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Popular Article

## TLRs: Revolutionary Site for Immunomodulatory Action in Poultry

**Khushboo Panwar<sup>1</sup>, Esha Sinha<sup>1</sup>, Gorre Venu<sup>1</sup>**

Division of Veterinary Microbiology, ICAR- Indian Veterinary Research Institute  
Izatnagar, Bareilly- 243122, Uttar Pradesh, India

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### Introduction

Toll-like receptors are a group of pattern recognition receptors (PRRs) that play a crucial role in the innate immune system. They are involved in recognizing pathogen-associated molecular patterns (PAMPs) present on various microorganisms, such as bacteria, viruses, and fungi. When a TLR detects these patterns, it triggers a signaling cascade that leads to the activation of immune responses to combat the invading pathogens.

In poultry, TLRs are expressed on various immune cells, including macrophages and dendritic cells. When these cells encounter pathogens, TLRs recognize specific PAMPs on the pathogens' surfaces. This recognition triggers a signaling cascade that activates the immune response to combat the infection.

Some key points about the role of TLRs as immunomodulatory sites in poultry are:

**Pathogen Recognition:** Different TLRs recognize different types of pathogens, allowing the immune system to detect a wide range of microorganisms.

**Activation of Immune Response:** Upon pathogen recognition, TLRs activate immune cells to produce pro-inflammatory cytokines and other molecules that help recruit and activate other immune cells, thus initiating an immune response.

**Antigen Presentation:** TLR activation also plays a role in antigen presentation, where immune cells process and present antigens from pathogens to adaptive immune cells (such as T cells and B cells) to trigger a specific immune response.

**Immunization and immunomodulation:** TLR agonists have been studied as potential adjuvants in

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poultry vaccines, as they can enhance the immune response and improve the efficacy of vaccines.

**Genetic Variability:** Different poultry species and breeds may have variations in the types and expression levels of TLRs, which can influence their immune responses and susceptibility to certain diseases.

In poultry, as in other vertebrates, TLRs are essential for recognizing and responding to pathogenic infections. Although there are several TLRs identified in chickens and other avian species, the specific TLRs present can vary among different bird species.

For example, in chickens (*Gallus gallus domesticus*), ten TLRs have been identified, including, TLR1LA and TLR1LB, TLR2-1 and TLR2-2, TLR3, TLR4, TLR5, TLR7, TLR15 which is related to TLR2 phylogenetically and TLR21 which seems to be orthologous to amphibians and pieces.

**Immunomodulatory Function of TLR Agonist:** Different TLR agonists have distinct immunomodulatory functions based on the specific TLR they activate. Here are some common TLR agonists and their immunomodulatory functions:

**TLR1 Agonist:** TLR1 is one of the TLRs found in poultry and is involved in recognizing microbial components, especially those from bacteria. The activation of TLR1 triggers an immune response that aims to clear the invading pathogens. Agonists for TLR1 have been investigated as potential immunostimulants in poultry to enhance their immune responses against bacterial infections. By stimulating TLR1, researchers aim to enhance the innate immune system's ability to detect and respond to bacterial threats more effectively.

**TLR2 agonists:** Lipoteichoic acid (LTA), Induces pro-inflammatory responses, such as the production of cytokines like interleukin-1 (IL-1) and tumor necrosis factor-alpha (TNF-alpha). Peptidoglycan (PGN), Stimulates cytokine production and promotes the activation of immune cells, including dendritic cells and macrophages. Pam3CSK4, Induces the production of pro-inflammatory cytokines and activates neutrophils.

**TLR3 agonists:** Polyinosinic: polycytidylic acid (Poly I:C), Activates antiviral responses and enhances the production of type I interferons (IFNs).

**TLR4 agonists:** Lipopolysaccharide (LPS), Potent inducer of pro-inflammatory responses, including the production of cytokines and chemokines.

**TLR5 agonists:** Flagellin, Induces the production of pro-inflammatory cytokines and chemokines.

**TLR7 agonists:** Imiquimod (R837) and Resiquimod (R848), Induces the production of type I IFNs and pro-inflammatory cytokines. Used in certain topical creams for the treatment of skin conditions



and viral infections. And various research is going on as potent immunomodulators in poultry.

**TLR15 Agonist:** TLR15 is a relatively recently discovered member of the TLR family, and its precise role in poultry immunity is still being elucidated. TLR15 is primarily expressed in the gastrointestinal tract and respiratory system of chickens. Activation of TLR15 has been shown to induce the production of pro-inflammatory cytokines and promote the recruitment and activation of immune cells. TLR15 agonists are being investigated as potential immunomodulators in poultry like some fungal proteases, with the aim of enhancing immune responses and improving disease resistance.

**TLR21 Agonist:** TLR21 is another important TLR in poultry, and its agonists have also been studied for their immunostimulatory effects. TLR21 is known to recognize and respond to unmethylated CpG motifs present in the DNA of certain viruses and bacteria. CpG oligodeoxynucleotides (CpG ODNs), Induces type I IFN production and promote Th1-biased immune responses. Activation of TLR21 helps in initiating an immune response against these pathogens, thus contributing to the host's defense mechanisms. Researchers have explored the potential of TLR21 agonists to boost the immune response in poultry, leading to improved protection against viral and bacterial infections.

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