

## Why Covid-19 Vaccine Still not Invented to Relieve the Globe from Pandemic

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### ABSTRACT

**Background:** Covid-19 pandemic shocked and locked whole world in year 2019 and 2020. Maximum death occurred in USA followed by Italy and Spain. Objective- Discuss and analyse various type of vaccines of Corona virus on basis of its antigen S protein with compare to other viruses.

**Methods:** Collecting data of Covid 19 vaccination preparation from internet and other all social network sources and afterwards discussing them.

**Result:** According to available information, in Germany and UK, the vaccine developed from chimpanzee's Corona virus is ahead of every other type as now they got permission of even testing on human volunteers.

**Conclusion:** Even though whole world community of scientists are working on the finding out of treatment as well as vaccine against Covid 19, on emergency basis, full flagged effective specific vaccine will be not available to common man before about one year, till that time social distancing and lockdown only can control the spread, morbidity and mortality in the whole globe.

**Keywords:** Covid-19; Virus; Antigen; S protein

### INTRODUCTION

A vaccine is a type of treatment aimed at stimulating the body's immune system to fight against infectious pathogens, like bacteria and viruses. They are, according to the World Health Organization, "one of the most effective ways to prevent diseases." The human body is particularly resilient to disease, having evolved a natural defense system against nasty disease-causing microorganisms like bacteria and viruses [1]. The defense system our immune system is composed of different types of white blood cells that can detect and destroy foreign invaders. Some gobble up bacteria, some produce antibodies which can tell the body what to destroy and take out the germs, and other cells memorize what the invaders look like, so the body can respond quickly if they invade again [2]. Vaccines are a really clever fake-out. They make the body *think* it's infected so it stimulates this immune response. For instance, the measles vaccine tricks the body into thinking it has measles. When you are vaccinated for measles, your body generates a record of the measles virus. If you come into contact with it in the future, the body's immune system is primed and ready to beat it back before

you can get sick [3]. The very first vaccine was developed by a scientist named Edward Jenner in the late 18th century. In a famous experiment, Jenner scraped pus from a milkmaid with cowpox a type of virus that causes disease mostly in cows and is very similar to the smallpox virus and introduced the pus into a young boy. The young boy became a little ill and had a mild case of cowpox. Later, Jenner inoculated the boy with smallpox, but he didn't get sick. Jenner's first injection of cowpox pus trained the boy's body to recognize the cowpox virus and, because it's so similar to smallpox, the young man was able to fight it off and not get sick. And you know the rest of history; this smallpox vaccine had eradicated the disease smallpox from the earth. Vaccines have come an incredibly long way since 1796. Scientists certainly *don't* inject pus from patients into other patients, and vaccines must abide by strict safety regulations, multiple rounds of clinical testing and strong governmental guidelines before they can be adopted for widespread use. Vaccines can be classified first into two groups, 1. Live attenuated vaccines 2. Inactivated vaccines which can be divided in to A. Whole killed vaccines B. Subunit vaccines (also called acellular vaccines),

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which again further divided into I. Toxoid Vaccines II Conjugate vaccines III Recombinant vaccines [4].

Among all above types, toxoid vaccine is out of consideration, as Covid 19 is a virus. According to me the easiest type to prepare is whole killed vaccines but with Covid 19, while killing or inactivating process, the desired antigenicity of spike antigen S should have to be kept intact. The method of whole killed vaccine developing for Covid 19 by this method, one has to find out the method of inactivation in which Covid 19's spike antigen S should remain unaffected. Even though killed vaccine's effect does not last long, it serves best in such urgent situations [5]. The live attenuated vaccines are far better and even long lasting then killed vaccines but at the same time requires long time in preparing it, either by finding out of other species of corona virus with almost same antigenicity but no pathogenicity is there, even should infect human cells. Germany and UK claimed that they found out Chimpanzee's corona virus for this purpose and under phase III testing, it means testing on human volunteers but its efficacy and side effect on human is still to be tested [6]. Today, an effective vaccine against HIV does not exist. A vaccine that can prevent infection would teach the immune system to respond to HIV by making antibodies that can bind to the virus and stop it from infecting cells, or by promoting other immune responses that kill the virus [7].

No vaccine is 100% effective, and this is likely to be the same for HIV, or even with Covid -19. Some people who receive a vaccine will not respond strongly enough to the vaccine and will not be protected, as in the case of the seasonal flu vaccine. But finding at least a partially effective vaccine remains of critical importance for the HIV response, and more even with Covid-19 due to its more contagious nature and capacity to lock all most whole globe at a same time, as all successful disease elimination strategies have included a vaccine among their arsenal [8]. Most vaccines against other diseases stimulate the production of antibodies that 'neutralise' viral infectivity, but in the case of HIV, neutralising antibodies do not clear the infection. This is because HIV reproduces so fast, and mutates so quickly, that antibodies produced against the virus quickly become ineffective against newer viruses. Millions of new viruses are produced each day and each one is slightly different from previous generations of the virus [9]. Antibodies against HIV are only likely to be effective if they can bind to regions of the virus that vary little between viruses.

Another issue is that HIV has several sub-types which are concentrated in different regions of the world. For example, sub-type B is common in North America and Europe, but sub-type C is common in southern and eastern Africa [10]. Any vaccine must either be effective against all sub-types or different vaccines must be developed against various sub-types. A vaccine might also stimulate the production of immune system cells called T-lymphocytes that can clear HIV-infected cells. But HIV has also evolved to suppress some immune responses that are important in the early stages of a viral infection. Another challenge in vaccine development is finding efficient ways to deliver HIV proteins safely in ways that will allow the immune system to recognise HIV and respond to it without establishing an infection. HIV integrates into human cells and uses those cells

to reproduce, so live or attenuated whole-virus vaccines are unsuitable for use in HIV [11]. Instead, HIV proteins need to be engineered in ways that make them harmless but still recognizable to the immune system. These proteins or sequences of viral material must be delivered using a vector another harmless virus such as canary pox or a common cold virus. This presents them to the immune system. Researchers are still working to understand what they call the 'correlates of protection' the immune system markers which show that a person is protected against HIV after vaccination. These measurements must be assembled from observations in clinical trials and animal studies. With Covid-19, the virus behavior is not as vigorous changing like HIV, so sooner or later and even before HIV vaccine, Covid-19, vaccines should be invented as far as the development of vaccine sciences technology indicates. Vaccines contain a handful of different ingredients depending on their type and how they aim to generate an immune response [12]. However, there's some commonality between them all.

The most important ingredient is the antigen. This is the part of the vaccine the body can recognize as foreign. Depending on the type of vaccine, an antigen could be molecules from viruses like a strand of DNA or a protein. It could instead be weakened versions of live viruses. For instance, the measles vaccine contains a weakened version of the measles virus [13]. When a patient receives the measles vaccine, their immune system recognizes a protein present on the measles virus and learns to fight it off. A second important ingredient is the adjuvant. An adjuvant works to amplify the immune response to an antigen. Whether a vaccine contains an adjuvant depends on the type of vaccine it is. Some vaccines used to be stored in vials that could be used multiple times and, as such, contained preservatives that ensured they would be able to sit on a shelf without growing other nasty bacteria inside them [14]. One such preservative is thimerosal, which has garnered a lot of attention because it contains trace amounts of easily cleared ethylmercury. Its inclusion in vaccines hasn't been shown to cause harm, according to the CDC. In places like Australia, single-use vials are now common, and thus preservatives such as thimerosal are no longer necessary in most vaccines.

## MAKING A COVID-19 VACCINE

The pathogen at the center of the outbreak, SARS-CoV-2, belongs to the family of viruses known as *corona viruses*. This family is so named because, under a microscope, they appear with crown like projections on their surface. In developing a vaccine that targets SARS-CoV-2, scientists are looking at these projections intensely. The projections enable the virus to enter human cells where it can replicate and make copies of itself. They're known as "spike proteins" or "S" proteins. Researchers have been able to map the projections in 3D, and research suggests they could be a viable antigen in any corona virus vaccine [17].

That's because the S protein is prevalent in corona viruses we've battled in the past ~ including the one that caused the SARS outbreak in China in 2002-03. This has given researchers a head start on building vaccines against part of the S protein and, using animal models, they've demonstrated they can generate an immune response[18]. There are many companies across the

world working on a SARS-CoV-2 vaccine, developing different ways to stimulate the immune system. Some of the most talked about approaches are those using a relatively novel type<sup>2</sup> of vaccine known as a "nucleic acid vaccine." These vaccines are essentially programmable, containing a small piece of genetic code to act as the antigen. Biotech companies like Moderna have been able to generate new vaccine designs against SARS-CoV-2 rapidly by taking a piece of the genetic code for the S protein and fusing it with fatty nano particles that can be injected into the body. Imperial College London is designing a similar vaccine using corona virus RNA its genetic code. Pennsylvania biotech company Inovio is generating strands of DNA it hopes will stimulate an immune response. Although these kinds of vaccines can be created quickly, none have been brought to market yet.

Johnson & Johnson and French pharmaceutical giant Sanofi are both working with the US Biomedical Advanced Research and Development Authority to develop vaccines of their own. Sanofi's plan is to mix coronavirus DNA with genetic material from a harmless virus, whereas Johnson & Johnson will attempt to deactivate SARS-CoV-2, essentially switching off its ability to cause illness while ensuring it still stimulates the immune system.

On March 30, Johnson & Johnson said human tests of its experimental vaccine will begin by September. We have a candidate that has a high degree of probability of being successful against the covid-19 virus, said Alex Gorsky, CEO of Johnson & Johnson, during an interview with NBC News' Today[19]. "Literally within the next few days and weeks, we're going to start ramping up production of these vaccines."

DIOSynVax, a vaccine development company working out of the University of Cambridge, is trying to eschew the traditional pathways to vaccine creation with a new platform. The company's approach uses computer modelling of the virus's structure to determine weak spots in the SARS-CoV-2 DNA places it can target to drive an immune reaction without causing any harm to the patient. "What we end up with is a mimic, a mirror image of part of the virus, but minus its bad parts," said Jonathan Heeney, CEO and founder of DIOSynVax, in a statement. "What remains is just the magic bullet, essentially, to trigger the right type of immune response".

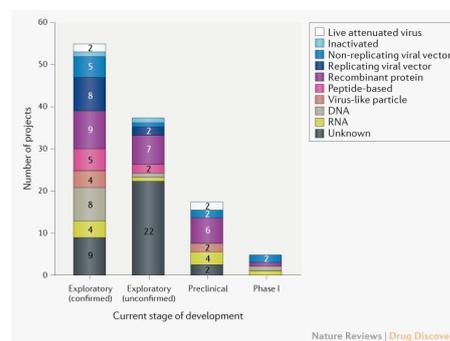
Some research organizations, such as Boston Children's Hospital, are examining different kinds of **adjuvants** that will help amplify the immune response. This approach, according to the Harvard Gazette, will be targeted more toward the elderly, who don't respond as effectively when vaccinated. It's hoped that by studying adjuvants to boost a vaccine, the elderly can be vaccinated with a mix of ingredients that would supercharge their immunity [20].

Vaccines have been produced against several diseases caused by coronaviruses for animal use, including for infectious bronchitis virus in birds, canine coronavirus and feline coronavirus.

Previous projects to develop vaccines for viruses in the family Coronaviridae that affect humans have been aimed at severe acute respiratory syndrome (SARS) and Middle East

respiratory syndrome (MERS). Vaccines against SARS and MERS have been tested in non-human animal models[21]. As of 2020, there is no cure or protective vaccine for SARS that has been shown to be both safe and effective in humans. According to research papers published in 2005 and 2006, the identification and development of novel vaccines and medicines to treat SARS was a priority for governments and public health agencies around the world. There is also no proven vaccine against MERS. When MERS became prevalent, it was believed that existing SARS research may provide a useful template for developing vaccines and therapeutics against a MERS-CoV infection. As of March 2020, there was one (DNA based) MERS vaccine which completed phase I clinical trials in humans, and three others in progress, all of which are viral-vectored vaccines, two adenoviral-vectored (ChAdOx1-MERS, BVR5-GamVac), and one MVA-vectored (MVA-MERS-S).

Public information on the specific SARS-CoV-2 antigen(s) used in vaccine development is limited. Most candidates for whom information is available aim to induce neutralizing antibodies against the viral spike (S) protein, preventing uptake via the human ACE2 receptor. However, it is unclear how different forms and/or variants of the S protein used in different candidates relate to each other, or to the genomic epidemiology of the disease [22]. Experience with SARS vaccine development indicates the potential for immune enhancement effects of different antigens, which is a topic of debate and could be relevant to vaccine advancement (Figure 1).



**Figure 1:** Pipeline of COVID-19 vaccine candidates by technology platform.

Exploratory projects (split into confirmed and unconfirmed) are in the early planning stage with no in-vivo testing, and preclinical projects are at the stage of in-vivo testing and/or manufacturing clinical trials material [23].

Candidate	Vaccine characteristics	Lead developer	Status
mRNA-1273	LNP-encapsulated mRNA vaccine encoding S protein	Moderna	Phase I (NCT04283461)
Ad5-nCoV	Adenovirus type 5 vector that expresses S protein	CanSino Biologicals	Phase I (NCT04313127)

INO-4800	DNA plasmid encoding protein delivered by electroporation	Inovio S Pharmaceuticals	Phase I (NCT04336410)
LVSMENP-DC	DCs modified with lentiviral vector expressing synthetic minigene based on domains of selected viral proteins; administered with antigen-specific CTLs	Shenzhen Geno-Immune Medical Institute	Phase I (NCT04276896)
Pathogen-specific aAPC	aAPCs modified with lentiviral vector expressing synthetic minigene based on domains of selected viral proteins	Shenzhen Geno-Immune Medical Institute	Phase I (NCT04299724)

**Table 1:** Clinical-phase vaccine candidates for covid-19.

A APC, artificial antigen-presenting cell; CTL, cytotoxic T lymphocyte; DC, dendritic cell; LNP, lipid nanoparticle; S protein, SARS-CoV-2 spike protein. Source: ClinicalTrials.gov website; WHO.

## DIVERSITY OF TECHNOLOGY PLATFORMS

A striking feature of the vaccine development landscape for COVID-19 is the range of technology platforms being evaluated, including nucleic acid (DNA and RNA), virus-like particle, peptide, viral vector (replicating and non-replicating), recombinant protein, live attenuated virus and inactivated virus approaches (Figure 1). Many of these platforms are not currently the basis for licensed vaccines, but experience in fields such as oncology is encouraging developers to exploit the opportunities that next-generation approaches offer for increased speed of development and manufacture. It is conceivable that some vaccine platforms may be better suited to specific population subtypes (such as the elderly, children, pregnant women or immuno compromised patients) [24].

Considering the candidates in Table 1, the novel platforms based on DNA or mRNA offer great flexibility in terms of antigen manipulation and potential for speed. Indeed, Moderna started clinical testing of its mRNA-based vaccine mRNA-1273 just 2 months after sequence identification. Vaccines based on viral vectors offer a high level of protein expression and long-term stability, and induce strong immune responses. Finally,

there are already licensed vaccines based on recombinant proteins for other diseases, and so such candidates could take advantage of existing large-scale production capacity [25].

For some platforms, adjuvants could enhance immunogenicity and make lower doses viable, thereby enabling vaccination of more people without compromising protection. So far, at least 10 developers have indicated plans to develop adjuvanted vaccines against COVID-19, and vaccine developers including GlaxoSmithKine, Seqirus and Dynavax have committed to making licensed adjuvants (AS03, MF59 and CpG 1018, respectively) available for use with novel COVID-19 vaccines developed by others.

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## RESULTS AND DISCUSSION

A COVID-19 vaccine is a hypothetical vaccine against coronavirus disease 2019 (COVID19). Although no vaccine has completed clinical trials, there are multiple attempts in progress to develop such a vaccine [15]. In late February 2020, the World Health Organization (WHO) said it did not expect a vaccine against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative virus, to become available in less than 18 months. The Coalition for Epidemic Preparedness Innovations (CEPI) which is organizing a US\$2 billion worldwide fund for rapid investment and development of vaccine candidates indicated in April that a vaccine may be available under emergency use protocols in less than 12 months or by early 2021 [16].

By 8 April 2020, 115 vaccine candidates were in development, with four organizations having initiated Phase I-II safety and efficacy studies in human subjects. Five of the vaccine candidates were in Phase I safety studies. In developing a vaccine for SARS-CoV-2, scientists need to find a viable antigen that will stimulate the body's immune system into defending against infection.

## CONCLUSION

Industry benchmarks for traditional vaccine development paradigms cite attrition rates for licensed vaccines of more than 90%. The approaches being applied for COVID-19 development which involve a new virus target and often novel vaccine technology platforms and novel development paradigms as well

are likely to increase the risks associated with delivering a licensed vaccine, and will require careful evaluation of effectiveness and safety at each step. In order to assess vaccine efficacy, COVID-19-specific animal models are being developed, including ACE2-transgenic mice, hamsters, ferrets and non-human primates. Bio safety-level 3 containment measures are needed for animal studies involving live-virus challenges, and the demand for these capabilities is likely to require international coordination to ensure that sufficient laboratory capacity is available.

Finally, strong international coordination and cooperation between vaccine developers, regulators, policymakers, funders, public health bodies and governments will be needed to ensure that promising late-stage vaccine candidates can be manufactured in sufficient quantities and equitably supplied to all affected areas, particularly low-resource regions. CEPI has recently issued a call for funding to support global COVID-19 vaccine development efforts guided by three imperatives: speed, manufacture and deployment at scale, and global access.

The Coalition for Epidemic Preparedness Innovations (CEPI) is a foundation that takes donations from public, private, philanthropic, and civil society organisations, to finance independent research projects to develop vaccines against Emerging Infectious Diseases (EID). CEPI is focused on the Organization's (WHO) "blueprint priority diseases", which includes: the Middle East respiratory syndrome-related corona virus (MERS-CoV), the Severe acute respiratory syndrome corona virus 2 (SARS-CoV-2), the Nipah virus, the Lassa fever virus, and the Rift Valley fever virus, as well as the Chikungunya virus and the hypothetical, unknown pathogen "Disease X". CEPI investment also requires "equitable access" to the vaccines during outbreaks, although subsequent CEPI policy changes may have compromised these criteria. In the year 2020, CEPI was identified as a "key player in the race to develop a vaccine" for the Corona virus disease 2019.

Hereby lastly we urge the global vaccine community to collectively mobilize the technical and financial support needed to successfully address the COVID-19 pandemic through a global vaccination program, and provide a strong base to tackle Covid-19 pandemics. As all global vaccine community collectively presumed that it may take about one year to prepare specific vaccine for Covid 19, by scientific manner, and I also represent the same. Even though at last but not least we hope that all above scientific presumptions may prove wrong and tomorrow only Covid 19 vaccine will be invented, which free the globe from this horrible pandemic within one or two months only.

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