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Intestinal health and mucosal immunity in the young animal

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One of the strategies to maintain optimal gut health in animal production in the absence of antibiotic growth promoters is to support the active immunity of the animal. Immunity at the level of the digestive system is concentrated in the mucosal immune system of the gut associated lymphoid tissue (GALT). Therefore, the GALT is the obvious target if we want to increase intestinal immunity.

M cells and dendritic cells sample the intestinal contents and bring pathogens in close contact with macrophages, B and T cells in specialized regions in the intestinal epithelium like e.g. the Peyer's patches (inductive site). Macrophages destroy the pathogen and stimulate the B and T cells to launch an immune response that is specific to this pathogen. Depending on the pathogen and the co-stimulatory signals this response can be the activation of cellular (cytoxic T lymphocytes (CTL)) or humoral (antibodies) immunity. Antibodies (IgA) are secreted at the effector site and transported through the epithelial cells to neutralize the pathogens already in the intestinal lumen. Macrophages thus act at the first line and stimulate a whole cascade of events leading to final antibody production.

The intense contact between intestinal contents and immune cells at the mucosa offers opportunities to modulate intestinal immunity via the feed. While immunostimulating activities are claimed on many feed additives like phytoproducts, organic acids, chelates, pre- and probiotics and many others these additives mostly have only bacteriostatic effects or indirect effects on the immune system. On the contrary, it has been widely demonstrated that β-glucans have a direct immunostimulating effect. More specifically they bind to a receptor on macrophages and increase their activity towards stimulation of B and T cells. As a consequence, increased antibody titers after vaccination and better protection after challenges with a pathogen have been observed when β-glucans were incorporated in the feed. However, not all β-glucans are equally effective and their interaction with the receptor on the macrophage depends on their primary and secondary structure (degree of polymerization (DP) and degree of substitution (DS)).

Since immunization and challenge trials are laborious, time consuming and therefore very costly we propose to develop a model system based on *in vitro* assays that can be used to evaluate the immunomodulating property of feed additives. Β-glucans with different purity, DP and DS can thus be compared. Most if not all sources of β-glucans that are used in feed are impure or semi-purified compounds that contain a variety of oligosaccharides including mannan-oligosaccharides or MOS. These molecules can interfere with the attachment of pathogenic bacteria (e.g. enterotoxic Escherichia coli or ETEC) to the intestinal epithelial thus reducing their colonization. Next to immunomodulation this is another aspect of the possible positive effect of these compounds on gut health. In our lab, interference of attachment of bacteria to the intestinal epithelium can also be quantified *in vitro*.

As outlined above, once a pathogen is sampled out of the intestinal contents a local immune response in the intestinal mucosa is generated in different steps. At first macrophages and other phagocytic cells (like dendritic cells ; non-specific immunity) take up the pathogen. They destroy the

pathogen with enzymes and O-radicals and process it for presentation to local T cells. Phagocytic cells also secrete pro-inflammatory cytokines that stimulate the activity and proliferation of those T and B cells that are most fit to attack the type of pathogen that was presented by the phagocytic cell (specific immunity). Finally the B cells will produce antibodies (IgA) that can be secreted in the intestinal lumen to neutralize the pathogens.

The benefits and values of these assays are that the activity of all the samples within each test will be comparable. Also, the results will give an activity profile of each sample, indicating at what level the immunological response is most probably modulated when the sample is included in the feed. Furthermore, the capacity of a sample to interfere with attachment of *E coli* is a measure of protection against attachment and colonization of the intestinal epithelium *in vivo*. And finally, validation of the results of the *in vitro* screening towards gut health and protection against pathogenic challenges will have to be performed by *in vivo* tests