Recent Advances in Vaccine Technologies

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KEYWORDS

• Vaccines • Inactivated • Attenuated • Subunit • Peptide • Vector • DIVA • Nucleic acid

KEY POINTS

- Traditional vaccine technologies are based on killed/inactivated and live/attenuated approaches.
- Novel killed/inactivated vaccination strategies include antigen subunit, protein, and peptide vaccines.
- Novel live/attenuated vaccination strategies include modified live, marker/differentiating infected from vaccinated animals, vector, and nucleic acid vaccines.
- New vaccine technologies often find their first commercial application within veterinary medicine.

INTRODUCTION

Most vaccines that are available today rely on either inactivated (killed) or live attenuated (weakened) technologies. Such approaches have been successfully used to address many of the important veterinary and human diseases. However, both techniques have their limitations and associated potential problems.

Inactivated vaccines must be totally innocuous and noninfective. Problems with field outbreaks in the past have occasionally been attributed to incomplete inactivation. Such problems should not, and would not, exist if more reliable inactivants, inactivation procedures, and innocuity testing were used within the manufacturing process. Furthermore, because the manufacture of such vaccines involves the culture of large amounts of the infectious agent, there is a potential hazard to the personnel involved and the environment. Vaccines grown in eggs, tissue culture, or simply culture medium may contain unwanted "foreign" proteins, which could affect immunogenicity or be potentially allergenic/reactogenic. Finally, inactivated vaccines have certain limitations on their mode of presentation and as a consequence the nature of the immune response they can elicit. The response to vaccination may be limited

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and of short duration with adjuvants or immunostimulants required to enhance their overall immunogenicity/efficacy.

Attenuated vaccines must be precisely controlled and characterized in order to provide the required level of protective immunity without causing significant disease symptoms within the host animal. There is also a low risk that the attenuated antigen may revert to full virulence, and careful reversion to virulence safety studies must be carried out. Furthermore, in culturing the vaccine antigen, it is possible that other infectious agents may be introduced that could themselves lead to undesired side effects when the vaccine is used in the field.

Because of these and other reasons, including protective efficacy, economy of manufacture, and whether the infectious agent can be produced in vitro, scientists have turned their attention more and more to the new vaccine technologies. These vaccine technologies include split-product, subunit, isolated protein, peptide, marker vaccine, live vector, and nucleic acid approaches.

KILLED VACCINE STRATEGIES

Natural Split-Product and Subunit Vaccines

By identifying suitable subunit, protein, or peptide antigens as vaccine candidates, natural split-product and subunit vaccines must be delivered to the target animals in order to elicit the desired protective immune response. The simplest and most basic form of subunit vaccine is one in which the infectious agent has simply been disassembled or broken up into its component parts. Some current influenza vaccines, known as split-product vaccines, consist of formalin inactivated virus that has been treated in order to lyse the viral envelope and release both the external envelope proteins and the internal nuclear and matrix proteins. A further refinement has been to use the purified envelope glycoproteins hemagglutinin and neuraminidase alone in a subunit vaccine in order to reduce the risk of any toxic side effects. Unfortunately, split-product and subunit vaccines for influenza have tended to have reduced immunogenicity when compared with whole virus products. Attempts to improve this situation have concentrated on modifying antigen presentation by delivering the viral glycoproteins within lipid vesicles, which can be composed of either virus-derived lipids (virosomes) or added nonviral lipids (liposomes).[1] In this way, artificial "empty" viruses can be created that can display improved immunogenicity. Polymeric preparations of isolated proteins in the form of micelles are also more immunogenic than the protein monomer.[2] In recent times, such multimeric presentation systems are often collectively referred to as virus-like particles or VLPs.[3] A development that offers both polymeric presentation and built-in adjuvant activity, for further enhancing immunogenicity, is the immunostimulating complex or ISCOM.[4] The first successful commercial veterinary application of this technology was for equine influenza,[5] and these vaccines have been studied for mucosal delivery.[6] Split product and cell culture subunit vaccines are also currently marketed for feline leukemia virus (FeLV) disease. Although each has been shown to be immunogenic, their overall degree of efficacy particularly in the face of an oronasal challenge has been inconsistent. However, once again by presenting the surface glycoprotein gp70/85 of FeLV in an ISCOM, neutralizing antibodies were elicited in all vaccinated cats, and complete protection was demonstrated against a subsequent oronasal challenge.[7]

As well as these new generations of veterinary viral subunit vaccines, many current bacterial vaccines are based on toxin or pilus subunits. Although antitoxin antibodies will neutralize the harmful effects of the bacterial infection, antipilus antibodies will block colonization by preventing attachment. Good examples are the F4 (K88),