## **Nanotechnology**

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Nanotechnology is opening new therapeutic possibilities of fighting against COVID-19 by enabling new prevention, diagnosis, drug delivery, and treatment methods. Nanomedicine is known as the branch of medicine involved in preventing and curing various diseases using nanoscale materials, such as biocompatible nanoparticles and nanorobots, for various applications, including diagnosis, delivery, and sensing. In addition, nanomedicines have exhibited important features, such as efficient transport through fine capillary blood vessels and lymphatic endothelium, longer circulation duration and blood concentration, higher binding capacity to biomolecules such as endogenous compounds including proteins, higher accumulation in target tissues, reduced inflammatory or immune responses, and oxidative stress in tissues.

Keywords: COVID-19; SARS-CoV-2; nanotechnology; detection; treatment

### 1. Introduction

Nanotechnology is being seriously investigated for its potential in developing therapeutics, vaccines, diagnostic techniques, and strategies to reduce the healthcare burden of patients with Coronavirus disease (COVID-19) or SARS-CoV-2 infection. The unique properties of nanoparticles, such as their small size, enhanced solubility, better target reachability, improved half-life, reduced side-effects, and surface adaptability, are utilized to bring out a much-needed clinical transformation that could be effective directly against the virus [1][2]. In addition, researchers are now looking into nanotechnology to develop improved assays and nanosensor-based diagnostic techniques to improve the delivery of medications and increase the circulation time of the drugs. Thus, nanotechnology seems to hold the potential to bring in innovative alternatives effective against the virus.

# 2. Nanotechnology-Based Approaches in Preclinical and Clinical Studies: In Vitro and In Vivo

#### 2.1. Nano-Based Approaches in Pre-Clinical Studies

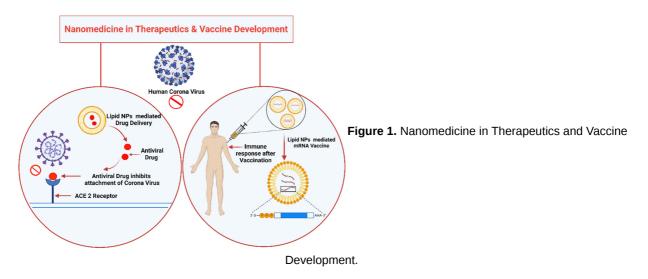
COVID-19 immune-based preclinical therapeutic approaches such as virus-binding molecules; inhibitors of specific enzymes involved in viral replication and transcription; small-molecule inhibitors of helicase, proteases, or other proteins critical for the virus survival; host cell protease; endocytosis inhibitors; and siRNA inhibitors are all potential therapeutic options for SARS-CoV-2 [3]. In addition, the effects induced by monoclonal antibodies (mAb) in COVID-19 patients may also improve the development of vaccines and increasingly specific diagnostics [4]. Moreover, every single one of these tools needs to be assessed regarding clinical efficacy and safety before treating infected patients.

#### 2.2. Nano-Based Approaches in Clinical Studies

Currently, nanotechnology-based formulations have been developed and commercialized for common viral infections. Several companies are moving away from conventional treatment and prevention strategies and switching over to nanotechnology to develop various types of vaccines and therapeutics, e.g., dexamethasone, a COVID-19 therapeutic agent introduced via various nanoformulations in the treatment of COVID-19. Completing phase 3 clinical trials of Pfizer's liposomal mRNA vaccine (BNT162b) can be considered a significant achievement in nanomedicine [5].

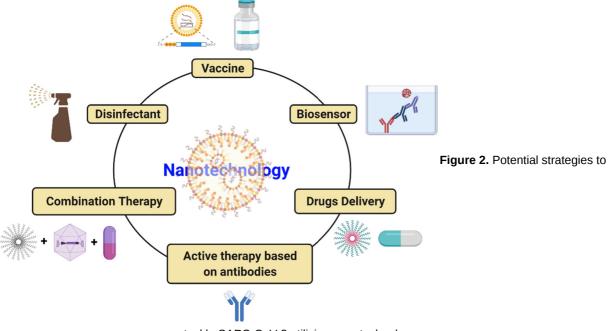
mRNA- and DNA-based vaccines would have little efficacy without nanomedicine components. According to recent research, nanomaterials may effectively inactivate the SARS-CoV-2 virus, as nanomaterials have been used to inhibit viruses of other members of the Coronaviridae family [6]. Many vaccine candidates under development for the SARS-CoV-2 vaccine have safety and efficacy in the clinical and pre-clinical stages [7]. ModernaTX, Inc. used lipid nanoparticles (LNP) to encapsulate mRNA-1273, which encodes the full-length SARS-CoV-2 S protein (NCT04283461). Cells that express this viral protein will present SARS-CoV-2 antigen to T cells, eliciting an immune response against the virus [8], which helps prevent premature degradation during drug delivery. Other clinical studies are testing diverse anti-

inflammatory agents to reduce lung inflammation (pneumonia), the leading cause of death in COVID-19 patients. These contain antibodies targeting inflammatory factors such as IL-6 and complement protein C5 or the CD24Fc conjugate that blocks TLR activation. Two clinical studies include the anti-angiogenic drug bevacizumab (anti-VEGF mAb) for the reduction of lung edema. A new antibody in clinical development is meplazumab, which blocks the binding of SARS-CoV-2 S protein to CD147 molecule on human cells, thereby reducing the virus's infection ability. Additional immunosuppressive agents are also being tested, such as the JAK1/JAK2 inhibitor baricitinib and the antimalarial drug hydroxychloroquine sulfate. While optimal treatment regimens are still under study, different dosing and schedules are being reported by clinicians [9]. The immune response by using lipid NPs-mediated drug delivery and mRNA vaccine is shown in Figure 1.



## 3. Future Perspectives to Tackle COVID-19 Using Nanotechnology

COVID-19 has introduced the scientific community to a global challenge it has perhaps never had to face before. However, it has also taught scientists and the population that this kind of situation could occur again. Therefore, cutting-edge tools, notably nanotechnology, should be solidly developed to tackle SARS-CoV2 infection. Nanoparticle-based medicine is a very effective tool with the potential to reduce the burden of illness. Nanoparticles that are much smaller than a micrometer have received exceptional attention in managing COVID-19 disease caused by SARS-CoV2 due to their distinctive properties (suitable size, simple preparation, minimal cost, effortless modification, etc.). Nanotechnology-based approaches for combating COVID-19 include the innovation of tools for speedy, precise, and sensitive diagnosis of SARS-CoV2 infection, production of efficient disinfectants, efficient delivery of mRNA-based vaccines into human cells, and delivery of antiviral drugs into the host. Nanotechnology is being geared up for implementation in the fight against SARS-CoV2 infection in a wide range of areas, as shown in Figure 2.



tackle SARS-CoV-2 utilizing nanotechnology.

Despite the recent progress and intensive studies on nanotechnology-based tools to mitigate COVID-19, several important challenges are remaining to be addressed when attempting to tackle COVID-19: (i) early, portable, rapid,

exceedingly sensitive, and reasonable development of diagnostic kits; (ii) potential use of nanomaterials to avoid the conventional restriction associated with antiviral drugs; (iii) nanoparticle-based vaccine development to fight against SARS-CoV-2 and other pathogens; (iv) combination therapy by utilizing nanoparticles as a delivery system; (v) development of nanobiosensors for rapid and early detection of viruses; and (vi) nanomaterial-based disinfectant agents that can kill pathogens.

Some of the drawbacks of nanoparticles, such as cell toxicity, genotoxicity fibrosis, inflammation, immunotoxicity, and oxidative stress, are key issues to be solved before their use with patients. Nevertheless, we anticipate that many advances will soon be accomplished in COVID-19 diagnosis, treatment, and therapy using nanotechnology-based strategies. In addition, nanotechnology-based tools will probably be utilized in the treatment of COVID-19 and emerging pathogens. This can be achieved by nanotechnology-based therapeutic antibodies or mRNA- or protein-based vaccines, which specifically deliver the active drugs/epitopes to the host's targeted organs and provide rapid detection of these viruses. Finally, the greatest challenge will be transferring nanomaterial technology to actual clinical applications and production feasibility on a large scale.

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