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Genes Transfer is the Main Process for Prediction of a Drug or Vaccine Against SARS-C0V-2

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ABSTRACT

Gene transfer is emerging as a method for a rapid response to the SARS-CoV-2 epidemic. Both experimental therapeutic solutions and vaccines are subject to preclinical and in some clinical cases. Many of these approaches make use of gene transfer techniques that, especially vaccines, allow a faster initial development pathway than conventional approaches. The unprecedented urgency of this global crisis may cause these antiviral drugs and genetic vaccines, if safe and effective, to be spread on a larger scale than anything else will be available for all people. Depending on the regulatory approval pathway, it may also happen at a pace never seen before in drug development as a result of gene transfer. Hopefully, in the coming days, the clinical trials of will end and the vaccines become available everywhere.

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Introduction

Over the course of 6 months, the SARS-CoV-2 pandemic has directly or indirectly affected everyone on the planet. At this time, more than 4 million people have been infected from nearly every country in the world. More than 300,000 individuals died. Fortunately, most of the infected persons survive, and many of them are intact. Unfortunately, others have severe symptpmes, irreversible damage to their lungs, heart, or kidneys. The individual, economic, psychological, and societal devastation of this event is rare in the modern epoch [1].

The genetic sequence of SARS-CoV-2, was released on 11 January 2020, triggering intense global R&D activity to develop a vaccine against the disease. The scale of the humanitarian and economic impact of the COVID-19 pandemic is driving evaluation of next-generation vaccine technology platforms through novel paradigms to accelerate development, and the first COVID-19 vaccine candidate entered human clinical testing with unprecedented rapidity on 16 March 2020 [2].

How did we come to the conclusion that 30 kilobases of nucleotides are capable of causing such damage? The science is clear: a virus with a moderate mortality rate, a surprisingly long half-life in the droplets and surface of an RNA virus, the ability to spread without symptoms and, first of all, lack of immunity in a population are the main factors that allow this viral tsunami to roll around the world with little From braking or without inhibition [3].

The main cause here is the biological complex related to the viral pathogen. However, the governments play a pivotal role in this crisis as well. They have the power to control this virus by imposing the home quarantine, to slow down and ultimately reduce the rates of the epidemic. History will judge their execution at the local, national cooperation and global levels. Now is the time for acting decisively to get out of the nightmare of COVID-19. It is clear that in this unique setting with a lot of thingummy, data collection and driven, decision-making and scientific prowess are the main tools that must rely on to escape from this global catastrophe. Currently days, experts in epidemiology, economics, biomedicine, psychology and other fields are driving more signs than ever before. This crisis explains whether that ignoring the science of the past, present and future is misplaced if the goal of policymakers are protecting our health, constituents, economies, and job [4].

Escape from Openings

Our system and our community play a major role in finding escape ports from this dark tunnel. First, many of you are on the frontline as medical practitioners (or research scientists putting their pipettes to help at the university hospital). Your steadfast determination and sacrifice saves lives, and you have the highest degree of gratitude. Second, those who stay at home, after shutting down your laboratories and companies, and protecting others while doing so, have made effective personal and professional sacrifices to bring down the R, flatten the curve, or protect your neighbor's vulnerable family member [5].

To return to a new version of normality, population (or herd) immunity must be established. The immunity of the population reduces the chance of the virus spreading, as the majority of the hosts in the population have acquired protective immunity against the pathogen, in this case SARS-CoV-2. Herd immunity can be achieved in one of two ways: either through natural infection of a large portion of the population, which inevitably leads, in the

absence of an effective antiviral drug, to significant morbidity and mortality rates, or a vaccine that is safe and available to all [6].

Genetic Vaccines

The majority of the first vaccines for SARS-CoV-2 in clinical development are genetically dependent. The speed of the transition from the first published sequence of the virus to the start of clinical trials has been remarkably fast, due in part to the agility of molecular biology, decades of learning from our field, and certainly the response of various commercial companies such as Moderna, Janssen (Johnson & Johnson), BioNTech, and Inovio with Deep experience and capabilities in the basic system. Aside from speed, these methods all share an additional benefit over other conventional vaccine methods, which is their ability to enhance both humoral and cellular immunity. Conventional vaccines are slightly delayed although the majority of the more than 100 programs worldwide are inactivated, attenuated, recombinant or tried and true peptide subunits [7].

There are three main classes of gene-based vaccines: DNA, mRNA and virus vector vaccines. Most of these seek to induce immunity to the SARS-CoV-2 spike (S) protein by encoding an open reading frame for the S-gene or gene fragment in a gene-based vaccine design, figure (1). So far, clinical trials have begun in each of these three categories. In March, Moderna (MA) with a lipid mRNA made of nanoparticles entered phase 1 safety studies in partnership with the National Institutes of Allergy and Infectious Diseases (NIAID) at the National Institutes of Health. Around that time, CanSino (China) had brought in a candidate HPV type 5 vaccine for human safety studies. In April, BioNTech (Germany) (mRNA) in partnership with Pfizer and Fosun began their RNA vaccine-based human studies, as did Inovio (PA) with a DNA immunization approach, and the University of Oxford's Jenner Institute with an adenocarcinoma vector for chimpanzee (now (Jointly with AstraZeneca). Many of these clinical studies are now entering the second phase in larger populations to measure efficacy and immunity initially. The organizers allowed Oxford / AstraZeneca to skip the traditional Phase 1 studies, presumably due to the prior use of the vector platform in vaccine studies, and it is already following infection prevention trials in 6,000 healthy people. The speed with which these entities and the regulators overseeing their activities have responded to the urgency of the situation is unprecedented [8,9].

Figure 1: 3D structure of spike protein of SARS-CoV-2 according to the similarity to SP 5X58A

In addition to the aforementioned gene-based methods, 3 other programs are already in the clinic with an inactivated virus, and another 100 are in preclinical development, 1 of which are AAVCOVID tracked by our group at Mass Eye and Ear (Boston, Massachusetts) in partnership with MAS Hospital. General (Boston, Massachusetts) and the Gene Therapy Program at the University of Pennsylvania (USA) [10].

Some questions should be considered: Is there a lot of effort? not enough? Which one will make it? Are they ultimately competing for the same resources, hindering us in reaching a vaccine solution? Is there a place for more than one vaccine? These and many other questions will likely remain unanswered for some time. The novelty of this viral enemy, the unprecedented nature and scale of this crisis, the first phase of the ever-changing situation, and the paralyzed world leaves us with many missing data points to answer any of these questions with any certainty. In the absence of these predictors of success, one places chips in as many areas of this unfortunate roulette table as possible, with the goal of validating as many methods as possible to create an effective vaccine [11].

What we can do at this moment is to clarify the basic parameters and features that any vaccine should be successful. I apply it here with some specificity to each of the gene-based methods under study. Safety is an indispensable feature of any vaccine as it is administered to a large number of healthy people. Small differences in the safety features of the suspended vaccines could be materially important in screening the different vaccine programs for the coming months. A major concern with any vaccine is that, in rare cases, it has been observed that certain experimental vaccines for some pathogens can enhance infection or disease, which has been previously seen in some vaccines for dengue and respiratory syncytial virus. Although not fully understood, this enhancement appears to be due to a quality of the immune response and a lack of appropriate equivalent antibody responses compared to the uninformed antibody binding activity [12].

Vector regimens with a broad clinical record in gene therapy can decline the safety of those platforms, often at dramatically higher doses, with adenoviruses (AAV) and stromes have now been used clinically for more than 20 years. In addition, all of these vector systems have established a base of expertise as a vaccine method as well. Adenovirus has been used extensively in gene-based immunization, with DNA and mRNA fully lagging behind, and AAV lagging in this aspect.

Effectiveness (or strength and level of protection afforded to residents) is an obvious key to success, but it is not the whole story. Efficacy is determined by the consistency of the effect across subjects, the amount and quality of the immune response (as mentioned previously), and durability. Gene transfer modalities have a common feature here as the endogenous expression of their transgenes activates both cellular and humoral immunity, in contrast to many conventional vaccine methods that predominantly activate antibodies. The efficiency and auxiliary effect of gene delivery will influence the size and appearance of the host response, and are known to differ between AAV, Ad, mRNA and DNA approach. Given that there is as yet no clarity about the connections that protection vaccine approaches should achieve, it will remain difficult to measure success until animal production challenge studies and / or human protection experiments are matched with specifics [13].

Canadian biopharmaceutical company Medicago announced that it had succeeded in producing a virus-like particle (VLP) from the coronavirus 20 days after obtaining the SARS-CoV-2 gene sequence. Medicago produced VLP using plant-based technology. VLP production is the first step in developing a vaccine for COVID-19 that will now undergo pre-clinical testing to ensure its safety and efficacy.

Medicago does not work with live virus but does use plants. Their technology inserts a genetic sequence into Agrobacterium, a soil bacterium, that plants eat. The plant begins to produce the protein that can then be used as a pollen. If the virus begins to mutate, as expected for SARS-CoV-2, they can only upgrade production with new factories.

Conclusions

Researchers are still ongoing to find a vaccine or drug to limit the spread of the outbreak. Most researches take different methods of transferring the required genes, especially the Spike protein of SARS-CoV-2, the main protein which the virus enters the host cell. Hopefully, in the coming days, the clinical trials of will end and the vaccines become available everywhere.

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