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Investigation of P53 regulation and identification of targeted receptors that associated with common poultry diseases

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Abstract
Poultry farming is a significant sector in the agricultural industry, providing a vital source of protein for human consumption. However, the industry faces challenges from various viral diseases that can lead to significant economic losses and impact food security. In spite of Vaccination, Viral diseases include Avian Influenza (AI), Infectious bronchitis (IB), Infectious Bursal Disease (IBD) infectious laryngotracheitis (ILT), Newcastle disease (ND) and bacterial diseases such as Necrotic enteritis (NE) and avian pathogenic E. coli (APEC), and other diseases are common over the world. Understanding the mechanisms of viral entry and replication in avian cells is crucial for developing effective strategies to combat these diseases. Central to this understanding are the receptors present on avian cells, which play a pivotal role in the recognition and binding of viral pathogens. The identification and characterization of viral antigens associated with poultry viral diseases are critical for the development of effective vaccines and diagnostic tools. Understanding these antigens enables researchers to design targeted immunization strategies, improve disease management, and enhance the overall health of poultry populations. As the poultry industry continues to evolve, ongoing research into viral antigens and their interactions with the host immune system will be essential for combating viral diseases and ensuring food security. This study explores the crucial receptors in poultry that are significantly associated with various diseases by fetching previous studies in which (Sialic Acid Receptor, chCD44, specific cellular receptor(s) with viral envelope glycoprotein,, sialoglycoconjugates, Purinergic Receptors (PRs), Toll-Like Receptors (TLR1A), Sialic Acid Receptor, C-type lectin receptor, dectin-1, host glycosaminoglycans (GAGs),A family of variable lipoproteins (VlhA), cytadhesin molecule GapA and other cytadherence-related molecules such as CrmA extracellular matrix (ECM) proteins, Tva Receptor, Tvj Receptor glycoproteins (gB, gD, and gC) Receptor) are identified to be upregulated during infections with those diseases, also detecting common viral diseases using Rapid test and unveil the expression of P53 in identified diseases in broilers farms using spectrophotometry quantification procedure. Because of their roles in immune response, and potential applications in disease resistance and vaccine development. The analysis is based on the most recent and reliable scientific literature available. Quantitative analysis of p53 expression revealed a significant upregulation across all experimental groups relative to the control. The control group exhibited minimal basal levels of p53, whereas the IBD group demonstrated a moderate increase. Notably, the ND and IB groups showed marked elevations in p53 concentration, which were statistically significant ($p<0.01$ and $p<0.001$, respectively). The AI group displayed the highest expression level, with a highly significant difference compared to the control ($p<0.001$). The progressive increase in p53 expression among the disease groups suggests a correlation between disease severity and activation of p53-dependent cellular stress responses.
The study revealed that each disease is correlated with a specific receptor and P53 is overexpressed during infection in poultry. Future studies are recommended in this direction.

Keywords: Sialic acid receptor, purinergic receptors (PRs), TLR1A, C-type lectin receptor, dectin-1, P53

Introduction
The poultry industry is a cornerstone of global food security, providing affordable protein in the form of eggs and meat. However, the industry faces constant threats from infectious diseases, many of which are exacerbated by immunosuppressive conditions.

Immunosuppression in poultry, defined as a dysfunction of the immune system leading to increased susceptibility to diseases, is often linked to specific receptors that mediate immune responses. Understanding these receptors is essential for developing disease-resistant poultry breeds, improving vaccine efficacy, and mitigating economic losses (Akter *et al*., 2025; Milby-Blackledge, Farnell, Swaggerty, & Farnell, 2025; Sayed *et al*., 2025; Yan *et al*., 2025; X. Zhang *et al*., 2025) [3, 57, 72, 84].

Poultry diseases pose a significant challenge to the global poultry industry, which is a critical source of food protein and economic stability worldwide. The immune system of poultry, particularly the role of specific receptors, plays a pivotal role in disease resistance and susceptibility.

Host recognition by the virus

Unlike living cells, many viruses lack a plasma membrane or the structures necessary to sustain life. Some viruses consist of nothing more than an inert protein shell filled with DNA or RNA. To replicate, viruses need to enter a living cell that acts as a host, then commandeer the host's cellular machinery (An, Liu, Ren, Mo, & Zhou, 2025; Chen, Yu, Yan, Yuan, & He, 2025) [84]. Viruses typically attach to cell-surface receptors on the target cell. For instance, the virus responsible for human influenza (flu) attaches exclusively to receptors on the membranes of respiratory system cells. Differences in the chemical makeup of the cell-surface receptors of different hosts mean that a virus that infects one species (e.g., humans) will not infect another species (e.g., chickens). In comparison to humans, though, viruses have tiny amounts of DNA or RNA, so viral reproduction can happen at lightning speed. Viral replication is error-prone, so mistakes will give rise to variants in newly replicated viruses; these variants could mean that the viral proteins that interact with receptors on the surface of host cells could evolve to be able to bind to receptors on a new host (Ilbagi, Kanakala, Masonbrink, Lozier, & Miller, 2025) [39]. These kinds of alterations occur spontaneously and frequently in the reproductive cycle of a virus, but the changes only matter if a virus with newly cultivated binding properties encounters a receptive host. This scenario can happen with influenza in situations in which animals and people are in close contact, such as poultry and swine farms. Once a virus has jumped to a new host, it can spread rapidly. Scientists keep a close eye on viruses they can observe for the first time (emerging viruses), hoping that monitoring may help prevent global infectious viruses (Roy *et al*., 2025) [71].

Enzyme-linked receptors, receptors are associated with an enzyme called a linked receptor that serves as a signal for the transport of calcium ions into the cell. In some cases, the receptor itself has an intracellular domain that acts as an enzyme. Other enzyme-linked receptor has a short intracellular domain that directly interacts with an enzyme (Chai *et al*., 2024) [15]. When a ligand binds the extracellular domain, a signal is transduced across the membrane to activate the enzyme. Turning on the enzyme sparks a series of events inside the cell that finally trigger a response. Entry receptors result in virus entry by endocytosis/pinocytosis or by inducing fusion/penetration. The effect of this binding cannot be undone (T. Li *et al*., 2024; Mukae, Yoshii, & Oishi, 2024) [59]. They have usually been designated as "co-receptors". Entry receptors are typically less accessible for the virion, which eschews this issue by first binding to adhesion receptors, which increase the likelihood of binding to the entry receptor. For bacterial viruses, binding to the entry receptor is termed irreversible adsorption, according to experimental data (Fadaee, Mahrooghi, Lahouty, Oskouei, & Nezhadi, 2025) [29].

Viral attachment to host entry receptor

A specific region of DNA in chickens associated with disease resistance after scientists successfully identified the DNA region in the chickens for the disease resistance. However, breeding companies will select animals that look similar with a higher general disease resistance, which results in lower antibiotic use and higher animal welfare. One region in the chicken's DNA accounts for a large part of the difference in potential disease resistance between the birds, this region of DNA carries one of the key sensors for priming the immune system, which could explain why some chickens get sick and others not (Ophelie, Christelle, Maxime, Romuald, & Joelle, 2024) [63]. Poultry housing systems can provide a hotbed of pathogen spread, while the reduced use of antibiotics and the transition to group housing of layer chickens have increased the demand for a more resilient layer chicken. In an earlier study, scientists discovered that birds have natural antibodies to inhibit and ward off further infection in the body, but those antibodies also sound the alarm and spark the actions of other immune system components. Earlier studies have demonstrated that the natural antibody (Nab)levels are higher in layers that showed an increased chance of survival, and are heritable and can therefore be manipulated through breeding (Cho *et al*., 2025) [21].

Key Poultry Receptors and Their Roles in Disease Susceptibility

1. Toll-Like Receptors (TLRs)

Toll-like receptors (TLRs) are a family of pattern recognition receptors (PRRs) that play a critical role in the innate immune system by recognizing pathogen-associated molecular patterns (PAMPs). In chickens, TLRs are vital for initiating immune responses against bacterial, viral, and fungal infections. The region had several genes in it. At the DNA level, it is very challenging to ascertain the difference that accounts for the difference in NAb level. “It’s likely this difference is driven by the Toll-like receptor 1A (TLR1A) gene, which makes this our primary candidate. TLR1A is a member of the TLR family, which is an important component of the immune system. This is a family of receptors, a sort of sensor, that detects common features on pathogens. “They recognize some pieces that are on many bacteria or viruses. Donc its sensors have a very wide function. But the link to NAb is new. Diagnostics and immunogenicity are both highly dependent on antigens, especially the VP2 protein, of birnaviruses. Infectious pancreatic necrosis virus (IPNV) and infectious bursal disease virus (IBDV) are members of the group of viruses known as birnaviruses; these notable differences in antigenic properties are important for strain identification and differentiation. The next paragraphs expand on the pertinence of the main defined features of birnavirus antigens (Nihashi, Ono, Kagami, & Takaya, 2019) [61]. In Poultry Diseases, TLR4: TLR4 is one of the most studied receptors in poultry immunology. It recognizes lipopolysaccharides (LPS) from Gram-negative bacteria, triggering a cascade of immune responses. Research has shown that TLR4 polymorphisms are associated with variations in disease resistance among chicken breeds. TLR2 and TLR7: These receptors are involved in recognizing bacterial lipopeptides and viral single-stranded RNA, respectively. Their activation leads to the production of pro-

inflammatory cytokines, which are crucial for controlling infections such as avian influenza and Newcastle disease. Applications in Genetic studies on TLR4 have paved the way for breeding disease-resistant poultry lines. For example, selective breeding programs targeting TLR4 variants have shown promise in reducing susceptibility to bacterial infections. And TLR-based adjuvants are being developed to enhance the efficacy of vaccines against infectious diseases in poultry.

2. Cellular Receptors for Avian Leukosis Virus (ALV)

Avian leukosis virus (ALV) is a tumor-inducing retrovirus that affects chickens. The virus enters host cells through specific cellular receptors, making these receptors critical determinants of susceptibility. In Poultry Diseases, Tva Receptor: Subgroup A ALVs utilize the Tva receptor, a member of the low-density lipoprotein (LDL) receptor family, for cell entry. Variations in the Tva receptor gene can influence susceptibility to ALV.Tvj Receptor: Subgroup J ALVs use the Tvj receptor, which belongs to the butyrophilin family. This receptor has been linked to the wide host range of ALV-J, particularly in Chinese local chicken breeds (J. Chen *et al*., 2025; Galikova *et al*., 2025; X. Zhang *et al*., 2025) [84, 31]. Identifying and modifying receptor variants through genetic engineering can lead to the development of ALV-resistant chicken lines. For instance, receptor-specific mutations have been proposed as a strategy to block virus entry (Shin, Kim, Woo, Park, & Han, 2025) [74].

3. Pattern Recognition Receptors (PRRs)

In addition to TLRs, other PRRs, such as nucleotide-binding oligomerization domain (NOD)-like receptors and C-type lectin receptors, are also crucial for pathogen recognition and initiation of immune responses. Purinergic receptors (PRs) have been identified as novel therapeutic targets for a variety of viral infections, including herpesviruses, necessitating their evaluation in relation to Marek's disease (MD) (de Geus & Vervelde, 2013) [23]. MD is a herpesvirus-induced malignancy in chickens and an economically important pathogen in the poultry industry (Boodhoo, Blake, Fazel, Shoja Doost & Sharif, 2025; Bu *et al*., 2025) [11, 13]. MD is caused by the disease-modifying viral load virus (MDV), which has a life cycle similar to that of the human varicella-zoster virus; the virus is secreted from infected skin epithelial cells and enters the host through the respiratory tract. This report investigates natural MD (MD) infection in MD-resistant White Leghorn chickens (WL) and MD-susceptible Pure Columbia chickens (PC), and investigates the PR response to disease progression. Samples from infected chickens, either without clinical signs of MD (infected) or with clinical disease (sick), included whole lung lavage cells (WLLC) and liver tissue. RNA was extracted and analyzed by RT-qPCR using gene-specific primers targeting P1, P2X, and P2Y members of the PR family. PR signaling is a potentially relevant clinical and research aspect of MDV replication (Akbar, Fasick, Ponnuraj, & Jarosinski, 2023) [1] and MD pathology. The NDV envelope contains two glycoproteins that mediate viral entry: hemagglutinin-neuraminidase (HN) and fusion protein (F). HN is a receptor-binding protein that recognizes and binds to sialic acid-glycoconjugates on the cell surface and also exhibits receptor-cleaving (sialidase) activity. These receptors are involved in the recognition of intracellular pathogens and fungal infections. For example, NOD-like receptors recognize bacterial peptidoglycans, leading to the activation of inflammasomes and the production of interleukin-1β (IL-1β), a key proinflammatory cytokine.

4. Main Newcastle Disease Virus antigens

1. Hemagglutinin-Neuraminidase (HN) Protein(AG)

It is a major ND antigen that induces the generation of neutralizing antibodies. It is commonly the Target of vaccines because a major target of the immune response, facilitating the attachment of the virus to host cells by binding to sialic acid receptors, and promoting the spread of the virus by cleaving sialic acid residues from infected and neighboring cells. 2. Fusion (F) Protein3.Nucleocapsid (N)Protein:4. Matrix (M) Protein:5. Phosphoprotein (P): Avian influenza Antigens Proteins and other elements of avian influenza are central to viral entry into host cells and to the immune response. The antigens include. Hemagglutinin (HA) Protein. One of the key surface proteins of the virus. Present in 18 subtypes (H1 to H18) in influenza viruses. Function: Attaches the virus to host cells by binding sialic acid receptors on the surface of the cell. Mediates the fusion of the viral envelope with the host cell membrane, thereby allowing the virus to enter host cells. Its Immunological Significance is a major antigen that induces the synthesis of neutralizing antibodies. The virus is typed according to this protein (H5, H7, etc.), with H5 and H7 belonging to highly pathogenic avian influenza (HPAI). 2. Neuraminidase (NA), the second major surface protein. Influenza viruses exist in 9 subtypes (N1 to N9). Name: Neuraminidase of the virus Train of Thought:

To propagate the virus, it cleaves sialic acid residues on the cell surface, which hinders virus clumping. Immunological Significance: Target of neutralizing antibodies that block viral transmission. Combined with HA to differentiate viral strains (E.g., H5N1, H7N9) 3. Accessory and Internal Proteins HA and NA are the main antigens, but other viral proteins also play a role in immunity and diagnostics: Nucleoprotein (NP): Encases the viral RNA. Targeted for use in diagnostic assays such as ELISA or PCR, Matrix Proteins (M1 and M2): Structural support to the virus. Some antiviral drugs target M2. Polymerase proteins (PB1, PB2, PA): Comparing the proteins encoded by the viral polymerase genes lijnen viral assembly and replication in host cells. Crucial in shaping viral evolution and mutations. For relevance to classification and epidemiological significance: Highly Pathogenic Avian Influenza (HPAI), e.g., H5N1 and H7N9 strains with specific HA and NA subtypes causing high poultry mortality. Low Pathogenic Avian Influenza (LPAI): This type only causes mild or no symptoms, but under certain conditions, it can mutate to the highly pathogenic kind. Application in Vaccine Development The vaccines of AIV are essentially developed by targeting HA and NA proteins, whereupon, due immune response is implemented. Vaccines are adjusted based on circulating strains to maximize their effectiveness.

6-Infectious laryngotracheitis antigen ILT

The herpes virus causes a contagious viral disease that infects poultry (Kang, Brocklehurst, Haskell, Jarvis, & Sandilands, 2025) [43]. Alphaherpes virus 1 Glycoproteins: The glycoproteins of the viral envelope are by far the most immunogenic antigens. These are involved in viral attachment, entry, and interaction with the host immune system. The key glycoproteins include. gB (Glycoprotein B): Required for viral penetration and fusion with the host cell membrane. One key target for neutralizing antibodies. gC (Glycoprotein C): Involved in viral attachment to its host cells, Key for triggering the immune response. gD (Glycoprotein D): Essential for viral attachment and entry.

Used as a strong antigen for use in development of recombinant vaccines. gE (Glycoprotein E): Tegument Proteins: Located between the viral envelope and capsid, contributing to viral replication and immune modulation. Examples: VP8 and VP16. Capsid Proteins: They also provide structural stability to the virus and serve as a target for recognition by the host immune system. Major Capsid Protein (MCP): Essential for the assembly of the viral capsid and plays a role in immune recognition. Immediate Early Proteins: These are regulatory proteins that govern viral replication and immune evasion (Aydin *et al*., 2025; Chacon *et al*., 2025; Cui *et al*., 2025) [6, 14, 22].

7. Infectious bursal disease virus (IBDV), which targets bursa B lymphocytes.

IBDV causes severe immunosuppressive disease in chickens and causes significant economic losses to the poultry industry. To date, the functional receptors to which IBDV binds and its ability to enter host cells remain unknown. In this study, we used mass spectrometry to identify host proteins in chicken bursal lymphocytes that interact with VP2. We identified the chicken transmembrane protein cluster of differentiation 44 (chCD44) and examined its interaction with the IBDV major capsid protein VP2. Overexpression and knockdown experiments demonstrated that chCD44 promoted IBDV replication. Furthermore, soluble chCD44 and anti-chCD44 antibodies blocked viral binding. Receptor reconstitution results demonstrated that chCD44 overexpression conferred viral binding to uncontrolled cells. Importantly, although IBDV was unable to replicate in uncontrolled cells overexpressing chCD44, the virus was able to enter uncontrolled cells with the help of chCD44. Our results demonstrate that chCD44 is a cellular receptor for IBDV, facilitating viral binding and entry to target cells through interaction with the IBDV VP2 protein. Infectious bursal disease virus (IBDV) causes a severe immunosuppressive disease in chickens, resulting in significant economic losses for the poultry industry. However, the specific mechanisms by which IBDV invades host cells remain incompletely understood. Chicken CD44 chCD44 likely facilitates IBDV binding to and entry into B lymphocytes, thereby acting as a cellular receptor for IBDV. With the emergence of viral variants, avian influenza (AI), avian influenza (IBD), and inflammatory bursal disease (IBD) have become major pathogens, causing significant economic losses to the poultry industry. Viruses rely on hosts to complete their life cycles and bind to specific receptors for entry into host cells. The study of viral receptors is crucial for understanding infection mechanisms and developing antiviral drugs. For example, sialic acid receptors have been identified as important entry receptors for avian influenza, Newcastle disease, and infectious bronchitis, and serve as targets for the development of therapeutic antibodies, antiviral drugs, and vaccines against these viruses. Specific antigens within pathogens are responsible for cellular receptor binding, particularly for infectious bursal disease virus (IBDV) (A. Liu *et al*., 2022). Bursal B lymphocytes are the target cells of infectious bursal disease virus (IBDV), which causes a severe immunosuppressive disease in chickens and causes significant economic losses to the poultry industry. The functional receptor for IBDV binding and entry into host cells remains unknown. In this study, we investigated chicken bursal lymphocyte host proteins that interact with VP2 using mass spectrometry. We found that the major capsid protein, IBDV VP2, interacts with the chicken transmembrane protein cluster of differentiation 44 (chCD44). Overexpression and knockdown experiments demonstrated that chCD44 promoted IBDV replication. Furthermore, soluble chCD44 and anti-chCD44 antibodies inhibited viral binding. Receptor reconstitution results demonstrated that overexpression of chCD44 failed to confer viral binding to the conditioned cells. Importantly, although IBDV failed to replicate in non-conditioned chCD44-overexpressing cells, (Kannaki, Priyanka, Abhilash, & Haunshi, 2021) [44].

8. Avian influenza Antigens

Proteins and other elements of avian influenza are central to viral entry into host cells and to the immune response. The antigens include:

Hemagglutinin (HA) Protein: One of the key surface proteins of the virus. Present in 18 subtypes (H1 to H18) in influenza viruses. Function: Attaches the virus to host cells by binding sialic acid receptors on the surface of the cell. Mediates the fusion of the viral envelope with the host cell membrane, thereby allowing the virus to enter host cells. Its Immunological Significance is a major antigen that induces the synthesis of neutralizing antibodies. The virus is typed according to this protein (H5, H7, etc.), with H5 and H7 belonging to highly pathogenic avian influenza (HPAI) (Nugroho *et al*., 2025; Pal, Pal, & Baviskar, 2021; Puga-Torres, Navarrete, & de la Torre, 2025) [62, 64, 66].

Neuraminidase (NA) is the second major surface protein. Influenza viruses exist in 9 subtypes (N1 to N9). Name: Neuraminidase of the virus. Train of Thought to propagate the virus, it cleaves sialic acid residues on the cell surface, which hinders virus clumping. Immunological Significance: Target of neutralizing antibodies that block viral transmission. Combined with HA to differentiate viral strains (E.g., H5N1, H7N9) (Gao *et al*., 2025) [32]; Accessory and Internal Proteins, HA and NA are the main antigens, but other viral proteins also play a role in immunity and diagnostics: Nucleoprotein (NP): Encases the viral RNA. Targeted for use in diagnostic assays such as ELISA or PCR, Matrix Proteins (M1 and M2): Structural support to the virus. Some antiviral drugs target M2. Polymerase proteins (PB1, PB2, PA): Comparing the proteins encoded by the viral polymerase genes and viral assembly and replication in host cells. Crucial in shaping viral evolution and mutations. For relevance to classification and epidemiological significance: Highly Pathogenic Avian Influenza (HPAI), e.g., H5N1 and H7N9. Strains with specific HA and NA subtypes cause high poultry mortality. Low Pathogenic Avian Influenza (LPAI): This type only causes mild or no symptoms, but under certain conditions, it can mutate to the highly pathogenic kind. Regarding Application in Vaccine Development, the vaccines of AIV are essentially developed by targeting HA and NA proteins, whereupon, due immune response is implemented. Vaccines are adjusted based on circulating strains to maximize their effectiveness.

9. *Mycoplasma gallisepticum*

Among the tiniest self-replicating organisms is *Mycoplasma gallisepticum*. It results in long-term respiratory illnesses, which cost the poultry business a lot of money. Because of its ability to evade the immune system, *M. gallisepticum* can remain in the host after invasion, leading to a chronic infection that lasts for a long time. Mycoplasmas employ extremely intricate immune evasion tactics, which have been deciphered by recent studies. Because of their high frequency of size and expression cycle variations, *M. gallisepticum* antigens can avoid the host humoral immune response being activated. In addition to invading non-phagocytic chicken

cells, *M. gallisepticum* controls microRNAs to alter tracheal epithelial cells' apoptosis, inflammation, and cell proliferation during the course of the illness. It has been demonstrated that *M. gallisepticum* temporarily triggers the inflammatory response before Investigation into the role of purinergic receptors (PRs) in Marek's disease (MD), a herpesvirus-induced cancer in chickens that is a significant pathogen for the poultry industry, is necessary because PRs have been identified as potential therapeutic targets for a variety of viral infections, including herpesviruses. MD is brought on by the MD virus (MDV).

10. Poxviruses

Enter host cells by binding to receptors that are highly conserved between different species, such as glycosaminoglycans. Poxviruses are divided into families that differ greatly from one another (Ali & Salama, 2024) [4], and both human and animal health can be affected negatively. The family comprises 18 genera within the subfamily Chordopoxvirinae, that is responsible for infecting vertebrates. Like other viruses, poxviruses can infect cells by entering through specific species receptors, like many other viruses, whose species are different, such as glycosaminoglycans. This enables the pathogen to infect different animals, as vascular species do not contain specific receptors, and productive infections do not stem from the host species, but rather from the extent to which the poxvirus is capable of counteracting the immune system (2). In the poxvirus family, the variation is extensive from within the different genus phenotypically and genotypically to the unique frames of species. For instance, cowpox viruses have an entire gene assortment of 214 intact genes, while all Old World orthopox viruses share 109 core genes, and variola virus commons 162 active genes and 17 that are deactivated, but might code for functional proteins. Many of the accessory genes that assist in immune response and host range evasion can account for this difference in gene content. Old-world orthopox viruses, cowpox viruses, tend to have the broadest host variety. In contrast, only animals are infected by the more specialized variola virus (Elshwihdi, Kammon, & Asheg, 2025; Fulton, Hengesbach, & Dodd, 2025; Klikha *et al*., 2024; Radaelli, Zanotto, Brambilla, Adami, & De Giuli Morghen, 2024; Trefry *et al*., 2024; Zhu *et al*., 2025) [27, 30, 47, 68, 76, 87].

11. *Aspergillus fumigatus*

Host innate immunity is crucial for the control of *A. fumigatus*. While the immune responses to *A. fumigatus* in humans and mice have been extensively investigated (18-20), the immune responses in chickens infected with *A. fumigatus* have not been fully explored. Multiple pattern recognition receptors (PRRs) are involved in the recognition of *A. fumigatus*, particularly Toll-like receptors (TLRs) and C-type lectin receptors (CLRs). Furthermore, different PRRs recognize distinct components of the fungal cell wall. TLR2 and TLR4 have been shown to be involved in the recognition of fungal DNA and zymosan. TLR4-deficient mice are more susceptible to infection with *A. fumigatus* than control mice. TLR2 signaling is crucial for the cellular response to *A. fumigatus* in both mice and humans. The C-type lectin receptor Dectin-1 recognizes *A. fumigatus* β-glucan in mouse alveolar macrophages and is involved in inducing a proinflammatory response in alveolar macrophages against *A. fumigatus*. After recognition by this receptor, a subsequent immune response mediated by PRR is triggered, and proinflammatory cytokines (such as TNF-α, IL-1β, IL-6, and chemokine Cxcl-8) are induced to participate in the defense against *A. fumigatus*. In contrast, *A. fumigatus* evades the attack of the host immune system by regulating or inhibiting related signaling pathways (28, 29). It is well known that the physiological and anatomical characteristics of the chicken respiratory tract are very different from those of mammals, and its innate immune system is also different from that of mammals. For example, the chicken TLR21 can recognize CpG DNA, while the mammalian TLR9 can recognize CpG DNA (Lima-Gomes *et al*., 2024) [53]. Therefore, the pathogenicity and immune response of *A. fumigatus* in chickens may also be different. Host innate immunity plays a crucial role in the control of *A. fumigatus*. Many literatures have studied the immune response of humans and mice to *A. fumigatus*. However, the immune response of chickens infected with *A. fumigatus* is still lacking. Different pattern recognition receptors, especially Toll-like receptors (TLRs) and C-type lectin receptors (CLRs), are responsible for the recognition of *A. fumigatus*. Furthermore, different fungal recognition receptors can recognize different parts of the fungal cell wall. TLR2 and TLR4 have been found to play a role in the recognition of fungal DNA and zymosan. TLR4-deficient mice are more susceptible to infection with *A. fumigatus* than control mice. Both human and mouse cells require TLR2 to respond to *A. fumigatus*. The C-type lectin receptor Dectin-1 can recognize *A. fumigatus* β-glucan on mouse alveolar macrophages and is required for the initial stage of the *A. fumigatus* proinflammatory response in alveolar macrophages. Recognition of cell-bound PPRs triggers a series of subsequent immune responses and the production of direct proinflammatory cytokines TNF-α, IL-1β, IL-6, and the chemokine Cxcl-8 to defend against *A. fumigatus* (El-Shemy *et al*., 2023) [26].

TLR3, present in innate immune cells, participates in preliminary virus recognition. Following the infection with the IBV-M41 strain, TLR3 mRNA expression was increased, as well as the upregulation of TLR3 and TLR7 mRNA in the trachea and lungs of chicks after intra-tracheal infection of the Conn strain (Bashir *et al*., 2019) [8]. Nephro-pathogenic IBV infection markedly elevates the expression of chicken myeloma differentiation antigen 5 (MDA5) in the kidneys, indicating the action of chicken MDA5 against IBV infection. Chicken mannose-binding lectin (MBL), a member of the type collectin family, possesses antiviral activity against IBV, since it blocks viral S1 protein attachment and prevents the infection of the tracheal epithelial cells of chickens. Furthermore, MBL is also said to be important in the regulation of both innate and adaptive immunity to IBV. Further, a high level of MBL is believed to facilitate the clearance of IBV from the trachea (Barjesteh, Taha-Abdelaziz, Kulkarni, & Sharif, 2019) [7].

The p53 protein, known as the “guardian of the genome,” helps protect cells by stopping damaged or infected cells from dividing or causing them to die. During viral infections, p53 can limit the virus’s ability to spread by triggering these defenses. However, many viruses have developed ways to block or destroy p53 so they can keep reproducing. For example, the human papillomavirus (HPV) makes a protein that removes p53, which can lead to cancer. In some cases, like influenza or HIV infections, p53 becomes more active, which helps fight the virus but can also cause cell damage. Overall, p53 plays an important role in controlling viral diseases, and understanding it can help scientists find better treatments (Beyaz, Aslan, Gok, Ozercan, & Agca, 2023; L. Yang *et al*., 2025) [10].

Materials and Methods

End note library was created to summarise the receptors associated with different pathogens in poultry using ENDNOTE X7 version purchased in 2017 manchester UK https://support.clarivate.com/Endnote/s/article/EndNote-Download-link-for-older-EndNote-versions?language=en_US Results shown in Table 1.

Rapid test was performed according to manufactural AffiVET® laboratories Cat: LSY-20094, and LSY-20054, the principle of this test is to capture antibodies on a the surface where the antigens of the tested diseases are attached. Broilers chickens from different farms were admitted to veteranary clinics with sympoms of Avian Influenza (AI), Infectious bronchitis (IB), Infectious Bursal Disease (IBD) infectious laryngotracheitis (ILT), Newcastle disease (ND) diseases and Rapid test were carried out to confirm the diagnosis then post mortem findings were performed for further confirmation. And serum were collected for p53 parameter.

P53 Expression was measured using colorimetric method according to (Beyaz *et al*., 2023) [10] using spectrophotometry and 96 well plate, the principle of spectrophotometry is that a substance absorbs or transmits light over a specific range of wavelengths, and this absorption is directly proportional to the concentration of the substance in fluid (serum of chickens).

Results and Discussion

Rapid test Results in (Fig. 1) revealed positive reaction for AI, IB. IBD, ND antigens.

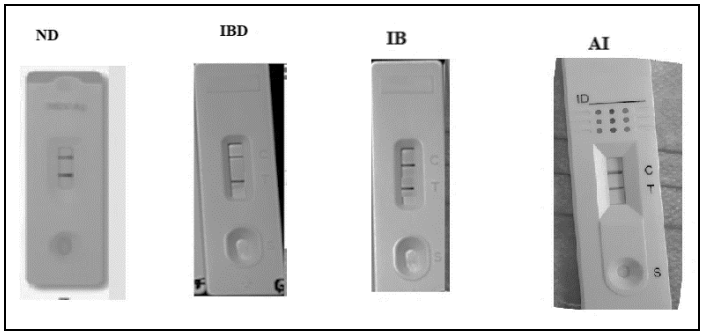

Fig 1: Results of immunoassay, Positive Result: A visible line at the test line (T) position indicates the presence of the disease antigens as an indicator of infection.

Expression of P53

The graph (fig. 2), shows that p53 expression significantly increases in all infected or diseased groups compared to the control. The Control group has very low p53 levels, while the IBD group shows a moderate increase. ND and IB groups display further elevated p53 expression, with statistical significance ($p<0.01$ and $p<0.001$, respectively). The AI group exhibits the highest p53 concentration, suggesting strong activation of the p53 pathway. This pattern indicates that disease or infection severity may correlate with increased p53 expression, reflecting a cellular stress or immune response.

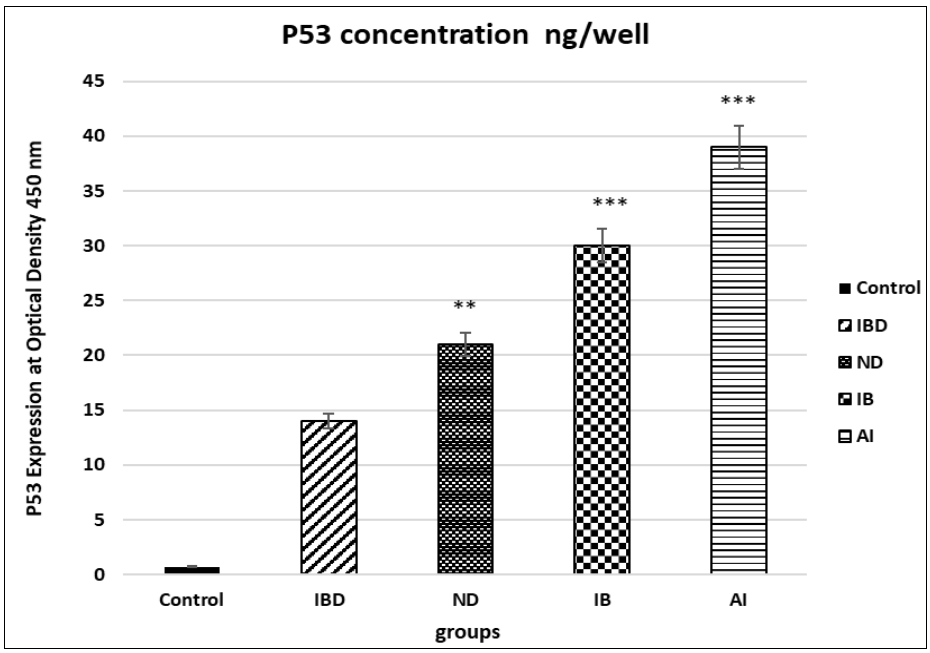

Fig 2: p53 concentration (ng/well) across five groups: Control, IBD, ND, IB, and AI. The y-axis represents *p53 expression* measured by optical density at 450 nm.

The elevated p53 expression observed in infected and diseased groups suggests that viral or inflammatory conditions trigger cellular stress responses that activate the p53 pathway. Since p53 is involved in controlling cell cycle arrest and apoptosis, its increased levels may represent a protective mechanism aimed at limiting viral replication and preventing damaged cells from proliferating (L. Yang *et al*., 2025; Y. Yang *et al*., 2025; Zhi *et al*., 2025) [81]. The highest p53 concentration in the AI group indicates a strong host defense reaction, possibly due to more severe infection or immune activation. These results support the idea that p53 plays a crucial role in the body's response to viral diseases and could serve as a potential biomarker for infection severity (Jansons *et al*., 2025; Jiang, Li, Dou, Han, & Fan, 2025; Latif *et al*., 2025; Liao *et al*., 2025) [40, 41, 48].

Conclusion

Immunity against viral diseases in poultry (table 1), such as Newcastle Disease, is induced by the HN and F proteins, explaining why vaccines against Newcastle Disease mostly target these antigens. Lentogenic strains are also used as live attenuated vaccines that induce immunity without causing

disease. Newcastle Disease Virus has two major antigens, which are the Hemagglutinin-Neuraminidase (HN) and Fusion (F) proteins. These proteins are responsible for attachment, entry, and dissemination of viruses and are the principal targets of vaccines and the immune response. The existence of neutralizing antibodies specifically targeting these antigens is crucial for the prevention and control of NDV infection. The Role of ILTV Antigens in Immunity. Viral glycoproteins (e.g., gB, gC, gD): Slant primary targets for neutralizing antibodies that block viral access to host cells. Generic vaccines induce humoral (antibody-mediated) and cellular immune responses. Capsid and tegument proteins: Have a minimal role in stimulating immune responses. Practical for diagnostic tests for ILTV infection. ILTV antigens, particularly the glycoproteins, also play a role in allowing the virus to escape antibody-mediated immunity by the host, which allows for the maintenance of the virus in infected birds. Nitric oxide acts as a marker of viral replication in poultry vaccines and recombinant mediating multiple immune responses towards glycoproteins (gB, gD, and gC). Inactivated vaccines use ILTV antigens so that protective immunity can be stimulated without disease induction.

The role of poultry receptors in disease susceptibility and resistance is a critical area of research with significant implications for the poultry industry. Toll-like receptors, cellular receptors for ALV, and other PRRs are at the forefront of this field, offering insights into the mechanisms of immune response and opportunities for genetic and nutritional interventions. By leveraging advanced genomic tools, vaccine technologies, and artificial intelligence, the industry can address the challenges posed by infectious diseases, ensuring sustainable poultry production and global food security. p53 is a pivotal regulator in poultry health, influencing antiviral defense, tumor suppression, and immune system function. Further research into p53's mechanisms could lead to improved disease management and prevention strategies in poultry farming.

Future work

The advent of CRISPR-Cas9 technology offers unprecedented opportunities to edit receptor genes, creating disease-resistant poultry lines. For example, modifying TLR4 or ALV receptor genes could significantly reduce the prevalence of bacterial and viral infections (Cheema *et al*., 2025; Rahimi *et al*., 2025; D. Zhang, Liu, & Zhong, 2025) [17, 84, 69, 13] and vaccine development.

Receptor-based adjuvants and vaccines targeting specific PRRs can enhance immune responses, providing long-lasting protection against infectious diseases. This approach is particularly promising for combating emerging pathogens such as avian influenza and Newcastle disease. Finally, Integration of Artificial Intelligence; Deep learning techniques, such as those used in smartphone-based disease detection frameworks, can complement receptor-based interventions by enabling early diagnosis and monitoring of poultry diseases.

Table 1: Summary of Identified receptors of known pathogens of common poultry diseases

No	Receptor	Antigen	Disease	Reference
1	Sialic Acid Receptor	HA, NA	Avian Influenza Virus AI	(Chang *et al*., 2023; Ichikawa *et al*., 2024; Kim *et al*., 2025; Lv *et al*., 2023; Song *et al*., 2025; C. Zhang *et al*., 2022) [38, 83, 75]
2	chCD44 specific cellular receptor(s) with viral envelope glycoprotein,	VP2	Infectious bursal disease IBD	(A. Liu *et al*., 2022)
3	sialoglycoconjugates	Hemagglutinin-Neuraminidase) Protein	Newcastle Disease ND	(Espejo, Goraichuk, Suarez, Breedlove, & Toro, 2025; Lee & Gladney, 2025; Neog, Kumar, & Trivedi, 2025) [28, 49, 60]
4	Purinergic Receptors (PRs)	Marek's disease tumor-associated surface antigen (MATSA)	Marek Disease MD	(Akbar *et al*., 2023; Akbar & Jarosinski, 2024) [1, 2]
5	TLR1A	certain parts present on many bacteria or viruses.	Many diseases	(Bovenhuis *et al*., 2022; Khan *et al*., 2024; Mitra, Bramberger, Bilic, Hess, & Liebhart, 2021; Nihashi *et al*., 2019) [12, 45, 58, 61]
6	Sialic Acid Receptor	S1	Avian Infectious Bronchitis IB	(Schwegmann-Wessels *et al*., 2011; Winter, Schwegmann-Wessels, Cavanagh, Neumann, & Herrler, 2006) [78]
7	C-type lectin receptor, dectin-1,	β-Glucan	*Aspergillus fumigatus*	(Belalmi *et al*., 2025; Dieste-Perez, Holstege, de Jong, & Heuvelink, 2025; Hatim & Denning, 2025; Wei *et al*., 2024) [9, 25, 35, 77]
8	host glycosaminoglycans (GAGs)	viral proteins	Avipoxvirus (avian pox)	(Elshwihdi *et al*., 2025; Fulton *et al*., 2025; Gentile, Carrasquer, Marco-Fuertes, & Marin, 2024; Klikha *et al*., 2024; H. Liu, Li, Tang, Ding, & Wang, 2024; Zhu *et al*., 2025) [27. 47, 87]
9	A family of variable lipoproteins (VlhA) cytadhesin molecule GapA and other cytadherence-related molecules such as CrmA extracellular matrix (ECM) proteins	Cellular receptors	*Mycoplasma gallisepticum*	(Gornatti-Churria *et al*., 2025; Hosny *et al*., 2025; Kachabi, Pourbakhsh, & Zahraei Salehi, 2025) [34, 37, 42]
10	Tva Receptor Tvj Receptor	Subgroup A ALVs	Avian Leukosis Virus (ALV)	(Xu *et al*., 2025; X. Zhang *et al*., 2025) [79, 84]
11	glycoproteins (gB, gD, and gC) Receptor	glycoproteins (gB, gD, and gC)	Infectious laryngotrachitis ILT	(Ponnusamy *et al*., 2025; Regragui *et al*., 2025) [65, 70]

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