for long-term storage which is a logistical obstacle to their impending distribution and administration.[8] Other than antigen delivery, nanoparticles can codeliver

Address for correspondence:
Shashwat S. Banerjee, Central Research Laboratory, MIMER Medical College, Talegaon Dabhade, Maharashtra, India. E-mail: shashwatbanerjee@mitmimer.com

adjuvants to aid prime the preferred immune responses. Adjuvants are immunostimulatory molecules that boost the body's immune response by acting as a depot for antigens, recruiting B and T cells to site of injection and upregulating cytokines and chemokines, when administered together with the vaccine. While the vaccine's objective is to stimulate lymphocytes to recognize and respond, not innate cells, the activation of the innate immune cells is essential to trigger the lymphocytes to obtain both B- and T-cell responses.[9,10] Conjugation and/or encapsulation of both the adjuvant and antigen in the same nanoparticle allow delivery to the same antigen presenting cell (APC) in a targeted and synchronous way. Many adjuvants have earlier been unsuccessful in the clinic due to toxicity issues. This codelivery can be beneficial in directing antigen and adjuvant activity only in APCs that have taken up the antigen, thereby minimizing side effects due to ineffective targeting.[11]

Exosomes secreted by the mesenchymal stem cells, have shown efficacy in mitigating symptoms associated with COVID-19.[12] The combinatorial strategy of immunomodulatory, tissue protective, and healing potential of exosomes along with antiviral drugs may reduce the severity of the COVID-19. Several clinical trials are underway to treat COVID-19 using exosome. For COVID-19 treatment, exosomes application can be split into three general categories. First, using mesenchymal stem cell secreted exosomal particles instead of cell therapy. Second, encapsulating specific miRNAs and mRNAs into exosomes and last, to transport drugs by exosomes as carriers for COVID-19 treatment. One of the major challenges that need to be addressed for exosomes as drug delivery platforms is their stability and functionality over a period of time.[13,14] Furthermore, keeping temperature low during handling and transportation also causes difficulty in their translational application.[15] To overcome these challenges, the applicability of freeze-dried exosomes has been evaluated to preserve them at room temperature. However, clumping of these nanosystems and degradation of their cargo might be a problem during the freeze-drying process. This can be rectified by addition of stabilizers such as sucrose, trehalose, and glucose that aid in replacing the hydration sphere surrounding the exosomes in the freeze-drying process, thereby avoiding their accumulation and maintaining their membrane integrity.[16]

Diagnostics are another important point regarding nanotechnology and COVID-19.[4] A number of diagnostic technologies are currently available to detect SARS-CoV-2, including polymerase chain reaction (PCR)-based nucleic acid tests and serological assays that identify antibodies formed during respiratory infection.[17] Viral genome detection by real-time-PCR is performed in the early stages of the disease, while serological tests such as enzyme-linked immunosorbent assay, chemiluminescence assay, immunofluorescence assay, or immunochromatographic test, among others are used to determine immunoglobulin (Ig) G and IgM antibody levels after 5–7 days or more than 10 days, respectively.[18-20] In some of these technologies, nanomaterials are an important component in the detection or transduction of the biochemical interactions. Recently, a rapid and simplified test based on the color change of Au NPs has been developed by attaching antisense oligonucleotides specific for two of the N-gene regions of SARS-CoV-2 to plasmonic gold nanoparticles (AuNPs). The test allows a naked-eye detection in about 10 min due to nanoparticle agglomeration in the presence of the target viral RNA.[21] In regions with low-resource medical infrastructure, as found in developing countries, such simple and cost-effective techniques could be of value.

In the present pandemic situation, it is critical for health care workers and general public alike to have appropriate protection to prevent SARS-CoV-2 spread. Moreover, toward prevention of COVID-19 spread, fabrication of face masks and other protective materials such as personal protective equipment (PPE) with ability to not only capture the aerosol droplets but also immobilize and kill the virus would be a significant step. New nanomaterials such as loading Ag and CuO NPs on such protective equipment can help to accomplish this function because these NPs have proven antiviral properties. The metal ions released for a prolong duration from the nanoparticles in a controlled manner may help to modulate the antiviral property of the surfaces.[22,23] Since in the spread of SARS-CoV-2, surface and aerosol contamination play a significant role, fabricating surface coatings with antiviral properties and efficient air filtering devices may help reduce viral load. Furthermore, the PPE kits currently being used have been found to frequently carry SARS-CoV-2 contamination.

CONCLUSION

With the deepening of our understanding of SARS-CoV-2 and advances in diagnostics and treatment of

COVID-19, we hope and believe that nanotechnology will play an important role in counteracting the current global public health risk.

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