In vivo imaging of antigen expression after DNA vaccination

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We are protected from infections by our immune system, which inactivates the invading bacteria or virus. The body recognizes the invader as being non-self through the proteins on its cell surface (antigens) and produces antibodies that bind to and inactivate it (antibody response) and/or cells that engulf and destroy the invader (cellular response).

Our immune system remembers agents against which a response has been raised, and so can respond more rapidly when the same agent invades in the future. This discovery was a breakthrough in medical science that allows people to be given long-term protection against a range of contagious diseases by stimulating long-lived antibody responses through vaccination.

Vaccination is achieved by introducing either specific antigens or live infectious agents that have been modified (attenuated) so that they are no longer able to cause disease, which prime the immune system to produce antibodies against that particular agent.

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Vaccination: the unmet need

Although there has been great success in vaccinations against diseases caused by bacteria and viruses that can be eliminated by an antibody immune response, e.g., measles, flu; effective vaccinations against disease-causing agents that must be removed by a cellular immune response, e.g., tuberculosis, malaria, have not yet been produced.

Since such diseases still cause substantial morbidity and mortality, there has been extensive research into understanding the mechanisms involved in generating long-lived cellular immune responses. This research has culminated in the development of a novel form of vaccination—DNA vaccination—that can engender both antibody and cellular immune responses.

DNA vaccination

Traditionally, vaccination has involved introducing the antigen against which an immune response is sought directly into the body. With DNA vaccination, the DNA sequence encoding the antigen (or antigens) of interest is introduced into the body within a plasmid and the antigens are then produced in situ[1]. The plasmid vector is taken up into cells where the protein encoded by the introduced DNA is produced. As the foreign protein begins to be degraded, the resultant peptides elicit a cellular immune response.

DNA vaccines have the additional advantages of being easy to manufacture so they can be produced quickly in response to changing needs, e.g., strain mutation, and be stored without the need for refrigeration[1].

Although pre-clinical animal studies of DNA vaccination proved highly successful, the same efficacy has not been consistently achieved in humans[2]. It has been suggested that poor antigen expression may play a role in limiting the efficacy of DNA vaccination in clinical trials. In order to address this theory, small animal whole body in vivo imaging has been used to monitor the level of antigen production after vaccination with the corresponding gene.

In vivo imaging of expression from transfected DNA

A recent study[3], the first of its kind, introduced plasmids containing DNA encoding a fluorescent protein (tdTomato, mCherry, Katushka, tdKatushka2) into newly born mice using intramuscular, subcutaneous or tattoo delivery. The fluorescent proteins were then detected through whole-body imaging using the In-Vivo MS FX Pro (Bruker Biospin).

Intramuscular delivery was shown to result in the highest level of protein expression; no signal was detectable in any animal after tattoo delivery. Although all the signals were weak, the strongest signal was obtained with tdTomato.

The mice also underwent DNA vaccination (intramuscular, subcutaneous and tattooing routes) against an influenza virus and subsequent exposure to the same influenza virus. Since the mice were very young, it was known that they had not been exposed to the virus previously and so could not have developed any acquired immunity. Weight loss among the non-immunized mice (an indication of a mouse being unwell) and the presence of cellular and antibody immune responses in the immunized, but not the non-immunized mice, confirmed that in all cases DNA immunization was successful.

Interestingly, the type of immune response elicited differed according to the route of immunization delivery. Immunization by tattooing and intramuscular immunization stimulated an antibody immune response, whereas a strong cellular response was observed after subcutaneous immunization.

Furthermore, immunity had been conferred despite low levels of protein expression being observed. Tattoo delivery elicited a strong antibody response although no protein expression was detected after vaccination by this route. This indicates that the ability of a DNA vaccine to induce an immune response is not solely dependent on the level of antigen produced; the degree of immunogenicity of the expressed antigen must also play a role. Consequently, in

vivo whole animal imaging of fluorescent proteins does not provide a tool for accurately predicting the level of immune response achieved through DNA vaccination. Further research is required to determine how to make effective DNA vaccines for clinical use.

References

1. McDonnel MW and Askari FK, The Emerging Role of DNA Vaccines. Medscape accessed July 2015. Available at http://www.medscape.com/viewarticle/715527_8
2. Saade F and Petrovski N. Technologies for enhanced efficacy of DNA vaccines. Expert Rev Vaccines. 2012;11(2):189–209. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3293989/
3. Kinnear E, et al. A Comparison of Red Fluorescent Proteins to Model DNA Vaccine Expression by Whole Animal In Vivo Imaging. PLoS ONE 2015;10(6). Available at: http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0130375

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