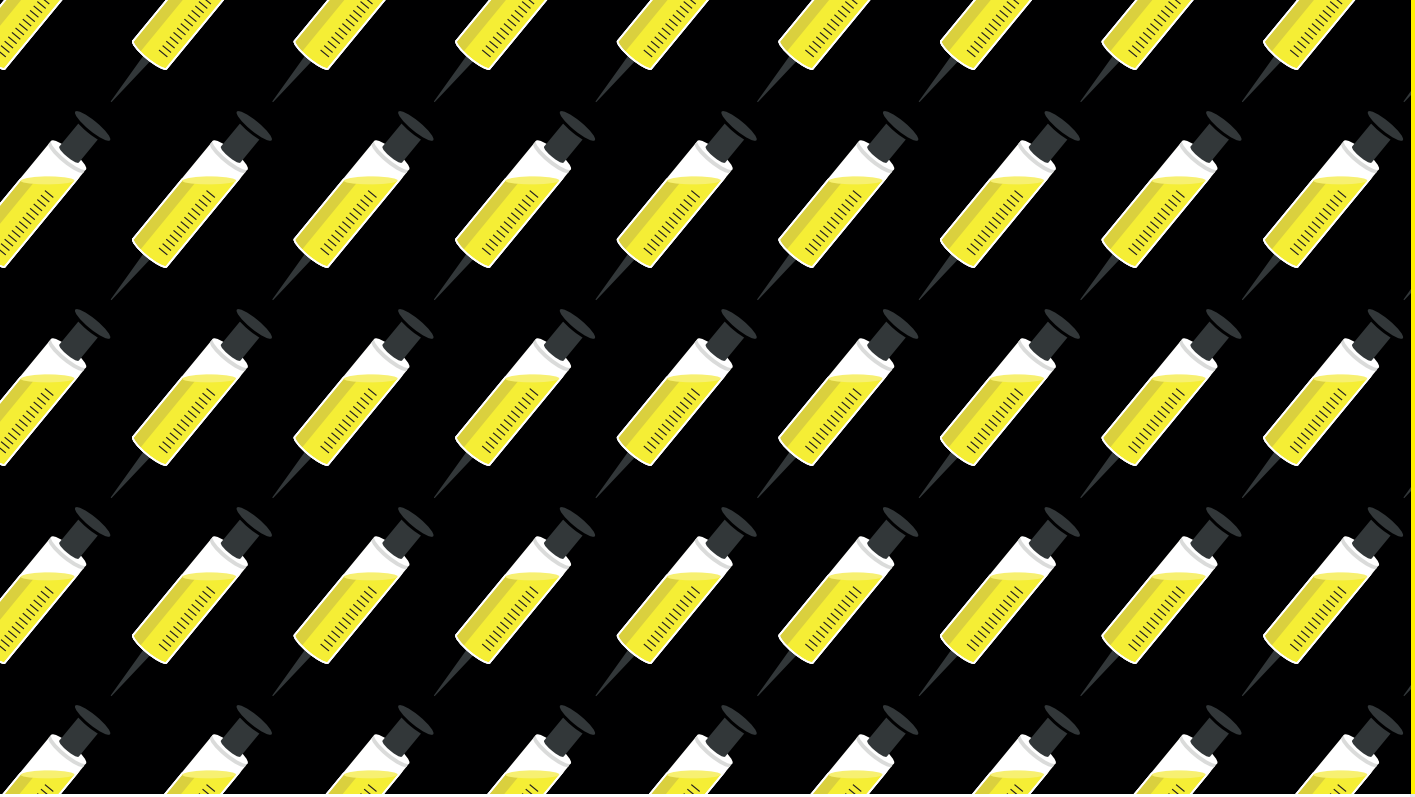

SARTORIUS

Success at Speed: Digging into Accelerated Vaccine Development

Part 3 – Vaccine Modalities

Virus-based vaccines were our first foray into immunization, but the field had to move on, embracing recombinant proteins, and now viral vectors and mRNA vaccines.

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In collaboration with

the Medicine Maker

Vaccine Modalities

Virus-based vaccines are the oldest form of vaccination, dating back to the 1700s, when Edward Jenner famously demonstrated how cowpox virus could provide immunity against smallpox. Created by producing and purifying an inactivated or attenuated version of the pathogenic virus, such vaccines have been used to combat many diseases, including rabies, polio, measles, mumps, rubella, and influenza. It's fair to say the approach has a long track record, but it's not perfect.

Traditional viral-based vaccines pose significant manufacturing challenges. The pathogenic virus has to be produced in large quantities to manufacture the vaccine, and some viruses, such as polio, rabies or SARS-CoV-2, are classified as biosafety level 3 (BSL3). The manufacturing process must also be tailored to the pathogen. For each new vaccine, you essentially start from zero, meaning long development timelines and the need to establish dedicated manufacturing facilities.

With the advent of molecular biology tools and increasing knowledge of immunity, recombinant subunit vaccines emerged. These vaccines consist of a recombinant disease specific antigen that can be recognized your immune system. Although development is simpler (manufacturers can begin with a well-known expression system) it is not a true platform approach. After all, the antigen expressed is unique and specific to the pathogen, and requires a tailored purification process. Furthermore, generating a strong T cell response can be challenging, although specific adjuvant can help.

Time for Vaccine Disruption

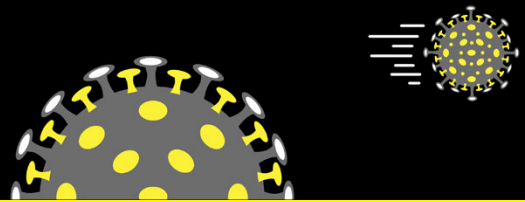
But what if we could turn the patient's own cells into mini-factories that pump out disease-specific antigen? Viral-vector-based vaccines and mRNA-based vaccines do just that and are considered disruptive approaches to vaccine production. Viral vector vaccines use genetically engineered viruses (for example, adenoviruses or poxviruses) to hijack the patient's cells into expressing antigen. On the other hand, mRNA-based vaccines deliver single-stranded mRNA molecules into the patient's cells (for example, via lipid nanoparticles), where they are translated into protein (antigen). →

→ These two approaches offer compelling advantages. Both safely mimic an infection (without a pathogen) and generate strong immune responses without the need for an adjuvant. And they are both true manufacturing platform approaches that can be applied to many different vaccines; the only aspect specific to the vaccine is the genetic code of the antigen.

Not only do such platforms speed development, they also offer significant manufacturing flexibility, as different vaccines can be produced in the same facility. mRNA-based vaccines also have the added advantage of being produced using cell-free processes, which keeps manufacturing relatively straightforward.

Overall, mRNA or viral-vector based vaccines offer significantly accelerated development timelines compared with viral or recombinant vaccines.

Tackling COVID-19



Researchers across the globe are exploring all four main modalities in the search for a COVID-19 vaccine; such a multi-pronged approach is sensible, as we do not yet completely understand the virus and the type of immune response it generates. Do we need a vaccine that generates a strong B cell response, a T cell response, or both? mRNA and viral vector vaccines usually generate a strong T cell response, while recombinant protein vaccines usually generate a strong B cell response. Early preliminary data indicate neutralizing antibody (B cell response) as a potential correlate of protection, and around 35 percent of COVID-19 vaccine candidates are using a recombinant subunit approach, with variety of expression systems, including bacteria, yeast, mammalian cell lines, and plants.

However, we can all agree that speed is of essence in this pandemic. And so the accelerated development and manufacturing timelines of platform approaches may mean that mRNA or viral-vectors reign supreme …

Remember that, prior to COVID-19, vaccines against SARS and MERS were in development, but aborted when the outbreaks were over. This highlights a significant problem in this field: vaccine development can be lengthy, but if it takes too much time then the outbreak may be over and the vaccine will have missed its biggest opportunity. If a vaccine is developed too late, it can hardly be considered a success – and its future is in doubt.

It is clear that we must learn how to safely and successfully accelerate vaccine development – not only for this pandemic, but also for the inevitable outbreaks of the future.

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