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Exploring the Potential of Gold Nanoparticle Technology and the Pan-Coronavirus Vaccine

Chanung Lee

Saint Mary's School, Republic of Korea

ABSTRACT

When facing the threat of viral COVID-19 mutations, current objectives remain rooted in creating a universal vaccine, or a pan-coronavirus vaccine, that is effective against all COVID-19 variants. While most current COVID-19 vaccines use mRNA, nonreplicating viral vectors, inactivated vaccines, and protein subunits, nanotechnology is emerging as a viable resource for developing protective immunity against COVID-19. With the possibility of new COVID-19 variants emerging, increasing funds to further gold nanoparticle research is as crucial as technological innovation. This study hypothesizes that using a combination of "push" and "pull" methods to increase R&D incentives in gold nanoparticle research can take pan-coronavirus vaccine developments one step closer to boosting long-term immunization and universal applicability. This study's limitations include the immediacy of the COVID-19 pandemic and an inability to evaluate nanotechnology vaccinations after they have been put on the market. With its emphasis on funding gold nanotechnology research via "push" and "pull" incentives, this study's implications include furthering global partnerships and contributing to the pan-coronavirus vaccine development with sensitivity to the rising risk of mutations and immunocompromised individuals.

Introduction

In 2023, the original Omicron variant is long gone ("What COVID-19 Variants Are Going Around in February 2023?" 2023)—with the threat of future subvariants replacing it. The race for a pan-coronavirus vaccine (Piore, 2022) calls for an innovative and universal vaccine delivery; we need a research approach that can identify a global "coronaviral universe" and create a vaccine that protects against all beta-coronaviruses and coronavirus mutations (Morens et al., 2022, para. 2). While most current COVID-19 vaccines use mRNA, nonreplicating viral vectors, inactivated vaccines, and protein subunits (Shaik et al., 2022; Feng et al., 2022), nanotechnology is emerging as a viable resource for developing protective immunity (Vashishta and Kumar, 2021) against emerging viral mutations of COVID-19. Nanotechnology, which utilizes nanoparticles that are just one billionth of a meter (Hagens et al., 2007), allows the vaccine to enter living cells and stimulate antigen-presenting cells to create immunogenicity (Dykman, 2020). Pati et al. (2018) find that over the past decade, nanoparticle-based vaccines have emerged to stimulate immune responses more efficiently than other vaccine methods by interacting with the immune system at a cellular level. While scientists in 2003 estimated that the nanotechnology market would grow $410 billion in just seven years (Pitkethly, 2003), by 2023, nanotechnology has evolved with the potential to meet the virus-neutralizing goals of the pan-coronavirus vaccine.

Recent researchers are honing in on gold nanoparticles as a particular source of COVID-19 vaccine potency. In vaccine deliveries, the flexibility of gold nanoparticles allows them to take on varying shapes, such as spheres, rods, or cubes (Zhao et al., 2014). According to Parrett (2022), the malleability of gold nanoparticles has been integral to research projects from the U.S., China, and Brazil, which have discovered that chiral gold nanoparticles can boost overall influenza vaccine efficacies by over 25 percent. With high-risk individuals in mind, is gold nanoparticle technology the "golden ticket" to deliver the universal vaccine?

With the possibility of new COVID-19 variants emerging, increasing funds to further gold nanoparticle research is just as important as developing the technology itself. As Forman et al. (2021) find, incentives to maintain

R&D incentives can be difficult, as vaccine developments come with high costs and hazards. Where “push” methods to increase R&D incentives rely on subsidizing research and “pull” methods reward innovation (Mueller-Langer, 2013), the urgency of the COVID-19 pandemic calls for both. In its exploration of the potential of gold nanoparticles in COVID-19 pan-coronavirus vaccine development, this study asks: 1) How does gold nanoparticle research contribute to goals of adapting to COVID-19 mutations? 2) Do nanotechnology vaccines utilizing gold nanoparticles benefit individuals with varying immune systems? 3) How do “push” and “pull” R&D incentives further the pan-coronavirus vaccine’s goals? This study hypothesizes that using a combination of “push” and “pull” methods to increase R&D incentives in gold nanoparticle research can take pan-coronavirus vaccine developments one step closer to boosting long-term immunization and universal applicability.

Mutations and Vaccine Deliveries

In 2023, the threat of COVID-19 is caused in part by “wild card” mutations. Mutations occur when a pathogen encounters a new environment, which can also heighten the deadliness of the mutations (Sridhar et al., 2021). As pathogens spiral into increasingly harmful forms, vaccines allow our bodies to develop a coded response to how these pathogens interact within our cells (Federman, 2014). The pan-coronavirus vaccine must be able to anticipate and defend against different types of interactions to prevent more virulent mutations. Dykman (2020) finds that when preparing antibodies and vaccines, it is critical to select the most ideal carrier; nanoparticle delivery systems allow penetration into macrophages that can improve the respiratory activity of cells, while also activating immune responses within genes. Some of the benefits of nanoparticle technology include their ability to trigger an especially strong immune response by identifying pathogens (Chen et al., 2021) and releasing cytokines. If future mutations of COVID-19 emerge, it is important to have a COVID-19 vaccine that is highly effective and universally useable, while utilizing the most optimal delivery system to prevent COVID-19 strains from mutating out of control.

Many contemporary, "non-universal" COVID-19 vaccines were created using pre-existing mRNA vaccine technology. When the coronavirus pandemic struck, the firms behind Moderna and Pfizer-BioNTech were working on a flu vaccine using messenger RNA (mRNA) technology, which is now widely known for the immune responses it triggers in response to COVID-19 (Beans, 2022). Yet where mRNA vaccines are easily developed using cloning and synthesis (Iwasaki and Omer, 2020), they do not suit every patient. In elderly patients, aging lung structures and functions can result in an increased risk of pneumonia and acute respiratory distress syndrome, among other illnesses (Har-Noy and Or, 2020). As the side effects of an mRNA or viral vector vaccine can overwhelm the respiratory system of an elderly patient, researchers have been looking for a vaccine delivery system that has fewer side effects and needs fewer doses (Pati et al., 2018). With their targeted delivery systems, nanotechnology vaccines can be non-invasive—meaning they can be subcutaneous and stimulate multiple cellular responses (Fahmy et al., 2017)—and may even require only a single dose.

The Possibilities of Gold Nanoparticles

Within nanotechnology vaccine research, the use of gold nanoparticles is linked to multicellular responses and the efficient use of antigens. Pati et al.’s (2018) Figure 1 shows the relationship between antigens and nanoparticles in a vaccine.

Figure 1

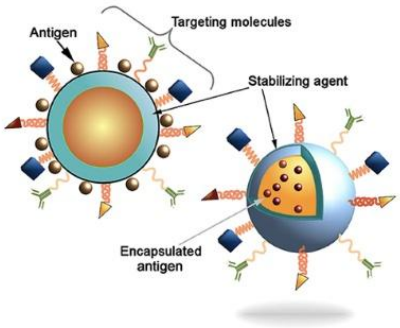

FIGURE 1. Schematic representation of the nanocarriers. Antigen can be conjugated to the nanoparticles surface or incapsulated into core of the particles. Decoration of the nanoparticles surface with targeting molecules (e.g., antibodies, Fab-fragments, peptides, etc) could further increase the delivery of particles into the antigen presenting cells (APCs) to induce innate and adaptive immune responses.

Figure 1. Schematic representation of nanocarriers. From "Nanoparticle vaccines against infectious diseases," by R. Pati et al., 2018, *Immunology*, *7*, para. 1. https://doi.org/10.3389/fimmu.2018.02224.

Where antigens trigger the immune system to create antibodies that fight off a virus, nanoparticles can specifically target crucial areas within the cell to maximize antigens. Zhao et al. (2014) discover that gold nanorods can be utilized as carriers for antigens drawn from the respiratory syncytial virus (a common respiratory virus) by effectively conjugating antigens to the surface. Although gold nanoparticles were used to rapidly diagnose COVID-19 in 2020 and 2021 (Pramanik et al., 2021), their application to the pan-coronavirus vaccine is still in the developmental stages. The notable success of gold nanoparticles in recent stages, however, supports theorists who believe that "a universal vaccine may be on the cards" (Lawton, 2021, para. 7).

Current breakthroughs with gold nanoparticles have been successful because they increase immunity *and* use different delivery methods from pre-existing COVID vaccines. According to Keenan (2023), in a 2022 study on COVID-19 vaccines, the immunogens formulated from gold nanoparticles "elicited an IgG immune response" and "generated high virus-neutralizing titers" (para 10) against the virus. Because one of the goals of the pan-coronavirus COVID-19 vaccine is lifelong immunity, gold nanoparticle vaccines are particularly relevant because they can be administered without a needle—and can be even more effective. Zimmer et al. (2022) observe that Emergex Vaccines, a British company, has developed a vaccine that utilizes gold nanoparticles with coronavirus peptides, triggering the immune system without relying on antibodies; Emergex completed its Phase 1 trial in November of 2022 and was administered to patients in January 2022, using arm patches. Where arm patches can be transported across the globe far more easily than mRNA vaccines, which require cold chain storage (Vu et al., 2021), gold nanoparticle research is an increasingly valuable investment, considering the potential of its global health outcomes. The methods of funding gold nanoparticle developments, however, will depend largely on R&D incentives.

R&D Incentives

Given the persistence of COVID-19, long-term funding (Abecassis, 2021) for nanotechnology research via R&D incentives is critical. According to Dimitri (2012), R&D incentives are described as either "push" or "pull" methods, while hybrid methods that incorporate both "push" and "pull" schematics are becoming more popular. Mueller-Langer (2013)'s Figure 2 shows the traditional divergence between "push" and "pull" programs.

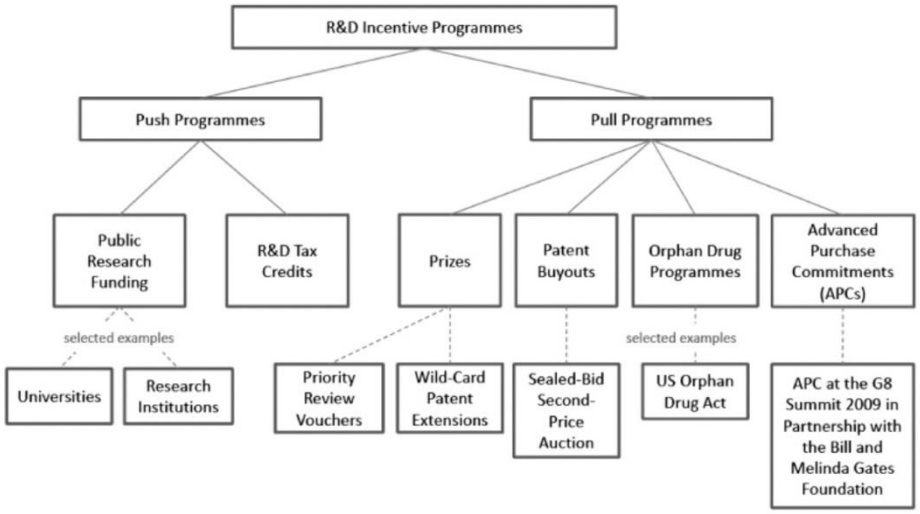

Figure 2. Push and pull incentive programs and selected examples. From "Neglected infectious diseases: are push and pull incentive mechanisms suitable for promoting drug development research?" by F. Mueller-Langer, *Health Economics, Policy and Law*, 8(2), 187. https://doi.org/10.1017/S1744133112000321.

According to Dimitri (2012), the difference between the "push" and "pull" incentives can be described as: while "push" programs rely on research grants from public institutions or charities and *directly* support drug discoveries, "pull" programs more *indirectly* support research efforts by increasing revenues or decreasing delivery costs. In the case of the COVID-19 pandemic, discovering a pan-coronavirus vaccine may be a huge, non-monetary "pull" factor in and of itself. Using a combination of "push" *and* "pull" factors to further nanotechnology research can simultaneously tackle the technological *and* public health challenges the pan-coronavirus vaccine currently faces.

Skeptics concerned about the obstacles researchers face when developing a pan-coronavirus vaccine are often met with goals of partnerships. As pan-coronavirus cynics, Forni and Mantovi (2021) wonder, "Will there be vaccines that will be able to protect the most fragile sections of the human population?" Additionally, Forni and Mantovi (2021) fear that it may not "be possible to overcome financial and political problems," preventing COVID-19 vaccines from being available "with equity for the entire population of the world" (para. 2). Yet if "push" and "pull" R&D incentives work hand-in-hand with one another and further nanotechnology vaccine research from research to delivery stages, global partnerships will be crucial to mitigating challenges and uncertainties. Moreover, public-private partnerships (PPPs) merge private for-profit and non-profit organizations to collaboratively exchange methods and benefits—and often play a central role in improving global public health initiatives (Druedhal et al., 2021). To realize the immunization potential of gold nanoparticle research, PPPs will need to invest in the *possibility* of a pan-coronavirus vaccine. Although the future after COVID-19 is unknown, what we do know is that investing in collaboration, knowledge, and innovation is a universal investment in global public health.

Methodology

This study is exploratory in nature and examines the possibilities of gold nanoparticle research in the hunt for a pan-coronavirus vaccine. Secondary sources utilized in this study include reports produced both before and during the COVID-19 pandemic, relevant journal articles, news articles, and vaccine highlights. This research project raises the following questions: 1) How can research on gold nanoparticles help the pan-coronavirus vaccine achieve its goal of mutation adaptation? 2) Are gold nanoparticle-based nanotechnology vaccinations beneficial for those with impaired immune systems? 3) How can "push" and "pull" R&D incentives assist scientists in achieving the objectives of the

pan-coronavirus vaccine? While this study's limitations include the immediacy of the COVID-19 pandemic and an inability to evaluate nanotechnology vaccinations after they have been put on the market, future researchers should conduct a comparative analysis of mRNA COVID-19 vaccines and nanotechnology vaccines using a focus group of individuals with immunosuppression. With its emphasis on funding gold nanotechnology research via "push" and "pull" incentives, this study's implications include furthering global partnerships and contributing to the pan-coronavirus vaccine development with sensitivity to the rising risk of mutations and at-risk individuals.

Conclusion

"The emergence of the omicron coronavirus is a clarion call for finding a pan-coronavirus vaccine" (Tingley, 2021, para. 11). With the threat of future mutations and the fear that current COVID-19 vaccines will not be able to adapt to new pathogens fast enough, the pan-coronavirus vaccine represents both a pressing technological need and the incentives to realize it. The current rise of viral mutations emphasizes the urgency of creating a pan-coronavirus vaccine with efficient delivery methods and universal applicability. With its malleability and efficient use of antigens, gold nanoparticle technology has emerged as a viable contender to meet the pan-coronavirus vaccine's objectives. The public health component of the technology, however, is rooted in R&D incentives that offer direct support to gold nanotechnology discoveries while decreasing delivery costs and increasing revenues. Although we may never live in a COVID-19-free world, perhaps the hope is that we are able to live *with it*—thanks to a pan-coronavirus vaccine—rather than destruct *because of* it. Global collaborations from scientists, researchers, and medical experts to public health specialists will be essential. If a universal vaccine is on the table, we will need to continue to mobilize to realize it.

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