With the ever-present threat of pandemics caused by emerging infectious diseases, the ability to quickly and effectively design, produce and administer novel vaccines is crucial. Inovio Pharmaceuticals is committed to revolutionising healthcare across the globe using next-generation vaccine development approaches and novel delivery methods. Whilst most current vaccines are given intramuscularly, there may be alternative target tissues equally able to invoke a strong immune response. Vaccines have already been developed for many common diseases, but despite this, there are many complex and devastating diseases with no available vaccines.

**THE NEXT GENERATION OF VACCINES**

DNA vaccines are different to conventional vaccines which can be made from the whole virus or bacteria itself, e.g., a whole inactivated virus vaccine. These are often referred to as first-generation vaccines. Other conventional vaccine approaches commonly involve a subunit of the pathogen-containing specific protein antigens, which alter the cells themselves. Next-generation vaccines consist of DNA which codes for specific proteins from a pathogen. DNA enters the cells and the cells use their own replication machinery to synthesise the pathogen proteins. Because these proteins are recognised as foreign, when they are processed by the host cells and displayed on their surface, the immune system is alerted, which then triggers immune responses. The DNA must be delivered in a vector, but no immune response to the vector itself, only the foreign proteins processed and displayed by the cells. Due to the inherent stability of DNA vaccines and Inovio’s optimised DNA storage formulation, they do not require storage at low temperatures. This is a major advantage over many current vaccines, as this issue often limits the distribution and use of vaccines in developing countries.

Inovio’s DNA vaccine platform can overcome many of the issues surrounding conventional vaccine platforms. These include the ability to induce robust immune responses, the flexibility to combine multiple antigens in a single vial, rapid design and production and improved storage stability. In other words, they do not necessarily need to be kept cold and can instead be stored at room temperature. The advantage of this is that specialised equipment is not required to store the vaccine, making it more accessible to clinicians and patients.

**EXISTING DNA VACCINES**

Although there are currently no approved DNA vaccines for human use, three DNA-based vaccines are approved DNA vaccines for human use. Inovio and their collaborators GeneOne have also been involved in the development of a vaccine against Zika virus and have tested this vaccine in a Phase I safety and immunogenicity trial. The vaccine was administered intradermally (into the skin), followed by an enhancing delivery process called electroporation (EP) which significantly increases the uptake of the DNA into the cells. The vaccine administration was well tolerated and 100% immunogenic.

Remarkably, from receipt of the viral vector to dosing a patient in the clinic, the Inovio trial was able to accomplish this in six months. This is an unprecedented timeline for vaccine development which speaks to the applicability of Inovio’s platform for meeting the challenges of emerging infectious diseases. Further work is still needed to assess the efficacy of the vaccine to protect humans against the virus, but it provides a promising solution to a disease which has devastating effects.

Vaccination against cancer is also getting closer to becoming a reality.

In the case of anti-cancer vaccines, the DNA constructs will code for one or more tumour associated antigens with the aim of being to elicit a tumour-specific immune response.

**ENHANCING VACCINE DELIVERY TECHNOLOGY**

Development of a next-generation vaccine requires a next-generation delivery approach to administer the vaccine. One of the many advantages of using DNA vaccines is that they can be designed and manufactured extremely quickly, in a matter of weeks compared to the several years it may take to develop and create the same solution using a conventional vaccine approach. This gives Inovio real-time tools to combat emerging diseases and pandemics.

The Inovio CELLECTRA® delivery device platform represents
alternative vaccine delivery tissue targets. The technology which the CELLECTRA® platform is based on, is called electroporation (EP). Using this technology, Inovio has so far conducted multiple clinical trials with over 1,700 subjects and administered approximately 6,000 doses of vaccine using electroporation.

Electroporation was first used in 1982 and is the process of using an electrical current to make the cell membrane temporarily more permeable, allowing better uptake of a vaccine. An attractive target for vaccine delivery is the skin as it is easily accessed and easily monitored. Furthermore, it has many resident antigen-presenting cells, crucial for eliciting robust and long-lasting immune responses.

Figure 4: Histological analysis reveals reporter gene expression localised to cells in the epidermis. Histological analysis of GFP and RFP expression after ID plasmid administration followed by SEP in guinea pig skin. A). GFP treated skin biopsies were removed, cryosectioned, stained with an antibody against K10 (a keratinocyte cell surface marker), Hoechst stained four hours post treatment, cryosectioned, DAPI stained and visualised using fluorescence microscopy (20x and 40x). An injection only control (no EP) is also shown. B). RFP treated skin biopsies were removed, cryosectioned, stained with an antibody against K10 (a keratinocyte cell surface marker), Hoechst stained and visualised using confocal microscopy. The figure was previously published in Vaccines, “Eliciting the Kinetics of Expression and Immune Cell Infiltration Resulting from Plasmid-DNA Delivery囿erved by Surface Dermal Electroporation”, 2013, Volume 1, Issue 3, 384-397; doi:10.3390/vaccines10318182 and is under the Creative Commons licence CC BY-NC-SA 3.0.

Resulting from Plasmid Gene Delivery Enhanced by Surface Dermal Electroporation

Genetic-based vaccines will revolutionise healthcare by presenting potential solutions to global health issues, such as cancer, HIV and flu.

The naked delivery of nucleic acid vaccines, in this case, DNA vaccines, is notoriously inefficient. Previous studies have shown that this often results in a weak or non-existent immune response to the vaccine. Therefore, EP offers an attractive enhancement to DNA vaccine administration. EP has been used extensively in the clinic targeting primarily either the muscle or the skin as target tissues. Inovio’s CIN EP-enhanced DNA vaccine Phase II trial was the first to demonstrate clinical efficacy.

As it has a local effect, EP can also be used to improve delivery to a target tissue of interest. Most importantly, DNA vaccines administered with EP can generate both T-cell and antibody responses.

INOVIO’S GOAL

Genetic-based vaccines will revolutionise healthcare by presenting potential solutions to global health issues, such as cancer, HIV and flu, and in addition to this, the preclinical development of a DNA-based vaccine delivery platform would make the technology suitable for mass vaccinations.

Inovio’s future aim is ultimately to use immunisation with DNA vaccines to protect against emerging infectious diseases in both developed populations and low and middle-income populations who may not currently have access to vaccines, whether this is for climatic, economic or technological reasons.

Figure 5: Efficient plasmid transfection of Guinea pig skin in vivo electroporation.

Guinea pig skin images 24 hours after treatment with GFP reporter plasmid by intradermal injection only (top panel), or intradermal injection with electroporation (lower panel).

References

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