INTRODUCTION TO MONOCLONAL ANTIBODIES:
Latest Advancement in Companion Animal Veterinary Medicine

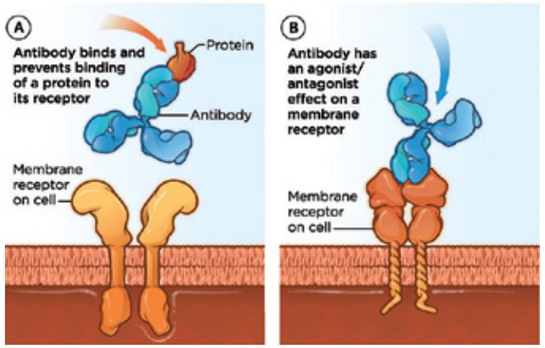
Innovations in human medicine and technology have long inspired new therapies and treatments in animal health. Biological therapy is the newest area being explored to help improve the health and quality of life of companion animals.

Biological therapy can take the form of vaccines, like immunotherapy, or therapeutic monoclonal antibodies. Examples of antibodies used in human health therapeutic areas include the development of Humira® for the treatment of rheumatoid arthritis and Xolair® for the control of asthma.

Monoclonal Antibodies (mAbs): A New Frontier for Animal Health*

All mammals produce antibodies to protect against foreign proteins or antigens introduced into the body. These are produced by a variety of plasma cells resulting in polyclonal antibodies. Scientists are now developing monoclonal antibodies that can be used therapeutically to mimic the immune system and to direct it against one specific antigen. The antibody is engineered with sequences compatible with the immune system of the target species (e.g., called "caninization" for the dog) so that the body does not recognize them as foreign.

These antibodies and therapeutic mAbs exert biological activity through various mechanisms. The antigen-binding fragment can interact with high specificity and affinity to soluble targets like cytokines in the blood and tissue interstitium to prevent these molecules from binding to their receptors and thus prevent cytokine activation of the receptor (A). Alternatively, an antibody or therapeutic mAb can bind to a target receptor on a cell surface to block its activation. These are described as antagonistic mAbs; most human mAbs fall under this category (B).



Monoclonal antibodies have three main safety advantages:
1) mAbs have very specific targets.
2) mAbs don't have intercellular activity—as a result, there are few anticipated side effects and reactions.
3) mABs are not metabolized by the kidney or liver but are catabolized within the cells resulting in amino acids, which are recycled within the body.

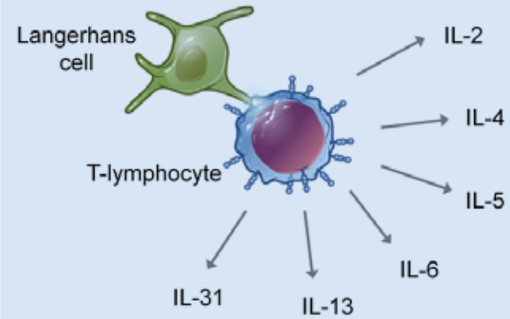
Applying Monoclonal Antibodies (mAbs) in Veterinary Dermatology

Capitalizing on knowledge from the development of human monoclonal antibodies, veterinary researchers are developing therapeutic mAbs for the treatment of many important and common conditions that affect the quality of life of dogs and cats such as osteoarthritis pain, chronic kidney disease, oncologic conditions, cardiac disease and atopic dermatitis.

The past decade has produced more insights into the pathophysiology of allergic skin disease—in particular, atopic dermatitis. Cytokines such as interleukin (IL)-2, -4, -6, -13 and -31 play an important role in orchestrating the cycle of itch as well as inflammation. Each of these cytokines plays a specific role in the production of clinical signs such as pruritus and inflammation.

Research has demonstrated that IL-31 plays a major role in the induction of pruritus in dogs with atopic dermatitis. It also has effects on keratinocytes and the inflammatory cells that are part of the condition. A mAb that inhibits the function of only IL-31 holds the potential to uniquely and specifically target the signs of atopic dermatitis without the side effects associated with broad-spectrum pharmacotherapy.

CYTOKINES INVOLVED IN CANINE ALLERGIC SKIN DISEASE



Many cytokines implicated in allergic skin disease (e.g., atopic dermatitis) are secreted from activated T-lymphocytes.

Effective therapies for atopic dermatitis inhibit T-cell and cytokine function. How they affect immune function or other organ systems may lead to differential safety profiles.

Learn More About mAb Therapy

This article provides a high-level view of mAb technology. More information is available at **www.itchcycle.com/antibodytherapy**.

* All data from: Olivry T, Bainbridge G. Advances in veterinary medicine: therapeutic monoclonal antibodies for companion animals. *Clinician's Brief*. http://www.cliniciansbrief.com/article/advances-veterinary-medicine-therapeutic-monoclonal-antibodies-companion-animals. Published March 2015. Accessed December 3, 2015.

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