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Popular Article

Application of transgenic plants in the production of vaccines and therapeutic antibodies in veterinary: an overview

Urfeya Mirza[1*], Shahnaz Anjum[2], Uiase Bin Farooq[3]
[1]Department of Veterinary Surgery and Radiology, Khalsa College of Veterinary and Animal Sciences, Amritsar
[2]Department of Botany, Lovely Professional University, Jalandhar, Phagwara, Punjab
[3]Department of Veterinary Surgery and Radiology, MR College of Veterinary and Animal Sciences, Haryana

Abstract

The production of vaccines and therapeutic antibodies using transgenic plants in veterinary medicine is a novel concept. Plants have a number of advantages in terms of production size and cost, as well as product protection, storage, and distribution and therefore can replace active vaccination with live virulent or attenuated vaccines with various disadvantages such as low immunogenicity, high manufacturing costs, antigenic heterogeneity between organisms, and the possibility of genetic material transfer to wild-type strains. Plants can act as cost-effective methods to prevent and control infectious animal diseases. In this article, the production of vaccines and therapeutic antibodies in transgenic plants for veterinary applications is focused upon.

Keywords: Antibiotic; Drugs; Immunity; Plant; Vaccine

Introduction

Infectious diseases are becoming more prevalent across the world. It is estimated that 58 percent of the 1,407 known human pathogen species are zoonotic, indicating they infect multiple hosts. Emerging and re-emerging infectious diseases are most likely caused by zoonotic pathogens (Woolhouse and Gowtage-Sequeria, 2005). As a result, providing strategies for animal welfare has an effect on human health. The rapid rise in antibiotic resistance around the world, as well as the possibility of residues in meat, milk, eggs, and the environment, has prompted the creation of alternative products for the treatment of infectious diseases. Antibiotics are being used for prophylaxis and growth promotion in animals, and efforts are being made to reduce the amount of antibiotics used.

Vaccinology in veterinary medicine covers a broader range of issues. Creation of cost-effective methods to prevent and control infectious animal diseases, consideration of animal health, and an emphasis on lowering the production costs of animals used as food are among them (Shams, 2005). Furthermore, mass vaccination campaigns have greatly reduced the use of veterinary medications, including antibiotics. Vaccines have had a positive effect on the environment by removing chemical contaminants from items like milk, eggs, and meat. Illness-related production losses can be avoided. Active vaccination with live virulent or attenuated vaccines is common, but it has disadvantages such as low immunogenicity, high manufacturing costs, antigenic heterogeneity between organisms, and the possibility of genetic material transfer to wild-type strains. Vaccination is still not a viable choice for post-weaned mammals, as well as animals with a limited lifespan, such as broilers. Low-cost systems and low-cost implementation strategies are also needed for the development of vaccines for veterinary use. As a result, an ideal expression mechanism for recombinant antibodies and antigens should be genetically modifiable, intrinsically stable, and cost-effective. It should be able to provide functional proteins with high antibody affinity, neutralization, and/or vaccination ability (Fischer and Schillberg, 2004). During the last 15 years, systems for producing antigens and antibodies in transgenic plants have been under development (Hood *et al.*, 2002; Koprowski, 2005; Ma *et al.*, 2003, 2005b). Plants have a number of advantages in terms of production size and cost, as well as product protection, storage, and distribution (Ma *et al.*, 2005a). In this article the production of vaccines and therapeutic antibodies in transgenic plants for veterinary applications is focused upon.

Plant-derived vaccines for veterinary purposes

Vaccine production and advancement are effective methods for combating infectious diseases in both wild and domesticated animals. To induce immunity, current strategies include intact or inactivated pathogen strains, as well as subunit vaccines manufactured commercially in bacteria, yeast, or mammalian cell cultures. Engineered plant viruses and transgenic plants have been used to create a number of veterinary candidate vaccines. There are summaries of plant-based vaccines for both veterinary and human medicine (Joensuu, 2006; Streatfield and Howard, 2003). The development of quick, effective, and safe systems for the generation of transgenic plants is a key prerequisite for vaccine production *in planta*. After the first study of active plant cell transformation (Fraley *et al.*, 1983), various plant expression systems have been established for molecular farming (Fischer and Schillberg, 2004). Four different methods are now generally used for the production of recombinant proteins (Horn *et al.*, 2004): Generation of stable nuclear transgenic plants, transplastomic plants, transient expression using a plant virus and transient expression via Agrobacterium infiltration. Another option is to grow plants that release the vaccine into a hydroponic medium as a part of the root exudates. However, due to the high dilution of the vaccines and the technological requirements for plant cultivation, such production systems are impractical. Model plants including Arabidopsis thaliana and tobacco are excellent candidates for preliminary research into generating stable transgenic plants expressing desired proteins. Veterinary vaccinations have also been made from edible leaves, such as spinach, alfalfa, and white clover; tubers/fruits, such as potato and tomato; and grains, such as maize and barley. Oral delivery provides convenience and defense against pathogens communicating with host mucosal surfaces by inducing mucosal immunity (Streatfield, 2005). Animal immunization by injection, on the other hand, almost always results in a systemic immune response. Plant viruses have been used to develop transient expression methods, which result in high levels of protein accumulation in the host plants due to the rapid amplification of an infectious plant viral genome (Pe´rez Filgueira *et al.*, 2003). Numerous veterinary candidate vaccines, primarily against virus infections, have been expressed in plants, in addition to the examples mentioned earlier. Examples are Foot-and-Mouth-Disease Virus (Dus Santos *et al.*, 2005), Newcastle Disease Virus (Berinstein *et al.*, 2005), Rinderpest Virus (Satyavathi *et al.*, 2003) and Rotavirus (Birch-Machin *et al.*, 2004). Plant systems have developed complete antigenic proteins as well as peptides representing major antigenic determinants.

Since the costs of development and application must be minimal, the expression levels of veterinary vaccines in plants are critical for the economic performance of such strategies. Low implementation costs for plant-based vaccines were achieved either through the oral delivery of crude plant material through "edible vaccines" or through the production of simple purification methods. There are only few clues for the purification of plant virus particles expressing antigenic epitopes using centrifugation (Marconi *et al.*, 2006) and of veterinary subunit vaccines using either affinity chromatography (Pe´rez Filgueira *et al.*, 2003) or anion exchange chromatography (Ashraf *et al.*, 2005) on a small scale. The majority of pathogens penetrate or colonize their hosts through the mucosal surfaces of the gastrointestinal, respiratory, or genital tracts. A mucosal vaccine that induces the production of serum (IgG) and mucosal antibodies (IgA) is needed to combat these infectors. Oral delivery of transgenic peanut leaves expressing the Rinderpest Virus hemagglutinin protein (H) to mice was used to accomplish this (Khandelwal *et al.*, 2003). Antibody levels in serum, colostrum, and milk of immunized gilts increase after a corn-based vaccine against Porcine Transmissible Gastroenteritis Virus (PTGEV), meaning that immunity can be passively passed to suckling piglets

(Lamphear *et al.*, 2004). Despite the fact that the expression of veterinary vaccine candidates in various plant species has been well studied and their immunogenicity assessed, plant-derived veterinary vaccines still face challenges. Other than barley (Joensuu *et al.*, 2006a), maize (Guerrero-Andrade *et al.*, 2006), white clover (Lee *et al.*, 2003) and alfalfa (Wigdorovitz *et al.*, 2004), which constitute the main components of animal feed, model plants are routinely used as expression systems; as a result, crop plants must be further grown for the development of veterinary vaccines. If plant-derived vaccines are to be administered by injection, purification technology is needed, and the production of low-cost purification methods is critical for commercial success.

Therapeutic antibodies for veterinary use from transgenic plants

Passive immunization with recombinant antibodies is seen as one of the most promising alternatives to fight infectious diseases, given the spread of antibiotic resistance and the emergence of new pathogens (Casadevall, 1998). Recombinant antibodies are yet to be successfully introduced into the animal health industry due to their high cost of goods. Plant-based processing offers a cost-effective solution to these issues. Plants also have a suitable mechanism for the oral delivery of recombinant biomolecules as part of a balanced diet. Infrastructure and downstream manufacturing costs, as well as major output losses, can thus be avoided. Despite advances in the development of antibodies in plants for human health, their use in veterinary medicine is small, with most potential product developers concentrating on vaccines. However, there have been some recent promising advances in the area of passive immunization. The focus has been on the creation and development of oral products for use in production animals for the prevention and/or treatment of some of the most common commercially important infectious diseases. The aim of most studies has been to administer the antibody molecule orally with no or minimal purification, making the product consistent with existing animal production cost structures. One big stumbling block is the heterologous protein's low concentration in plant tissue. Although attempts to resolve this limitation are being made in the literature, issues such as final product formulation and effectiveness, as well as long-term stability under farming conditions, have received little attention thus far.

Conclusions

The production of vaccines and therapeutic antibodies using transgenic plants in veterinary medicine is now catalyzed by a high demand for new, specific products, spurred by the ban of persistent drugs, particularly antibiotics, and this is where molecular pharming can provide better solutions. Any veterinary product's economic value is directly improved by increasing expression levels, especially in seeds.

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