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Pfizer-BioNTech COVID-19 vaccine explained

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With a variety of questions following its approval by regulatory bodies in the UK and US, many are focussed on communicating the precise mechanisms of the Pfizer-BioNTech mRNA vaccine to protect against COVID-19 or SARS-CoV-2. This piece aims to explore the contents of the vaccine and its exact effects upon injection into the muscle of the upper arm.

The vaccine developed by Pfizer-BioNTech is different from other pre-existing vaccines: rather than using weakened or inactivated forms of the pathogen (disease-causing particle), it contains genetic information in the form of mRNA. To account for the effects of this, it's important to acknowledge the body's cellular machinery and the effects that the invading virus has:

- All cells contain DNA. This is a very compact molecule that contains massive amounts of information encoded into its molecular structure. It contains instructions for your body on pretty much everything, from your eye or hair colour, to the exact details of chemical processes that take place in your digestive system.
- In order to mobilise (read and use) instructions in DNA, the cells convert DNA into messenger RNA – mRNA - in a process called transcription.
- This requires existing cell machinery called ribosomes to read the instructions in the mRNA molecules in a process called translation and use them to make proteins which are vital for all day-to-day function.
- The virus takes advantage of the cells' existing processes, hijacking the structures to reproduce its own genetic information (also in the form of mRNA) rather than that of the original, functional cell.
- Viruses hijack healthy cells' existing machinery to produce their own viral proteins which then go on to help produce more of the virus. This is what disrupts regular function and causes disease[1].

So what's inside the vaccine?

The vaccine also contains instructions (in the form of mRNA) for proteins. Mainly one small protein in particular: spike proteins. These are often represented by protrusions on the surface of the viral particle, shown in red (left). RNA molecules are very unstable and often 'fall apart', so they are packaged within lipid (fatty) nanoparticles[2]. The vaccine is designed to give the body a 'headstart' to protect against the virus[3]. The vaccine particles interact with the body's cells, fuse with them and release the spike mRNA into the cells. The cell then uses its own ribosomes to construct the spike proteins which, on their own, are relatively harmless. (Figure 2, below) The inserted mRNA is eventually destroyed by the cell, leaving no permanent trace.

What's the effect of having SARS-Cov-2 spike proteins in the body's cells?

Once they are constructed, spike proteins (and fragments of spike proteins) migrate to the surface of the cell and stick out tips. This is recognised by the body, specifically the body's immune system, and generates an immune response[4].

Figure 2, below: Creative rendition of interactions between vaccine particles and vaccinated cell. Shows how cellular machinery is used to synthesise spike proteins.

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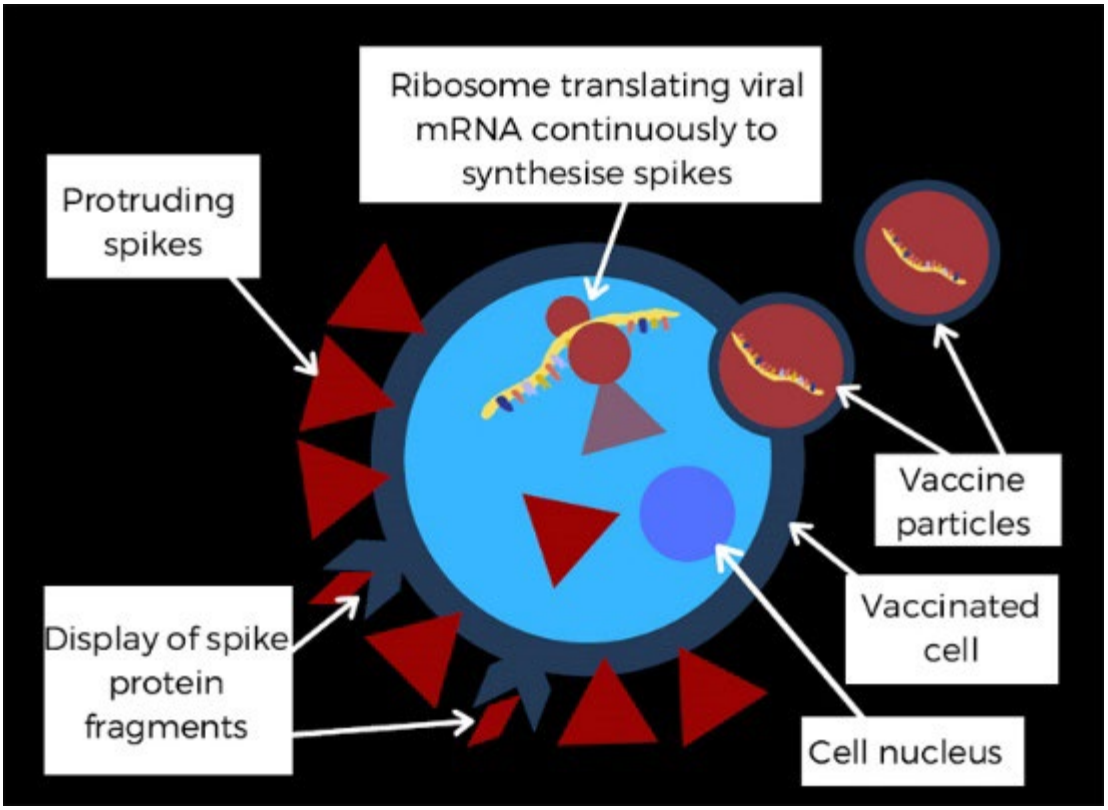

How does the immune system react once recognising the foreign protein fragments following vaccination?

Once the cell is recognised as foreign and infected, it is destroyed by the immune system, releasing its contents into its surroundings. The released spike proteins and their fragments are then collected by and displayed on the surface of an immune cell called an antigen-presenting cell. This can have several effects (Figure 3):

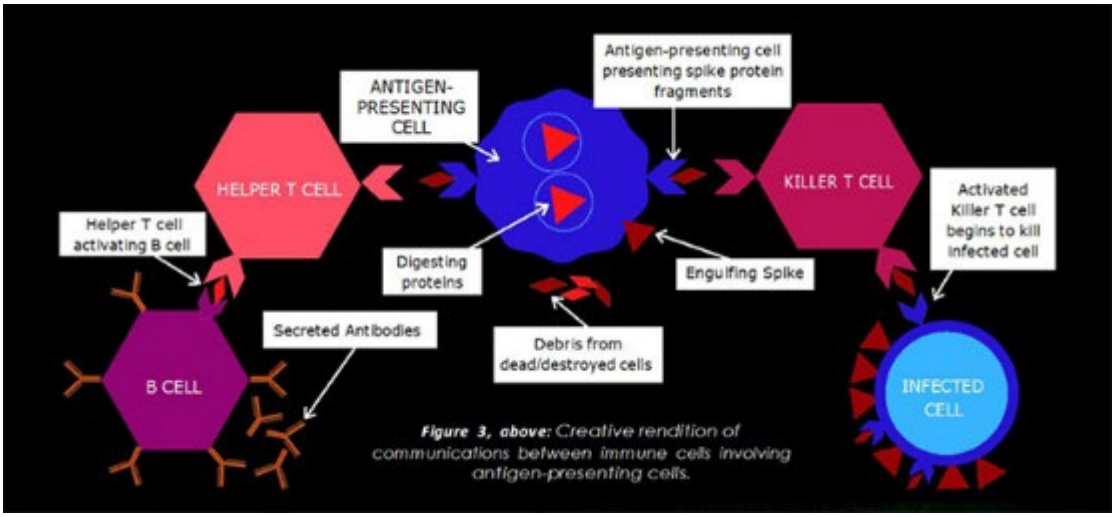

Figure 3, above: *Creative rendition of communications between immune cells involving antigen-presenting cells.*

The antigen-presenting cell activates a type of immune cell called the helper T- cell. Helper T-cells detect the fragments of proteins presented by the antigen- presenting cell and communicate with the rest of the body's immune system to help fight the infection.

Antigen-presenting cells also activate a type of immune cell called killer T-cells. These then seek out and destroy infected cells displaying spike protein fragments on their surfaces.

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Immune cells called B-cells then synthesise and secrete antibodies. These are protein molecules that the body produces in response to disease and uses to fight infections. Antibodies produced in response to the vaccine also have the ability to help fight SARS-CoV-2; they latch onto SARS-CoV-2 spike proteins, flagging them to the rest of the immune system to be destroyed. They also prevent further infection of other healthy cells by blocking the spikes from attaching to them (Figure 4).

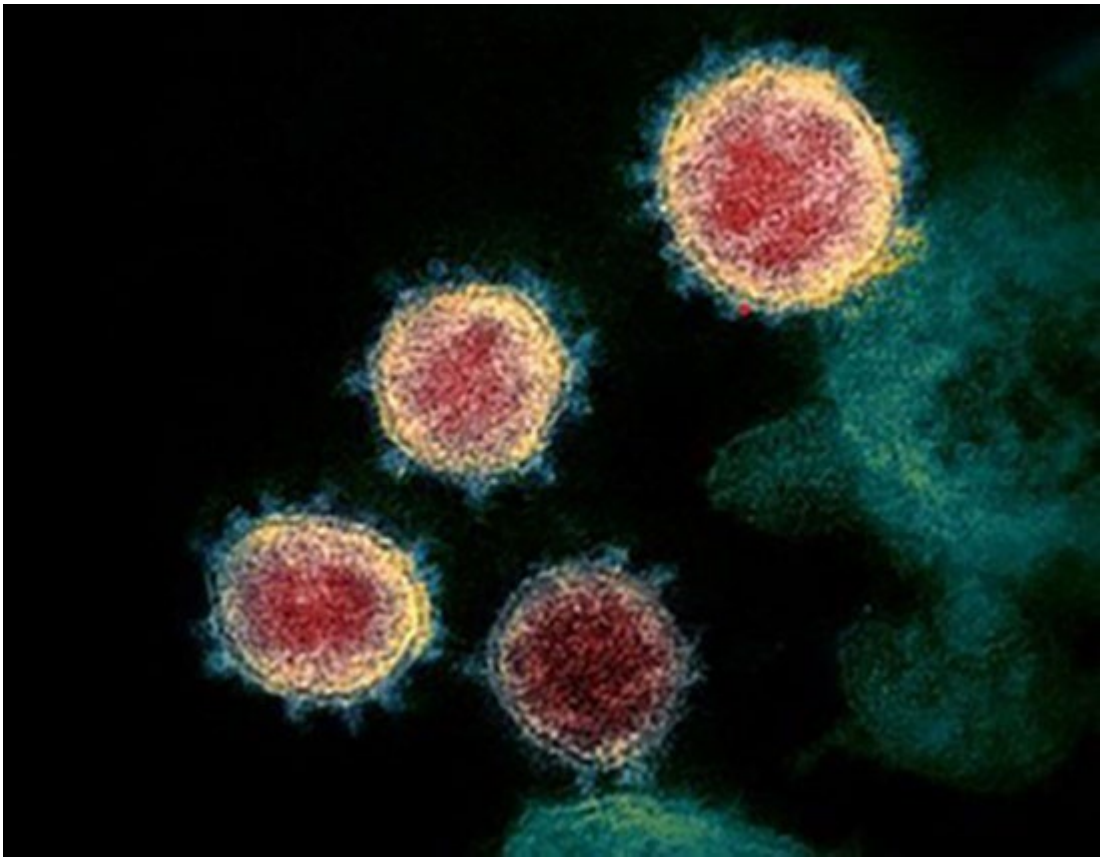

Figure 4:
Transmission electron microscope image shows SARSCoV- 2, causing COVID-19, isolated from a patient. The spikes on the outer edge of the virus give coronaviruses their name (corona = crown). The spikes act as a target for both immune response in disease and potential therapies. Source: NIAID-RML

The Pfizer-BioNTech vaccine requires two injections, given 21 days apart. It's possible that in the months after vaccination, the number of antibodies and killer T-cells in the body will decrease, as researchers still aren't sure exactly how long protection will last. However, the instructions to construct the disease-fighting antibodies are stored in the body's bespoke 'disease database' managed by immune cells called memory B-cells and memory T-cells[1].

The production of antibodies in response to vaccination gives the body's immune system a much-needed 'headstart' in fighting a potential SARS-CoV-2 infection. This means that the body can recognise and fight the virus by producing antibodies much more quickly than if the vaccine was not given. On 18th November 2020, Pfizer and BioNTech reported that primary efficacy analysis of the BNT162b2 vaccine demonstrates 95% effectiveness against COVID-19 beginning 28 days after the first dose[5].

Whilst the exact logistics of its use within healthcare systems are still being determined, it is certain that the use of an effective and safe vaccine will prove invaluable in the first stage of global recovery from the pandemic.

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