mRNA vaccines: The next generation tool to fight infections

Vaccines

Vaccines have been used by humans for over 225 years to prevent serious illness or death from infectious agents. Immunization currently prevents 4-5 million deaths every year [10]. The goal of vaccination is to show your body's immune system pieces of a pathogen (a microorganism that can cause you harm) prior to you being infected by the actual infectious organisms. Vaccination allows the body to educate immune cells involved in recognizing foreign invaders to eliminate them before they cause disease to you. Several vaccines have had complete successes such as wiping out smallpox in humans and rinderpest (a cattle plague) [1].

Traditional vaccines

Traditional vaccines can be divided into 3 types: inactivated, live-attenuated, and subunit vaccines. Examples of inactivated vaccines are the flu (shot), hepatitis A, polio (shot), and rabies. These vaccines are made by growing the pathogen in a controlled laboratory setting and killed in some manner making it incapable of causing disease. Live-attenuated vaccines include measles/mumps/rubella (MMR), rotavirus, smallpox, and chickenpox vaccines. For this type of vaccine, the pathogen is grown repeatedly in artificial conditions that damage its infectivity in its natural host. These defective pathogens can then be given to healthy people whose immune systems fight off the weakened virus without causing any disease. For subunit vaccines a small piece of the pathogen is created artificially and used as such or sometimes linked to other attenuated pathogen that express the fragment of another pathogen which induce immune response. As only pieces of the pathogen are used, there is no chance for illness from the pathogen [2].

Emerging Vaccines

Scientists and medical professionals are constantly working to improve vaccines in areas such as ability to make vaccines faster, cheaper, against newly emerging diseases, and more effective against the authentic pathogen. As technology improves, the options for creating vaccines have expanded greatly. mRNA vaccines are the result of this new technology, allowing scientists to very quickly make effective vaccines against new unknown pathogens. The COVID-19 vaccine designed by Pfizer--BioNTech and Moderna contain lipid (fat) entrapped mRNA encoding the spike protein from SARS-CoV-2 the causative agent of COVID-19 [3].

mRNA

All life is composed of DNA, RNA, and proteins (among other substances) [4]. DNA stores your genetic information and tells the cells of your body how to function properly. DNA has multiple genes, and it sends the messages of each gene for protein synthesis through mRNA, which reaches the cytoplasm and guides the ribosomal proteins to synthesize proteins. The proteins along with other biomolecules assemble into cells, cells group together into tissue, tissue to organs, until your entire body is built (Figure 1). Scientists can now create DNA and RNA outside of a cell and put together whatever messages they would like. This process is useful medically for replacing proteins that are missing in some sick people or to help manufacture vaccines.

mRNA vaccine

Typically, mRNA in your body is quickly made into protein and then broken down relatively fast while the protein sticks around to carry out additional functions. RNA is vulnerable to break down by proteins called RNases [5] and has a hard time getting into cells from outside. Foreign RNA inside cells triggers your immune response through its produced protein and is removed from cells quickly [6]. New technology is allowing RNA to be made outside of the cell and then returned to the cell to make protein based on what the new RNA instructs. This new RNA is made in such a way that they last a little longer than normal RNA and look more like natural RNA, preventing it from being broken down or recognized by the immune system [7] . Further, the RNA is protected by being encased in nanomaterials such as lipids which both protects the RNA and helps it get into cells [8]. This new RNA can make viral proteins which gets recognized by the immune system and produces the specific immunity.

Food and Drug Administration (FDA) approval process

Any new technology for use in humans undergoes rigorous testing before it is given to large numbers of people to ensure it is both safe and effective. The FDA regulates this process in the United States [9] with the following basic process; **Research and development-** scientists in the lab test whether their ideas for a vaccine work in laboratory or animal experiments. **Preclinical testing-** additional laboratory research and testing in animals to determine how the vaccine works and if it is likely to be safe and work well in humans. **Investigational New Drug Application** is filed with the FDA and scientists carefully study the preclinical data to ensure safety and efficacy. **Phase I clinical trial-**20–100 volunteers are given the vaccine to focus on safety and whether any adverse reactions occur. **Phase 2 clinical trial**- various dosages are tested on hundreds of people with varying health statuses and from different demographic groups, in randomized-controlled studies (some get the vaccine, some don't). **Phase 3 clinical trial**- the vaccine is given to thousands of people with studies looking at the effectiveness, and further safety evaluations occur. **FDA approval-** when enough testing has been completed, and the vaccine or drug has been shown to be both safe and effective, the product gains FDA approval for use in a specific treatment.

Different types of mRNA vaccines yet to come

Since mRNA vaccines have been shown to be safe and effective against COVID-19, we can expect to see more vaccines utilizing this technology in future human and animal vaccines. Further study on how long the immune response from these vaccines lasts will be critical to improving their usage and efficacy. Each new mRNA vaccine will go through the strict process of FDA approval before being released for public use.

Action items

It is a natural response for humans to be concerned about new technologies and vaccination in general. Overcoming these concerns and being vaccinated, if eligible, is critical to stopping the spread of certain diseases and to prevent you from getting seriously sick. If you have vaccine doubts the best course of action is to talk with your primary care physician. Doctors can discuss which vaccinations you should have and answer any concerns you may have with sound medical advice. If you have further questions, you can contact the Centers for Disease Control and Prevention (CDC) information number at (800) CDC-INFO or (800) 232-4636.

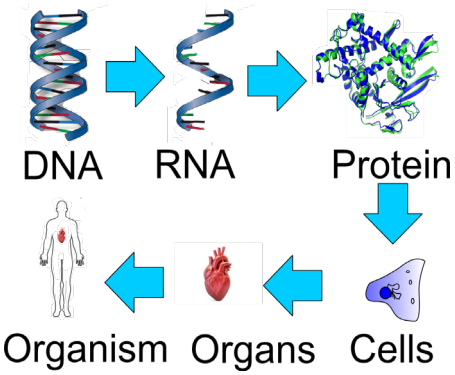

Figure 1 DNA and RNA as building blocks of life.

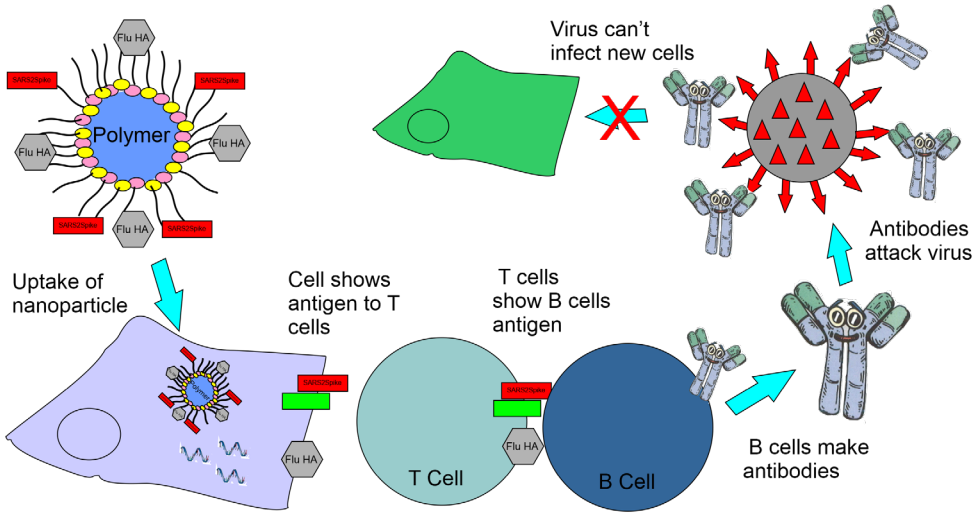

Figure 2. Nanoparticle vaccine function. Nanoparticle containing mRNA is taken up by host immune cells. Cells make the protein encoded by the RNA. The proteins are recognized by the host immune system. The activated host immune system makes specific antibodies and T cells to fight against the pathogen.

Citations:

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