Review Article

An Overview of Future Development Methods of Infectious Bronchitis Vaccines

Najmeh Motamed*

Department of Poultry Diseases Vaccine Research and Production, Razi Vaccine and Serum Research Institute, Agricultural Research, Education and Extension, Karaj, Iran.

Use your device to scan and read the article online

How to Cite This Article Motamed, N. (2024). An Overview of Future Development Methods of Infectious Bronchitis Vaccines. *Iranian Journal of Veterinary Medicine*, *18*(1), 1-12. http://dx.doi.org/10.32598/ijvm.18.1.1005406

http://dx.doi.org/10.32598/ijvm.18.1.1005406

ABSTRACT

Vaccines are major disease-controlling tools in human and animal practices. Vaccination controlled or even eradicated a long list of diseases worldwide. Classic viral vaccines are usually composed of live or inactivated whole viruses and have been produced for many years. However, they are unsuccessful, especially in persistent infections, fast-evolving viruses, complex and compound antigens, and emerging agents. Novel vaccine development technologies such as DNA, protein, or viral vector vaccines have revolutionized vaccine development and opened a new horizon for study and research in vaccine research and production vision. Newly-developed vaccines, or even most traditional ones, are based on new technologies, especially in human diseases where cost and complications in production can be ignored. However, in animal health, especially for commercial poultry production, the cost of development, simplicity, and mass application of large-scale production cannot be overlooked. In recent years, the significance of producing novel vaccines has been highlighted in parallel with technological advancement, especially with emerging novel variants of infectious bronchitis viruses—serious poultry pathogens for years. In this review, we will introduce some studies on novel vaccine development techniques and investigate the results of those vaccines in the protection of chickens and their clinical outcomes.

Keywords: Infectious bronchitis, Novel techniques, Variant, Viral vector vaccines

Article info:
Received: 28 May 2023
Accepted: 17 Jul 2023
Publish: 01 Jan 2024

*** Corresponding Author:**
Najmeh Motamed, Assistant professor.
Address: *Department of Poultry Diseases Vaccine Research and Production, Razi Vaccine and Serum Research Institute, Agricultural Research, Education and Extension, Karaj, Iran.*
Phone: *+98 (26) 34540500*
E-mail: *n.motamed@rvsri.ac.ir*

Introduction

Infectious bronchitis is a contagious viral disease with a high economic impact on the poultry industry. Schalk and Hawn first detected the disease in North Dakota in 1931. Since then, the disease has been distributed to different continents worldwide (Hajijafari Anaraki et al., 2022). The virus mainly affects the respiratory, kidney, and reproductive systems. Economic losses result from the high morbidity of the virus: Weight loss, condemnation at slaughterhouses, decreased egg production, and lower inner and outer egg quality. Nowadays, the strategies for disease control comprise a combination of good biosecurity and, most importantly, vast vaccination in broiler and breeder flocks (De Wit et al., 2010; Cavanagh, 2005).

Infectious bronchitis (IB) is caused by a single-stranded enveloped RNA virus belonging to the *Igacovirus* subgenus of the *Gammacoronavirus* genus and the *Coronaviridae* family confined to the avian population. The IB virus genome, the largest avian RNA virus, is 27 to 32 kb long. It encodes 4 structural proteins: Spike (S), matrix (M), nucleocapsid (N), and envelope (E). They are interspaced by 3 and 5 accessory genes and at least 15 nonstructural proteins encoded by the first two-thirds of the genome. S and N proteins were proposed to be immunomodulatory proteins in the virus.

The most important virus protein is the glycoprotein spike projecting from the virus's surface. It is responsible for bird immune system reactions and neutralizing antibody production in chickens. Infectious bursal disease (IBV) S-protein comprises 3400 nucleotides (Beheshtian et al., 2020). Furin or its related enzymes cleave S protein into S1 520 at the amino-terminal and S2 625 amino acids at the carboxyl-terminal in the Golgi complex of the host cell. Typically, S1-glycoprotein plays a significant role in host cell receptor binding and membrane fusion via cell-to-cell and virus-to-cell interactions, and S2 contributes to the fusion mechanism (Koch et al., 1990). A complication arises when the protein shows variability. It has at least 3 hypervariable regions at positions 24–61, 132–149, and 291–398 amino-acid residues. They continuously evolve into new variants different from classic strains, so natural or vaccinal protection against them cannot confront variant viruses (Lee et al., 2003). N protein attaches to the genome and causes the helical capsid complex.

Essential proteins in immunomodulation following virus infection or vaccination

As previously said, S1 is hypervariable. Unfortunately, sequence comparisons of variants with vaccines fail to identify the site of the gene responsible for protection induction. The highly conformational nature of S1 complicates the antigenic characterization of S1 and whether cell-mediated immune or humoral responses are the main protection mechanisms. Researchers have tried to map antibody-inducing sites and cell-mediated immune (CMI) response factors in S1 protein (Cavanagh et al., 1992; Wei et al., 2014; Ignjatovic et al., 2006; Ignjatovic & Galli 1995; Ignjatovic & Galli 1994). To date, 5 antigenic sites, which all were conformation dependent and responsible for virus neutralizing antibody production, have been mapped within the hypervariable region (HVR) of S1 at positions 24–61 and 132–149, as well as outside the hypervariable region at 291–398 (Kant et al., 1992; Kusters et al., 1989; Moore et al., 1997). Because of this, monoclonal antibodies are the primary tool used in antigenic epitope recognition on S1.

The S2 also induces antibodies to cross-react in ELISA and cell-mediated responses but not protective responses. The two antigenic sites in the N terminus of the S2 between 546-577 amino acids are reported to be immunodominant and cause cross-reactive antibodies (Kusters et al., 1989).

The N protein induces cross-reactive ELISA antibodies and CMI (Ignjatovic & Galli, 1994). However, it is not involved in disease protection. The carboxy-terminal portions of N protein has B cells epitopes; a region between 78–94 amino acid residues was mapped, which induces a T cell response in addition to protection (Jayaram et al., 2005). N protein functionally binds with the genomic RNA to form a helical ribonucleoprotein complex, thus aiding transcription, replication, translation, and packaging of the viral genome during replication (Jayaram et al., 2005).

RNA virus is dangerous because of its fast and continuous evolutions. Two critical phenomena in shaping the genome of coronaviruses are mutation and recombination (Domingo & Holland, 1997). It is difficult to define how the IBV genome evolves; however, three major theories have been hypothesized. First, the lack of proofreading in RNA polymerase may lead to mistakes in the genome, which, in turn, causes mutations (deletions, insertions, or point mutations of nucleotides). Second, multiple serotype infections or using different live attenuated vaccines leads to recombination and favors the

emergence of new variants (Kusters et al., 1989). Mutations in the hypervariable region of S1 affect its subpopulation and make new viruses of different pathogenicity and virulence. In this regard, quasi-species viruses are generated with a mixture of multiple genetic mutants of the same strains (Nix et al., 2000). The most common regions in the IBV genome for recombination are encoding regions of nsp 2, 3, and 16, plus the glycoprotein spike (Thor et al., 2011). Third, other suggested factors are the presence of immunosuppressive agents like Marek's disease, infectious bursal disease, and chicken anemia virus, which affect the evolutionary dynamic of the IBV (Bande et al., 2015).

Control and vaccination strategies

Several IBV strains and variants have been detected and classified by serotype and genotype. Some have limited geographical distribution (Italy 02; variant 2), and some are globally distributed, including M41, QX, and so on (Valastro et al., 2016). As mentioned, IBV is currently controlled by vaccination with live-attenuated and inactivated vaccines (Motamed & Bashashati, 2022, Motamed et al., 2021). Vaccination programs in one geographical area differ from other sites because vaccines typically induce restricted cross-protection between strains (De Wit et al., 2010). Live-attenuated vaccines are administered to young chicks through sprays or drinking water. In older ages, breeders and or laying may then be boosted with either live or inactivated vaccines (Sjaak de Wit et al., 2011). The ease of application favors live-attenuated vaccines; however, the risk of reversion to virulence and breakdown limits their application. Although the molecular mechanism of attenuation has not been discovered, it happens only with few consecutive level mutations. Hence, over passaging of the vaccine in the field provides reversion to virulence possibility (Oade et al., 2019).

Live-attenuated vaccines

The infectious bronchitis virus is a pathogen of economic and welfare concern for the poultry industry. Today, the most effective controlling tool is vaccination (Motamed & Bashashati, 2022). Live-attenuated vaccines are generated by serial passage of a virulent isolate in embryonated chicken eggs for at least 80 consecutive passages until attenuation is achieved. The mechanism of the attenuation is unknown (Motamed, 2022). This kind is the most widely-used vaccine with an old production history. In addition to high benefits, it has some disadvantages, such as reversion to virulence. Even with efforts to decrease virulence after more than 80-100 passages, severe outbreaks in the farm may occur. Also, tissue damage results in secondary bacterial infections or pathological disorders, especially in day-old chicks.

Another problem is the interference by maternal-derived antibodies. Finally, co-circulation of the vaccine virus and field viruses may lead to recombination events and the emergence of new variants. To reduce problems associated with vaccine reversion, researchers explored the options of using reverse genetic technology to create a vaccine virus that is potentially pathogenic in the host but capable of replication and inducing an immune response (Zhou et al., 2013). Exploring various virus clones showed that some vaccine strains, such as Ark, could not induce enough protection because of multiple virus subpopulations in a vaccine seed. So, protection did not reach the optimum, and chicks were still susceptible to the disease (Sjaak de Wit et al., 2011). The ability of some ArkDPI-derived vaccine viruses to persist and be selected in vaccinated chick may lead to a high frequency of Ark field viruses (Gholami et al., 2018). So, the persistence of the vaccine virus in the field offers the required materials for recombination with other circulating viruses or mutation, resulting in increased pathogenesis (Ndegwa et al., 2014).

Mutations and recombination contribute to the emergence of new variants following the intensive use of live, often multiple vaccines. Therefore, attempts have been made over recent years to develop new generation vaccines, such as subunit vaccines, to allow the use of a part of protective antigen but to vaccinate against different genotypes in the same vaccine (Ignjatovic et al., 2006).

Inactivated virus vaccines

Inactivated vaccines are used alone or in combination with live ones. Usually, they are administered to laying and breeder flocks at 12-18 weeks of age, and they cannot replicate. So, they do not revert to virulence; however, limitations are present. For example, their administration is difficult and impractical, especially in large settings; they have shorter immune duration with just antibody response and do not produce T cells. Thus, a prime boost with the live-attenuated vaccine is usually needed. Also, the elimination of the whole or parts of the carcass in slaughter because of the reactions in the injection site can happen. Slow release of antigen and long-lasting immunity throughout the laying period are achieved by intramuscular or subcutaneous injection of vaccines that incorporate an adjuvant and IBV that has been inactivated.

Researchers have taken many approaches to designing new vaccines against pathogenic microorganisms. These methods are dictated by the nature of the infection mechanism and pathogen and practical factors about its use (Motamed, 2022).

In light of COVID-19, which is classified in the Coronaviridae family with a fast-evolving nature, researchers have considered new-generation vaccine approaches for confronting viral diseases. We can no longer trust live or inactivated vaccines. We need to think about new methods with more flexibility in manipulation or substitution. We should reach a new vaccine with new emerging strains in a shorter time. The continuous fast pace of vaccine development and quality controls represents a substantial achievement that was impossible previously, strongly demonstrating the utility of modern technology vaccines in new emerging diseases.

Pathogen outbreaks

Considering new outbreaks, a live-attenuated vaccine usually takes 3 to 5 years to get official administration and distribution permission. However, according to studies, an emerged variant may persist not more than 4-5 years in an area. So it could be expected that neither a licensed variant vaccine, which is now a bit different from the predominant variant after 5 years, nor classic vaccines can fight effectively against field viruses. The same thing is expected over protectotype vaccination, which takes a long time and costs to be studied against variants. However, nowadays, protectotypes are considered as most effective vaccination method to make an optimum immune status in a flock (Sjaak De Witt et al., 2011). Over the last years, many reports declared that 793/B-like- and mass-like-based vaccine combination seems to provide broad protection against heterologous (Awad et al., 2015b; Awad et al., 2015a; Habibi et al., 2017) strains, such as Variant 2 and QX (Franzo et al., 2017; Lisowska et al., 2017). So, it is commonly adopted in most regions worldwide (Jordan, 2017). The vaccine industry has to develop rationally live vaccines. Past research has evaluated vaccines including the S glycoprotein as DNA or by viral vectors (Song et al., 1998; Yan et al., 2016; Toro et al., 2014; Zhao et al., 2017a; Shirvani et al., 2018; Ellis et al., 2018). Spike is the primary attachment factor and virus entry, making it a main target in the development of vaccines. Studies have shown it induces virus-neutralizing antibodies (Koch et al., 1990; Kant et al., 1992). Vaccines currently used against SARS-CoV-2 aim to generate neutralizing antibodies by following this method to deliver S protein (Folegatti et al., 2020; Jackson et al., 2020). The vaccine offers a reasonable degree of protection after multiple doses. They cannot stimulate complete protection in mild to moderate clinical disease or infection and replication of the SARS-CoV-2 (Ellis et al., 2018; De Wit et al., 2010). If the industry is going to be ready to respond to the newly-emerged viruses, it will have to develop and set up alternative techniques to ensure efficient reactions in a proper and fast manner

mRNA vaccines

mRNA vaccines have attracted considerable attention recently because they can accelerate vaccine development, improve safety and efficacy, and combat diseases that cannot be prevented by other methods. mRNA is a non-infectious agent. It is non-integrated and degraded by normal cellular processes shortly after injection, reducing the risk of toxicity and long-term side effects. Intracellular antigen expression by mRNA may produce strong T cell responses typically seen with viral vector-based or replication-defective virus-based vaccines (Gebre et al., 2022). Also, mRNA vaccines do not induce vector-specific immunity and counteract preexisting or newly developed vector immunity that can interfere with subsequent vaccinations (Gebre et al., 2022). In late 2020, Moderna and Pfizer launched their new mRNA vaccine against COVID-19. mRNA gene delivery system has numerous applications in cancer, vaccines, and disease. The concept of this method was initially developed in 1990. mRNA is a delivery system that encodes antigens of a specific pathogen in the host. Infected cells translate it, and the immune system recognizes the antigen. To increase stability and ease of entrance, mRNA is usually delivered in a lipid nanoparticle (LNP) without an immune response, allowing multiple LNP-mRNA use. The simple and fast nature of assembling new sequences in mRNA systems in vaccine formulas will promise mRNA vaccine pioneers in the near future (Folegatti et al., 2020).

Two main limiting reasons that hindered the research of novel IBV vaccines are considered. The first factor is cost. Poultry plants have a minimal profit margin, so any extra cost seems weighty. Classic live-attenuated and inactivated vaccines have a few costs per dose. Other standard recombinant vaccines commonly used against poultry pathogens (other than IBV) are still frequently used due to their ease of application and good efficaciousness, even though they are expensive. If a new IBV vaccine can match those specifications, its cost would not be an impediment. The second limiting reason is the method of application. Each vaccine should be applied in mass and compatible on a large scale.

Vaccine development in viral vectors

The recombinant viral-vectored vaccines hold promises for the commercial poultry industry. Adenovirus vector vaccines have also evolved to become promising vaccine platforms. Optimal adenovirus vaccine vector design involves the selection of uncommon vector serotypes. The structural components of Adenovirus (Ad) vectors can be harnessed and modified to enhance tropism, efficient delivery, and optimal antigen expression. Ad vectors can be rapidly developed and produced commercially, and the potency and stability characteristics of the vector support single-shot vaccines that do not require cryopreservation. However, this technology does have limitations. The issue of preexisting immunity or maternally derived immunity interferes with the live vector itself. It reduces the antigen uptake by the antigen-presenting cells and, consequently, the transgene expression and specific immune response.

Developing promoter vectors against multiple pathogens shows their flexibility and promises for current and future vaccine applications.

Vectors replicating or non-replicating viruses

At present, Fowlpox virus, Marek's disease virus, turkeys Herpes virus, Newcastle disease virus, and members of the Retroviridae family have been most extensively used as expression vectors. Genes of antigenic proteins of Newcastle virus, infectious bursal disease virus (IBDV) (Darteil et al., 1995), and infectious laryngotracheitis virus (Vagnozzi et al.; 2012) are inserted into these systems. They induced the appropriate immune reaction in chickens. Someone attempted to insert S1 in these viruses (Toro et al., 2014). They all had a different immune response to the homologous challenge. Still, they did not meet the vaccination requirements against IBV, especially mass application, which is not feasible commercially. Adenoviral vectors have efficient transduction in various cell types, are widely used in COVID-19 vaccine production, and reach into global consumption admissions (Mendonca et al., 2021). Hence, they can easily express inserted antigens accompanied by economic advantages of mass production of Ad-vectored viruses by cell lines in serum-free media and large bioreactors with simple chromatography separation techniques.

The potency of human Ad-vectored vaccines for immunizing chickens was reported by stimulating immune responses in chickens following intramuscular injection (Zeshan et al., 2010). Those adenoviruses are non-replicating, without causing tissue damage and tropism to different dividing and non-dividing cells, allow sustained antigen release with effective immune response, and reduce problems associated with reversion to virulence or mutation. However, a lack of posttranslational modifications, such as protein folding and glycosylation, can alter epitope arrangement and affect immunogenicity or vaccine efficacy. A recombinant adenovirus vaccine containing infectious bronchitis S1-glycoprotein showed a prominent antibody response, conferring 90%–100% protection. Zeshan et al. (2010) conducted a study on developing a human adenovirus-vector IB vaccine for use in ovo; they constructed a recombinant adenovirus expressing the *S1* gene of nephropathogenic IBV (*rAd-S1*) and reported that in ovo vaccination and then an intramuscular inoculation by rAd-S1 led to dramatic augmentation of cellular and humoral responses against homologous challenge, decreasing lesion and clinical signs. In a study, expressing the *N* gene of IBV by a replication-defective human adenovirus was evaluated in SPF chickens using immune response and protective efficiency against challenge. Despite the recognized immunogenic response, the N protein had no proliferative response to IBV in vaccinated chickens without significant protection. Some researchers have designed oral adenovirus vector vaccines to avoid neutralization of vectors by maternally derived or preexisting antibodies. Other advantages are the ease of application and lower handling associated stress, but they had no T cell responses, so complementary studies are needed to stimulate CMI.

A modified baculovirus, the BacMam virus, that mediates expression under the control of the mammalian promoter has emerged as a versatile and safe vector in the development of vaccines. In a study, an improved BacMam virus expressing *S1* of IBV was generated. S1 glycoprotein was displayed on the baculovirus envelope expressed in mammalian cells. The vaccine BV-Dual-S1 has elicited significant humoral and cell-mediated immunity in specific pathogen-free chickens. Protection rates of immunized chickens with BV-Dual-S1 reached 83% compared to 89% inactivated vaccine following the challenge with IBV-M41 (Zhang et al., 2014). Other vectors may replicate in bird bodies and have their specific effects. Shi et al. (2011) showed a recombinant fowlpox virus vaccine expressing *S1-IBV* gene and chicken *INF-y* gene [rFPV-IFN-S1] that enhanced humoral and CMI and protected birds against heterologous and homologous IBV challenge (Shi et al., 2011). In another study, the expression of *S1* gene with interleukin (IL)-18 in a fowlpox virus vector caused a significant increase in humoral immunity, CD4+, and CD8+ activity (Chen et

al., 2017). Metapneumoviruses, Newcastle disease virus, and duck enteritis viruses are other viral backbones for inserting S1 or S2, especially metapneumoviruses which can be massively used and replicate in the respiratory system and may stimulate the head-associated lymphoid tissue to a higher extent and produce high immune response (Falchieri et al., 2013; Li et al., 2016; Toro et al., 2014; Zhao et al., 2017b).

Subunit and peptide-based vaccines

Peptide subunit vaccines contain an antigenic portion of the pathogen, amino acid short segments presented to the immune system. Often, these peptides are synthetic and represent the immunostimulant antigen. *S1*- and *N*-gene epitopes have been used for neutralizing antibodies and cytotoxic T lymphocytes, respectively. Some vaccines showed promising results in protection challenges (Wei et al., 2014; Yang et al., 2009). A novel chimeric infectious bronchitis-Newcastle disease (IB-ND) virus-like particles (VLPs) vaccine constructed from the rF, rS, and M IBV proteins has been designed. It stimulates humoral and cell-mediated immunity, causes 100% protection against clinical signs, and reduces virus shedding (Wu et al., 2019). The immune response following administration of these vaccines must be enhanced by combining with factors such as cytokines adjuvants.

The second limitation is the method of administration, commonly by injection, which is not favored in large rearing settings and usually costs much more than other production methods. They may be expressed in *E. coli*, yeast, insects, etc. (heterologous expression system). Today, most under-investigation vaccines are based on purified subunit antigens or recombinant proteins. The hepatitis B virus (HBV) vaccine is among the best recombinant protein vaccines. A study has reported that synthetic peptide epitopes from S20 to S255 react well with polyclonal antibodies, demonstrating the potential use for poly-topic IB vaccines (Wang et al., 1995). Some researchers have focused on developing multi-epitope peptide vaccines against various IBV genotypes. Yang et al. (2009) demonstrated that an IBV multi-epitope vaccine based on *S1*- and *N-protein* genes can cause remarkable cell-mediated and humoral immune responses. The *Lactococcus lactis* bacterial system could deliver peptide IBV vaccines orally and with mucosal immune response induction (Cao et al., 2012; Cao et al., 2013).

Plasmid DNA vaccines

DNA vaccine does not involve a live vector and uses plasmids to express the DNA of the immunogenic portion of the pathogen genome. No licensed DNA vaccine for poultry use is available yet, primarily because of the administration route, which is injection. This problem can be overcome by oral or in ovo administration. The nanoparticle delivery system may protect the DNA from enzyme degradation and enhance mucosal responses. As DNA vaccines can be administrated in the presence of maternally derived antibodies, they could overcome poultry challenges related to vaccination at an early age. Other advantages are the ability to induce humoral and cell-mediated immunity, possible expression of multiple epitopes, safety, and lower cost production, especially compared with peptide vaccines. Short production time is a valuable tool for confronting emergencies. They can be combined with adjuvants and cytokines (Zuo et al., 2021; Yang et al., 2009).

Zuo et al. (2021) designed and developed a DNA vaccine based on Spike protein with consecutive nucleotide sequences. After two times intramuscular injections of the vaccine, 85% protection was observed against challenges with the M41 infectious bronchitis virus. The vaccine could stimulate humoral and cell-mediated immunity.

A designated S1-DNA vaccine, pDKArkS1-DP, based on Arkansas IBV, was developed. In ovo vaccination, followed by a live attenuated IB vaccine 2 weeks later, caused a high immune response and 100% protection against challenge. The DNA vaccine's efficacy and protection improve whenever a cationic liposome carrier is used. Alternatives to improve the effectiveness of that kind of vaccine are combination with specific adjuvants such as cytokines, whether mono- or polyvalent, DNA vaccines encoding nucleocapsid or S1 or even membrane protein with IL-2 chicken (GM-CSF). A liposome-encapsulated multi-epitope DNA vaccine from S1, S2, and N regions in intramuscular injection resulted in increased numbers of CD4+ and CD8+ cells and an 80% protective immune response in immunized birds (Leyson et al., 2017; (Jordan, 2017).

Reverse genetic vaccines

A reverse genetic vaccine is a new technology for manipulating viral genes and producing a new virus from a classic one. For example, a recombinant Beau-R-IBV vaccine was constructed by replacing the antigenic sites of *S1* of the Beau-IBV strain with *S1* from a pathogenic strain M41 and 4/91 strains (Armesto et al., 2011; Hodgson et al., 2004). These changes lead to protective responses without making the manipulated Beau-R strain to be pathogenic. Reversion to virulence, which is a

weak point for live attenuated vaccines, is abrogated and can be used in the presence of maternal immunity. Whether this vaccine generation will increase or reduce the mutation rate or selection pressure is not clearly understood (Zhou et al., 2013).

Previous research has focused on developing an attenuated recombinant IBV (rIBV), a molecular clone of the highly attenuated Beaudette-CK strain, for S1 expressing of other heterologous genotypes. The rIBV, as a vaccine backbone, mimics a natural infection to induce both local and systemic immune responses. Beau-R with the *S* gene of 4/91 strain could achieve 65% protection after homologue challenge (Keep et al., 2020; Keep et al., 2022b). The replication of rIBV Beau-R in the host is minimal and, in cell culture, is completely inhibited at a natural chicken body temperature of 41˚C. There was a hypothesis that the temperature sensitivity of the recombinant backbone is a desired character for the production of live-attenuated vaccines that are temperature sensitive and so restricted to causing virulent infection in chickens but have limited replication to induce immunity. Temperature sensitivity is not a new issue in virology and has been used to develop viral vaccines such as influenza (Keep et al., 2022a; Martinez-Sobrido et al., 2018).

Posttranslational modifications in different expression systems, including yeast, bacteria, plant, or baculovirus, influence the vaccine production outcome. For example, an attempt with the IBV vaccine on vaccinia could not produce enough antigen and then enough antibody responses, which is probably because of poor replication of the designed vaccine in avian cells and maybe the immune response of the mice to the vaccine that hindered the antigen-presenting for *IBV* gene (Bande et al., 2015). Another attempt to develop a baculovirus-based vaccine to produce the Korean KM91 strain S1-glycoprotein generated just 50% immunity because of post-translation modifications (Jung et al., 2022). The potato was chosen to express S1 of IBV using the cauliflower mosaic virus (35S) promotor gene (Zhou et al., 2004). The vaccine had promising results suggesting the method for food-based IB vaccines. Application of infectious bronchitis Beaudette virus as a background was a technology for a new generation of vaccines. The method was successful because it mimicked the virus replication cycle in the host without virulence but provided a possibility for vaccine production in cell culture, especially in the Vero cell, which is a licensed cell media to produce viral vaccines (Keep et al., 2022b). The delivery method and route of administration in vaccination can affect immune responses and significant histocompatibility complex responses. Live vaccines are administrated through water or spray. Inactivated vaccines are used via injection. The question is when you can use a vaccine in poultry as a mass application. It is beneficial and easy to use. Some vaccines have been designed to be administrated via feed, which is a very applicable route (Jordan, 2017). A DNA vaccine expressing S1-protein was administered orally with an attenuated *Salmonella enterica* strain (Jiao et al., 2011)—mucosal immune responses increased following oral or intranasal immunization. As a system to deliver the vaccine, *Lactococcus lactis* bacteria causes an effective immune response in mucosa (Peng et al., 2013).

Conclusion

The future vision is that an IBV vaccine should provide broad protection against variable genotypes or induce strong protection in response to challenges posed by emerging viruses. Novel-designed vaccines should escape maternal antibody effects, be user-friendly, and have a rapid and cost-effective development process, considering the constant evolution of the viruses and the emergence of new variants that might lack cross-protection with the classic vaccine's immunity. In light of novel technology, it is possible to develop vaccines that can reduce reversion to virulence. However, inactivation by maternal antibodies, especially following viral vectors and live-attenuated vaccines, is still a significant concern.

The recombinant vaccines, such as plasmid and multi-epitope vaccines, can deliver multiple antigens, inducing both humoral and cell-mediated immunity. New genotypes can also be manipulated and inserted into an established mechanism. Their preferences include oral or oculonasal routes for administration by developing these vaccines in novel delivery techniques such as nanoparticles or virus-like particles. Whether DNA or protein vaccines are produced in the future, it should be remembered that the protection is not 100%, and boosting with other kinds of vaccines must be contributed. These novel vaccines may be delivered by oral or mucosal route, but gaining the best protection requires repetition of vaccination.

Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this research.

Funding

This research did not receive any grant from funding agencies in the public, commercial, or non-profit sectors.

Conflict of interest

The author declared no conflict of interest.

Acknowledgments

The author would like to express her gratitude to her colleagues in the Poultry Vaccine Research and Production Department, Razi Vaccine and Serum Research Institute for their sincere efforts through vaccines production and developments.

References

Armesto, M., Evans, S., Cavanagh, D., Abu-Median, A. B., Keep, S., & Britton, P. (2011). A recombinant avian infectious bronchitis virus expressing a heterologous spike gene belonging to the 4/91 serotype. *PloS One, 6*(8), e24352. [DOI:10.1371/journal.pone.0024352] [PMID]

Awad, F., Forrester, A., Baylis, M., Lemiere, S., Ganapathy, K., & Hussien, H. A., et al. (2015). Protection conferred by live infectious bronchitis vaccine viruses against variant Middle East IS/885/00-like and IS/1494/06-like isolates in commercial broiler chicks. *Veterinary Record Open, 2*(2), e000111. [DOI:10.1136/vetreco-2014-000111] [PMID]

Awad, F., Forrester, A., Baylis, M., Lemiere, S., Jones, R., & Ganapathy, K. (2015). Immune responses and interactions following simultaneous application of live Newcastle disease, infectious bronchitis and avian metapneumovirus vaccines in specific-pathogen-free chicks. *Research in Veterinary Science, 98,* 127–133.[DOI:10.1016/j.rvsc.2014.11.004] [PMID]

Bande, F., Arshad, S. S., Bejo, M. H., Moeini, H., & Omar, A. R. (2015). Progress and challenges toward the development of vaccines against avian infectious bronchitis. *Journal of immunology Research, 2015,* 424860. [DOI:10.1155/2015/424860] [PMID]

Beheshtian, B., Haghighi Khoshkhoo, P. Akbariazad, G., & Hosseini, H. (2020). Phylogenetic study and investigation on the involvement of the Newcastle Disease virus in multicausal respiratory diseases of the broiler flocks in Qazvin Province, Iran 2014-2015. *Iranian Journal of Veterinary Medicine, 14*(2), 135-145. [DOI:10.22059/IJVM.2019.274487.1004961]

Cao, H. P., Wang, H. N., Yang, X., Zhang, A. Y., Li, X., & Ding, M. D., et al. (2013). Lactococcus lactis anchoring avian infectious bronchitis virus multi-epitope peptide EpiC induced specific immune responses in chickens. *Bioscience, Biotechnology, and Biochemistry, 77*(7), 1499–1504. [DOI:10.1271/bbb.130157] [PMID]

Cao, H. P., Wang, H. N., Zhang, A. Y., Ding, M. D., Liu, S. T., & Cheng, H., et al. (2012) Expression of avian infectious bronchitis virus multi-epitope based peptide EpiC in Lactococcus lactis for oral immunization of chickens. *Bioscience, Biotechnology, and Biochemistry, 76*(10), 1871–1876. [DOI:10.1271/bbb.120326] [PMID]

Cavanagh, D. (2005). Coronaviruses in poultry and other birds. *Avian Pathology, 34*(6), 439–448. [DOI:10.1080/03079450500367682] [PMID]

Cavanagh, D., Davis, P. J., Cook, J. K., Li, D., Kant, A., & Koch, G. (1992). Location of the amino acid differences in the S1 spike glycoprotein subunit of closely related serotypes of infectious bronchitis virus. *Avian Pathology, 21*(1), 33–43. [DOI:10.1080/03079459208418816] [PMID]

Chen, Y., Jiang, L., Zhao, W., Liu, L., Zhao, Y., & Shao, Y., et al. (2017). Identification and molecular characterization of a novel serotype infectious bronchitis virus (GI-28) in China. *Veterinary Microbiology, 198,* 108–115. [DOI:10.1016/j.vetmic.2016.12.017] [PMID]

Darteil, R., Bublot, M., Laplace, E., Bouquet, J. F., Audonnet, J. C., & Rivière, M. (1995). Herpesvirus of Turkey recombinant viruses expressing infectious bursal disease virus (IBDV) VP2 immunogen induce protection against an IBDV virulent challenge in chickens. *Virology, 211*(2), 481–490. [DOI:10.1006/viro.1995.1430] [PMID]

Sjaak de Wit, J. J., Cook, J. K., & van der Heijden, H. M. (2011). Infectious bronchitis virus variants: A review of the history, current situation and control measures. *Avian Pathology, 40*(3), 223-235. [DOI:10.1080/03079457.2011.566260] [PMID]

De Wit, J. J., Swart, W. A., & Fabri, T. H. (2010). Efficacy of infectious bronchitis virus vaccinations in the field: Association between the α-IBV IgM response, protection and vaccine application parameters. *Avian Pathology, 39*(2), 123–131. [DOI:10.1080/03079451003604639] [PMID]

Domingo, E., & Holland, J. J. (1997). RNA virus mutations and fitness for survival. *Annual Review of Microbiology, 51,* 151–178. [DOI:10.1146/annurev.micro.51.1.151] [PMID]

Ellis, S., Keep, S., Britton, P., de Wit, S., Bickerton, E., & Vervelde, L. (2018). Recombinant infectious Bronchitis viruses expressing chimeric spike glycoproteins induce partial protective immunity against homologous challenge despite limited replication in vivo. *Journal of Virology, 92*(23), e01473-18. [DOI:10.1128/JVI.01473-18] [PMID]

Falchieri, M., Lupini, C., Cecchinato, M., Catelli, E., Kontolaimou, M., & Naylor, C. J. (2013). Avian metapneumoviruses expressing Infectious Bronchitis virus genes are stable and induce protection. *Vaccine, 31*(22), 2565–2571. [DOI:10.1016/j.vaccine.2013.03.055] [PMID]

Folegatti, P. M., Ewer, K. J., Aley, P. K., Angus, B., Becker, S., Belij-Rammerstorfer, S., & Bellamy, D., et al. (2020). Safety and immunogenicity of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2: A preliminary report of a phase 1/2, single-blind, randomised controlled trial. *Lancet (London, England), 396*(10249), 467–478. [DOI:10.1016/S0140-6736(20)31604-4] [PMID]

Franzo, G., Massi, P., Tucciarone, C. M., Barbieri, I., Tosi, G., & Fiorentini, L., et al. (2017). Think globally, act locally: Phylodynamic reconstruction of infectious bronchitis virus (IBV) QX genotype (GI-19 lineage) reveals different population dynamics and spreading patterns when evaluated on different epidemiological scales. *PloS One, 12*(9), e0184401. [DOI:10.1371/journal.pone.0184401] [PMID]

Gebre, M. S., Rauch, S., Roth, N., Yu, J., Chandrashekar, A., & Mercado, N. B., et al. (2022). Optimization of non-coding regions for a non-modified mRNA COVID-19 vaccine. *Nature, 601*(7893), 410–414. [DOI:10.1038/s41586-021-04231-6] [PMID]

Gholami, F., Karimi, V., Ghalyanchi Langeroudi, A.., Hashemzadeh, M., & Vasfi Marandi, M. (2018). Genotyping of Infectious bronchitis viruses isolated from broiler chicken farms in Iran during 2015-2016. *Iranian Journal of Veterinary Medicine, 12*(1), 9-17. [DOI:10.22059/IJVM.2017.228730.1004797]

Habibi, M., Karimi, V., Langeroudi, A. G., Ghafouri, S. A., Hashemzadeh, M., & Farahani, R. K., et al. (2017). Combination of H120 and 1/96 avian infectious bronchitis virus vaccine strains protect chickens against challenge with IS/1494/06 (variant 2)-like infectious bronchitis virus. *Acta Virologica, 61*(2), 150–160. [DOI:10.4149/av_2017_02_04] [PMID]

Hajijafari Anaraki, M., Sheikhi, N., Haghbin Nazarpak, H., & Nikbahkt Brujeni, G. (2022). Real time detection of different variant strains of infectious bronchitis virus in trachea, lung and kidney of infected broiler chickens. *Iranian Journal of Veterinary Medicine, 16*(1), 57-63. [DOI:10.22059/IJVM.2021.321594.1005165]

Hodgson, T., Casais, R., Dove, B., Britton, P., & Cavanagh, D. (2004). Recombinant infectious bronchitis coronavirus Beaudette with the spike protein gene of the pathogenic M41 strain remains attenuated but induces protective immunity. J*ournal of Virology, 78*(24), 13804–13811. [DOI:10.1128/JVI.78.24.13804-13811.2004] [PMID]

Ignjatovic, J., & Galli, L. (1994). The S1 glycoprotein but not the N or M proteins of avian infectious bronchitis virus induces protection in vaccinated chickens. *Archives of Virology, 138*(1-2), 117–134.[DOI:10.1007/BF01310043] [PMID]

Ignjatovic, J., & Galli, U. (1995). Immune responses to structural proteins of avian infectious bronchitis virus. *Avian Pathology, 24*(2), 313–332. [DOI:10.1080/03079459508419072] [PMID]

Ignjatovic, J., Gould, G., & Sapats, S. (2006). Isolation of a variant infectious bronchitis virus in Australia that further illustrates diversity among emerging strains. *Archives of Virology, 151*(8), 1567–1585.[DOI:10.1007/s00705-006-0726-y] [PMID]

Jackson, L. A., Roberts, P. C., & Graham, B. S. (2020). A SARS-CoV-2 mRNA Vaccine - Preliminary report. Reply. *The New England Journal of Medicine, 383*(12), 1191–1192. [PMID]

Jayaram, J., Youn, S., & Collisson, E. W. (2005). The virion N protein of infectious bronchitis virus is more phosphorylated than the N protein from infected cell lysates. *Virology, 339*(1), 127–135. [DOI:10.1016/j.virol.2005.04.029] [PMID]

Jiao, H., Pan, Z., Yin, Y., Geng, S., Sun, L., & Jiao, X. (2011).Oral and nasal DNA vaccines delivered by attenuated Salmonella enterica serovar Typhimurium induce a protective immune response against infectious bronchitis in chickens. *Clinical and Vaccine Immunology : CVI, 18*(7), 1041–1045. [PMID]

Jordan, B. (2017). Vaccination against infectious bronchitis virus: A continuous challenge. *Veterinary Microbiology, 206,* 137–143. [DOI:10.1016/j.vetmic.2017.01.002] [PMID]

Jung, J. S., Lee, R., Yoon, S. I., Lee, G. S., Sung, H. W., & Kwon, H. M., et al. (2022). Genetic and immunological characterization of commercial infectious bronchitis virus vaccines used in Korea. *Archives of Virology; 167*(11), 2123-2132. [PMID]

Kant, A., Koch, G., van Roozelaar, D. J., Kusters, J. G., Poelwijk, F. A., & van der Zeijst, B. A. (1992). Location of antigenic sites defined by neutralizing monoclonal antibodies on the S1 avian infectious bronchitis virus glycopolypeptide. *The Journal of General Virology, 73*(Pt 3), 591–596.[DOI:10.1099/0022-1317-73-3-591] [PMID]

Keep, S., Stevenson-Leggett, P., Dowgier, G., Everest, H., Freimanis, G., & Oade, M., et al. (2022). Identification of Amino Acids within nonstructural proteins 10 and 14 of the avian coronavirus infectious bronchitis virus that result in attenuation in vivo and in ovo. *Journal of Virology, 96*(6), e0205921. [DOI:10.1128/jvi.02059-21] [PMID]

Keep, S., Stevenson-Leggett, P., Dowgier, G., Foldes, K., Webb, I., & Fones, A., et al.(2022). A temperature-sensitive recombinant of avian coronavirus infectious bronchitis virus provides complete protection against homologous challenge. *Journal of Virology, 96*(17), e0110022. [DOI:10.1128/jvi.01100-22] [PMID]

Keep, S., Stevenson-Leggett, P., Steyn, A., Oade, M. S., Webb, I., & Stuart, J., et al. (2020). Temperature sensitivity: A potential method for the generation of vaccines against the avian coronavirus infectious bronchitis virus. *Viruses, 12*(7), 754. [DOI:10.3390/v12070754] [PMID]

Koch, G., Hartog, L., Kant, A., & van Roozelaar, D. J. (1990). Antigenic domains on the peplomer protein of avian infectious bronchitis virus: Correlation with biological functions. *The Journal of General Virology, 71*(Pt 9), 1929–1935. [DOI:10.1099/0022-1317-71-9-1929] [PMID]

Kusters, J. G., Jager, E. J., Lenstra, J. A., Koch, G., Posthumus, W. P., & Meloen, R. H., et al. (1989). Analysis of an immunodominant region of infectious bronchitis virus. *Journal of Immunology (Baltimore, Md. : 1950), 143*(8), 2692–2698. [DOI:10.4049/jimmunol.143.8.2692] [PMID]

Lee, C. W., Hilt, D. A., & Jackwood, M. W. (2003). Typing of field isolates of infectious bronchitis virus based on the sequence of the hypervariable region in the S1 gene. *Journal of Veterinary Diagnostic Investigation, 15*(4), 344–348.[DOI:10.1177/104063870301500407] [PMID]

Leyson, C. M., Hilt, D. A., Jordan, B. J., & Jackwood, M. W. (2017). Minimum infectious dose determination of the arkansas delmarva poultry industry infectious bronchitis virus vaccine delivered by hatchery spray cabinet. *Avian Diseases, 61*(1), 123–127. [DOI:10.1637/11474-072216-ResNote] [PMID]

Li, H., Wang, Y., Han, Z., Wang, Y., Liang, S., & Jiang, L., et al. (2016). Recombinant duck enteritis viruses expressing major structural proteins of the infectious bronchitis virus provide protection against infectious bronchitis in chickens. *Antiviral Research, 130,* 19–26. [DOI:10.1016/j.antiviral.2016.03.003] [PMID]

Lisowska, A., Sajewicz-Krukowska, J., Fusaro, A., Pikula, A., & Domanska-Blicharz, K. (2017). First characterization of a Middle-East GI-23 lineage (Var2-like) of infectious bronchitis virus in Europe. *Virus Research, 242,* 43–48. [DOI:10.1016/j.virusres.2017.09.010] [PMID]

Martínez-Sobrido, L., Peersen, O., & Nogales, A. (2018). Temperature sensitive mutations in influenza A viral ribonucleoprotein complex responsible for the attenuation of the live attenuated influenza vaccine. *Viruses, 10*(10), 560. [DOI:10.3390/v10100560] [PMID]

Mendonça, S. A., Lorincz, R., Boucher, P., & Curiel, D. T. (2021). Adenoviral vector vaccine platforms in the SARS-CoV-2 pandemic. *NPJ Vaccines, 6*(1), 97. [DOI:10.1038/s41541-021-00356-x] [PMID]

Moore, K. M., Jackwood, M. W., & Hilt, D. A. (1997). Identification of amino acids involved in a serotype and neutralization specific epitope within the s1 subunit of avian infectious bronchitis virus. *Archives of Virology, 142*(11), 2249–2256. [DOI:10.1007/s007050050239] [PMID]

Motamed, N. (2022). Quantitative real time PCR for dynamic assessment of H120 vaccine virus. Agricultural Research, Education and Extension, Karaj, Iran. [Unpublished Research].

Motamed, N., & Bashashati, M. (2022). Comparative genetic features of S1 gene from six Massachusetts and Variant avian 2 infectious bronchitis viruses isolated in Iran. *Archives of Razi Institute, 77*(5), 1611-1619. [DOI:10.22092/ARI.2022.356836.1924]

Motamed, N., . Beshashati, M., & Fallah, M. H. (2021). [Molecular detection of Infectious Bronchitis virus in broiler chicken flocks (Persian)]. *New Findings in Veterinary Microbiology, 3*(2), 118-126. [DOI:10.22034/NFVM.2021.139269]

Ndegwa, E. N., Toro, H., & van Santen, V. L. (2014). Comparison of vaccine subpopulation selection, viral loads, vaccine virus persistence in trachea and cloaca, and mucosal antibody responses after vaccination with two different Arkansas Delmarva Poultry Industry -derived infectious bronchitis virus vaccines. *Avian Diseases, 58*(1), 102–110. [DOI:10.1637/10609-070613-Reg.1] [PMID]

Nix, W. A., Troeber, D. S., Kingham, B. F., Keeler, C. L., Jr, & Gelb, J., Jr (2000). Emergence of subtype strains of the Arkansas serotype of infectious bronchitis virus in Delmarva broiler chickens. *Avian Diseases, 44*(3), 568–581. [DOI:10.2307/1593096] [PMID]

Oade, M. S., Keep, S., Freimanis, G. L., Orton, R. J., Britton, P., & Hammond, J. A., et al. (2019). Attenuation of infectious bronchitis virus in eggs results in different patterns of genomic variation across multiple replicates. *Journal of Virology, 93*(14), e00492-19. [DOI:10.1128/JVI.00492-19] [PMID]

Peng, Q., Zeng, X. F., Zhu, J. L., Wang, S., Liu, X. T., & Hou, C. L., et al. (2016). Effects of dietary Lactobacillus plantarum B1 on growth performance, intestinal microbiota, and short chain fatty acid profiles in broiler chickens. *Poultry Science, 95*(4), 893–900. [PMID]

Seah, J. N., Yu, L., & Kwang, J. (2000). Localization of linear B-cell epitopes on infectious bronchitis virus nucleocapsid protein. *Veterinary Microbiology, 75*(1), 11–16. [DOI:10.1016/S0378-1135(00)00202-9] [PMID]

Shi, X. M., Zhao, Y., Gao, H. B., Jing, Z., Wang, M., & Cui, H. Y., et al. (2011). Evaluation of recombinant fowlpox virus expressing infectious bronchitis virus S1 gene and chicken interferon-gamma gene for immune protection against heterologous strains. *Vaccine, 29*(8), 1576–1582. [DOI:10.1016/j.vaccine.2010.12.102] [PMID]

Shirvani, E., Paldurai, A., Manoharan, V. K., Varghese, B. P., & Samal, S. K. (2018). A recombinant Newcastle Disease Virus (NDV) expressing S protein of Infectious Bronchitis Virus (IBV) protects chickens against IBV and NDV. *Scientific Reports, 8*(1), 11951. [DOI:10.1038/s41598-018-30356-2] [PMID]

Song, C. S., Lee, Y. J., Lee, C. W., Sung, H. W., Kim, J. H., & Mo, I. P., et al. (1998). Induction of protective immunity in chickens vaccinated with infectious bronchitis virus S1 glycoprotein expressed by a recombinant baculovirus. *The Journal of General Virology, 79*(Pt 4), 719–723. [DOI:10.1099/0022-1317-79-4-719] [PMID]

Thor, S. W., Hilt, D. A., Kissinger, J. C., Paterson, A. H., & Jackwood, M. W. (2011). Recombination in avian gamma-coronavirus infectious bronchitis virus. *Viruses, 3*(9), 1777–1799. [DOI:10.3390/v3091777] [PMID]

Toro, H., Zhao, W., Breedlove, C., Zhang, Z., Yu, Q., & Van Santen, V. (2014). Infectious bronchitis virus S2 expressed from recombinant virus confers broad protection against challenge. *Avian Diseases, 58*(1), 83–89. [PMID]

Vagnozzi, A., Zavala, G., Riblet, S. M., Mundt, A., & García, M. (2012). Protection induced by commercially available live-attenuated and recombinant viral vector vaccines against infectious laryngotracheitis virus in broiler chickens. *Avian Pathology, 41*(1), 21–31. [DOI:10.1080/03079457.2011.631983] [PMID]

Valastro, V., Holmes, E. C., Britton, P., Fusaro, A., Jackwood, M. W., & Cattoli, G., et al. (2016). S1 gene-based phylogeny of infectious bronchitis virus: An attempt to harmonize virus classification. *Infection, Genetics and Evolution, 39,* 349-364. [DOI:10.1016/j.meegid.2016.02.015] [PMID]

Wang, L., Parr, R. L., King, D. J., & Collisson, E. W. (1995). A highly conserved epitope on the spike protein of infectious bronchitis virus. *Archives of Virology, 140*(12), 2201–2213. [DOI:10.1007/BF01323240] [PMID]

Wei, Y. Q., Guo, H. C., Dong, H., Wang, H. M., Xu, J., & Sun, D. H., et al. (2014). Development and characterization of a recombinant infectious bronchitis virus expressing the ectodomain region of S1 gene of H120 strain. *Applied Microbiology and Biotechnology, 98*(4), 1727–1735. [DOI:10.1007/s00253-013-5352-5] [PMID]

Wu, X., Zhai, X., Lai, Y., Zuo, L., Zhang, Y., & Mei, X., et al.(2019).Construction and immunogenicity of novel chimeric virus-like particles bearing antigens of infectious bronchitis virus and Newcastle Disease Virus. *Viruses, 11*(3), 254. [DOI:10.3390/v11030254] [PMID]

Yan, S. H., Chen, Y., Zhao, J., Xu, G., Zhao, Y., & Zhang, G. Z. (2016). Pathogenicity of a TW-like strain of infectious bronchitis virus and evaluation of the protection induced against it by a QX-Like Strain. *Frontiers in Microbiology, 7,* 1653. [DOI:10.3389/fmicb.2016.01653] [PMID]

Yang, T., Wang, H. N., Wang, X., Tang, J. N., Gao, R., & Li, J., et al. (2009). Multivalent DNA vaccine enhanced protection efficacy against infectious bronchitis virus in chickens. *The Journal of Veterinary Medical Science, 71*(12), 1585–1590. [DOI:10.1292/jvms.001585] [PMID]

Zeshan, B., Zhang, L., Bai, J., Wang, X., Xu, J., & Jiang, P. (2010). Immunogenicity and protective efficacy of a replication-defective infectious bronchitis virus vaccine using an adenovirus vector and administered in ovo. *Journal of Virological Methods, 166*(1-2), 54–59. [DOI:10.1016/j.jviromet.2010.02.019] [PMID]

Zhang, J., Chen, X. W., Tong, T. Z., Ye, Y., Liao, M., & Fan, H. Y. (2014). BacMam virus-based surface display of the infectious bronchitis virus (IBV) S1 glycoprotein confers strong protection against virulent IBV challenge in chickens. *Vaccine, 32*(6), 664–670. [DOI:10.1016/j.vaccine.2013.12.006] [PMID]

Zhao, K., Li, S., Li, W., Yu, L., Duan, X., & Han, J., et al. (2017). Quaternized chitosan nanoparticles loaded with the combined attenuated live vaccine against Newcastle disease and infectious bronchitis elicit immune response in chicken after intranasal administration. *Drug Delivery, 24*(1), 1574–1586. [DOI:10.1080/10717544.2017.1388450] [PMID]

Zhao, R., Sun, J., Qi, T., Zhao, W., Han, Z., & Yang, X., et al. (2017). Recombinant Newcastle disease virus expressing the infectious bronchitis virus S1 gene protects chickens against Newcastle disease virus and infectious bronchitis virus challenge. *Vaccine, 35*(18), 2435–2442. [DOI:10.1016/j.vaccine.2017.03.045] [PMID]

Zhou, Y. S., Zhang, Y., Wang, H. N., Fan, W. Q., Yang, X., & Zhang, A. Y., et al. (2013). Establishment of reverse genetics system for infectious bronchitis virus attenuated vaccine strain H120. *Veterinary Microbiology, 162*(1), 53–61. [DOI:10.1016/j.vetmic.2012.08.013] [PMID]

Zhou, J. Y., Cheng, L. Q., Zheng, X. J., Wu, J. X., Shang, S. B., & Wang, J. Y., et al. (2004). Generation of the transgenic potato expressing full-length spike protein of infectious bronchitis virus. *Journal of Biotechnology, 111*(2), 121–130. [PMID]

Zuo, L., Yan, W., Song, Z., Li, H., Xie, X., & Gu, K., et al. (2021). Design and characterization of a DNA vaccine based on spike with consensus nucleotide sequence against infectious bronchitis virus. *Vaccines, 9*(1), 50. [DOI:10.3390/vaccines9010050] [PMID]

مقاله مروری

مروری آینده نگر بر روش‌های تولید واکسن علیه بیماری برونشیت عفونی

نجمه معتمد*

گروه تحقیقات و تولید واکسن بیماری‌های طیور، مؤسسه تحقیقات واکسن و سرم‌سازی رازی، تحقیقات، آموزش و ترویج کشاورزی، کرج، ایران.

Use your device to scan and read the article online

How to Cite This Article Motamed, N. (2024). An Overview of Future Development Methods of Infectious Bronchitis Vaccines. *Iranian Journal of Veterinary Medicine*, *18*(1), 1-12. http://dx.doi.org/10.32598/ijvm.18.1.1005406

http://dx.doi.org/10.32598/ijvm.18.1.1005406

چکیده

امروزه واکسن‌ها ابزار اصلی کنترل سلامت در جوامع انسانی و دامی هستند. فهرست طولانی‌ای از بیماری‌هایی که در سراسر جهان با واکسیناسیون کنترل یا حتی ریشه‌کن شده‌اند، وجود دارد. واکسن‌های ویروسی کلاسیک معمولاً از ویروس کامل زنده یا غیرفعال تشکیل شده‌اند و سال‌هاست که تولید می‌شوند، اما متأسفانه در برخی موارد به‌ویژه در عفونت‌های پایدار، ویروس‌های با رشد سریع، آنتی‌ژن‌های دارای ساختار پیچیده و کمپلکس و عوامل نوظهور چندان موفق نبوده‌اند. فناوری‌های جدید توسعه واکسن مانند واکسن‌های DNA، پروتئین ساب یونیت یا واکسن‌های ناقل ویروسی، توسعه واکسن را متحول کردند و طیف وسیعی از راه‌ها را برای دانشمندان درمورد مطالعه و تحقیق در تحقیقات تولید واکسن هموار کرده‌اند. بیشتر واکسن‌های سنتی یا حتی واکسن‌های جدید ساخته‌شده مبتنی بر فناوری‌های جدید هستند، به‌ویژه درزمینه بیماری‌های انسانی که می‌توان هزینه و خسارات تولید را به راحتی نادیده گرفت؛ اما در سلامت دام‌ها به‌ویژه برای تولید تجاری طیور، هزینه توسعه، سادگی کاربرد و روش استفاده آسان در سطح گله و امکان تولید در مقیاس‌های بزرگ، اقلام محدودکننده محسوب می‌شده است. در سال‌های اخیر در راستای پیشرفت فناوری و ظهور انواع جدیدی از ویروس‌های برونشیت عفونی که سال‌ها پاتوژن مهم طیور هستند، اهمیت تولید، تحقیق یا توسعه تکنیک‌های جدید تولید واکسن بیش از پیش برجسته شده است. در این بررسی، برخی از مطالعات در مورد تکنیک‌های جدید ساخت واکسن برونشیت عفونی معرفی و نتایج آن واکسن‌ها در حفاظت از جوجه‌ها و بروز علائم بالینی بیان می‌شود.

کلیدواژه‌ها: واکسن‌های mRNA، تکنیک‌های جدید، واریانت، وکتورای ویروسی واکسن

تاریخ دریافت: ۰۷ خرداد ۱۴۰۲
تاریخ پذیرش: ۲۶ تیر ۱۴۰۲
تاریخ انتشار: ۱۱ دی ۱۴۰۲

* **نویسنده مسئول:**
دکتر نجمه معتمد
نشانی: کرج، سازمان تحقیقات، آموزش و ترویج کشاورزی، مؤسسه تحقیقات واکسن و سرم‌سازی رازی، گروه تحقیقات و تولید واکسن بیماری‌های طیور.
تلفن: ۹۴۰۲۱۷۷ (۹۱۲) ۹۸+
رایانامه: *n.motamed@rvsri.ac.ir*