The COVID Crossroads:

How a Needle in Your Arm Will Put a Glass in Your Hand

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Introduction

No event in recent memory has devastated the global community so completely as the COVID-19 pandemic. What began in December 2019 as an unexplained outbreak of pneumonia in Wuhan City, China, spread and before it was able to be stopped ravaged almost every facet of our society, leading to the death of 1.9 million before its second Christmas (WHO, 2021). It can be comforting in a way to characterise the disease as an evil force, an invisible killer which targets especially the elderly and the infirm. This mystification however, only serves to grant the virus undue power, which must be treated through education.

The COVID-19 disease is caused by a virus called SARS-CoV-2, shown in Figure 1. The most important component of the virus is its RNA. Much like the DNA within you, the RNA in a virus acts as a genetic blueprint, containing all the information necessary for function, divided into sections called genes. Each gene contains the information for a different characteristic, in humans, eye colour and height for example and in SARS-CoV-2 one crucial gene will instruct the cell to create spike proteins.

Spike proteins are the second component of vital importance. They extend out from the spherical surface of the viruses and each one is tipped with a region called Receptor Binding Domain (RBD) which matches a specific region on human cells called ACE2, like a key to a lock (Krammer, 2020(a)).

The combination of these two parts are what make infection by SARS-CoV-2 such a deadly prospect. The virus is incredibly small, 100,000 of them laid side by side would only span a centimetre. They can, as a result be inhaled unknowingly and once inside the body, latch onto healthy human cells using the spike protein and its RBD. Through this bond, the virus can insert its RNA into the human cell, attacking it and forcing it to act as a factory, producing more copies of the virus.

The Solution

Being the product of roughly six million years of evolution, the human body has defences in place for situations like this, namely antibodies. Antibodies are small proteins created by the body in order to defend against invaders (Krammer, 2020(b)). When created, they are specific to the invader and as such can intercept and bind to them before they reach the human cells, as shown in Figure 2.

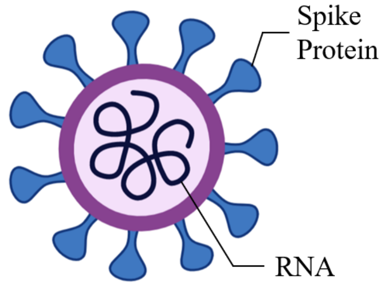

Figure 1. A Model of the SARS-Cov-2 Virus.

There is a problem however, the first time the body is exposed to an invader, the process to create these antibodies is time consuming and by the time the body has completed it, it may be too late to fight off the infection. However, after this initial exposure, the body retains memory cells which will recognize the same invader in future, meaning the specific antibodies can be created immediately. This is why vaccination is so crucial and why the recent breakthroughs hold so much promise for the future. At its core, vaccination exposes the body to harmful elements, such as the spike protein, and gives the body time to develop these memory cells, which in turn will quickly release specific antibodies in the event of an infection (Birney, 2020).

Approximately 140 vaccines are currently in development, which fall under four different methods (Callaway, 2020). This is the crossroads in the scientific community at the moment, as to the most effective way of navigating the crisis.

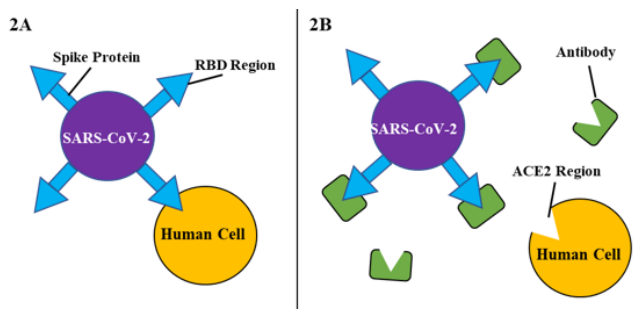

Figure 2. A model to show the impact and function of antibodies. In 2A, an example of a person without antibodies, the RBD can interact with ACE2 unobstructed, leading to infection. In 2B, the antibodies present in a person are able to bind to the RBD, which protects the human cell.

Virus Vaccines

This is the oldest method of vaccine production, used throughout history. For the elimination of polio and measles as death sentences, you have virus vaccines to thank. It is the simplest of the methods, less popular than its more modern counterparts but highly effective nonetheless. To create this vaccine, a virus in its natural state is taken, grown in favourable conditions and concentrated to produce a large amount of pure virus. It is then treated, either with heat or chemicals such as formaldehyde in order to harm the genetic information within the virus (Krammer, 2020(a)). Once treated, the surface is unchanged but the RNA has been damaged, making it unable to enter and infect human cells. It can now be delivered to a patient, who will develop antibodies without becoming infected.

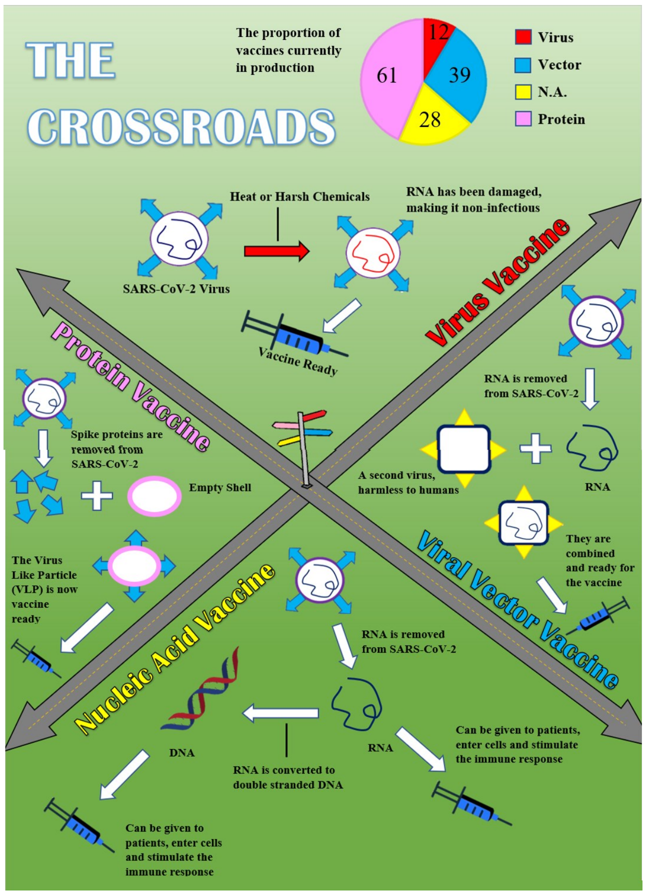

Figure 3. An infographic summarising the four most popular methods of SARS-CoV-2 vaccine production. Pie chart adapted from Callaway, 2020.

Viral Vector Vaccines

The second method available to researchers is the viral vector, which is less complex than it initially sounds. In this method, scientists take the gene in the viral RNA responsible for creating the spike proteins, and insert it into a different species of virus, which does not cause disease in humans. This second virus acts as a way of transporting this gene into human cells, which will read the gene and create a spike protein on its surface (Callaway, 2020). This will trigger the immune response and allow the specific antibodies to develop, whilst being harmless to the patient. One potential disadvantage is that a patient may be immune to this second virus and in that case, the treatment would be ineffective.

Nucleic Acid Vaccines

Nucleic acid is the NA in DNA and RNA, which codes for proteins and instructs the cell. This method is similar to the previous, opting to make human cells present the spike protein. It does this by taking a strand of RNA, with a gene which codes for the spike protein and implanting it into a patient. Alternatively, it can be converted into double stranded DNA before being given to the patient, before using a process called electroporation, which shocks the cell and creates holes the DNA can enter through (Khanh *et al.,* 2020). Once inside, cell machinery will read the gene and create the spike protein it codes for, presenting it on the surface and allowing antibodies to develop.

Protein based

It's a well-worn phrase that the simplest explanation is most often correct, whilst this may not be true in all cases, it is supported by the fourth and final method. The problem at its core is that we need to expose the human body to the spike protein in order for antibodies to develop and this fourth method does just that. Researchers take several of these spike proteins and attach them to an artificial empty shell, containing no genetic information (Krammer, 2020 (a)). This will result in a Virus-Like Particle (VLP). When given to a patient, the immune response will create antibodies and there is no risk of infection as the VLP contains no genetic material at all. A disadvantage of this method is it would require several treatments for long term immunity.

Conclusion

In conclusion, these are the four main vaccines currently being tested by researchers and each one represents a different potential route out of the COVID crisis, as shown in Figure 3. Whilst they use contrasting methods, they serve the same goal, returning us to normality, hopefully sooner rather than later.

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