

## **GUARDIANS OF THE GATEWAY: UNVEILING THE SECRET WORLD OF MUCOSAL IMMUNITY**

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### **OVERVIEW OF THE ISSUE**

Vaccines have long been the key to preventive medicine and that is even more true today as diagnostic capabilities continue to provide more precise and complete pictures of pathogen interaction. But, are mucosal vaccines really appropriate? As vaccinology continues to advance at warp speed, it is important for practitioners to understand the *why* behind the *how* of vaccine administration and efficacy.

The immune system is a complex and multi-layered protection apparatus for living organisms that is continuously adapting and improving. White blood cells are a large component of the immune system with three main categories: granulocytes, lymphocytes and monocytes. Basophils, eosinophils and neutrophils are the granulocytes with neutrophils making up the majority of white blood cells in the body. Monocytes represent less than 10% of all white blood cells in a normal system and function by simply destroying invaders, typically during chronic infections. Lymphocytes are further divided into B cells, T cells, and natural killer cells. B cells are responsible for producing antibodies or immunoglobulins (Ig).

Antibodies are large Y-shaped proteins that identify and neutralize foreign objects like bacteria and viruses. Antibodies recognize specific antigens on pathogen surfaces. Five basic types of immunoglobulins of interest are IgG, IgA (SIgA), IgM, IgE, and IgD.

IgE is responsible for the Type I hypersensitivity reactions and is most active during parasitic infections, autoimmune processes, and in venom protection. IgE actually provides a more robust response upon secondary exposure to an antigen.

IgG makes up 75-80% of immunoglobulins in circulation at any point in time, making it the most common Ig. IgG is the utility player of the Ig team as it functions in many different ways to protect against pathogens. It can bind to the pathogen and immobilize it for phagocytosis by other immune cells, activate complement, bind to and neutralize toxins, play a role in both Type I and II hypersensitivity reactions, lay the foundation for life-long immunity and is the only Ig to cross the placenta.

IgM is the largest Ig and is found in the peripheral blood and in circulating lymphatic fluid. It provides protection quickly in the face of infection, but is short-lived only lasting weeks rather than months or years like IgG. IgM is a powerful activator of Complement and also can activate inflammation, opsonization, and destruction of pathogens. IgM primarily protects the vascular system but can be released into the mucosal system via mucosal epithelial transport.

IgA is found in almost all secretions and acts mostly at the mucosal membranes serving as the first-line of defense for most pathogens when they attempt to enter the body naturally. IgA is

referred to as secretory IgA (SIgA) once it moves into the mucus layer, but many use the terms interchangeably. SIgA can bind to pathogens independent of antigenic specificity to trap invaders on the luminal surface and largely prevent invasion into tissues. SIgA is NOT efficient at activating Complement and so is less likely to trigger damaging inflammation upon activation when compared to IgG, IgE and other Ig's. SIgA can cross-link antigens expressed on pathogen surfaces thereby causing them to clump or clump up and make for easier removal.

Mucosally-administered vaccines typically stimulate local tissue immunity via IgA as well as systemic immunity through IgG production while parenterally administered vaccines stimulate only IgG production. In the case of pathogens with short incubation periods, this distinction makes a difference! If a pathogen enters through the respiratory tract unimpeded by IgA, then clinical signs may have time to develop in a short-incubation period before the IgG is triggered and the pathogen is eliminated. However, if IgA has been produced against the pathogen via a mucosal vaccine, then the pathogen is prevented from producing disease in the tissue at the point of entry, no matter the incubation period length, thereby reducing disease and shedding of the pathogen.

For incredibly contagious diseases with a complex of pathogens, such as Canine Infectious Respiratory Disease Complex, mucosal vaccination for Canine parainfluenza can be key to reducing potential for infection and rapid transmission among social dogs and mucosal administration of canine parainfluenza vaccine has been proven to decrease clinical signs and stop transmission when compared to parenteral vaccination alone.

Mucosal vaccination is safe, effective, and in some cases, may be superior to parenteral vaccination in preventing clinical disease and transmission of critical pathogens.

## References/Suggested Reading

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