Immune modulation: its importance for disease control and vaccination

Nowadays, the trend to reduce the prophylactic supplementation of animal feed with antibiotics is gaining traction in all parts of the world. However, supplementation with antibiotics led to reduced incidence of some diseases, increased growth rates, and improved feed efficiency in animal production.

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There is now, however, increasing evidence that such long term and non-specific exposure to antibiotics leads to bacterial resistance with significant impacts on the future efficacy of these critical drugs.

Consequently, several countries have restricted or banned the prophylactic use of antibiotics in animal feed. This gives a new urgency to the search for alternative strategies to maintain animal performance and protect animals from disease.

Additionally, the use of antibiotics to treat animals is under pressure. Therefore, veterinary and all other stakeholders need to change their strategy, moving away from a reactive treatment approach, to a preventive strategy, keeping animals healthy, consequently reducing the need for antibiotics.

There is a constant drive to use specific, clearly defined ingredients to help producers reach both aims reducing antimicrobials while maintaining animal health and productivity. An area not systematically targeted yet is the immune system of an animal.

Protecting immunity

Several well-known diseases have a down-regulation of the immune system as part of their strategy of infecting a host. Even some of the strategies aimed at maintaining health come at a cost in terms of productivity, such as intensive vaccination programmes. Not to forget young animals, whose immune system is immature, but nonetheless present.

Additionally, bridging the immunity gap – when the maternal immunity is gone and the newborn's immune system is not yet well developed – is crucial.

By priming the immune response with a feed supplement, it is possible to enhance animal health at a minimal energy cost. Even without a disease challenge there might be a need to assist the immune system.

By supporting the immune system there is a potential to lessen all those negative effects. Of course, modulating the immune system always comes with the fear of serious energy costs and loss in feed conversion.

The key is to target those species or ages that genuinely need support and to standardise the active ingredients and dosage to such an extent that an over-regulation can be avoided.

Treatment	Group	Aleta
1	Control without challenge	-
2	Control with challenge	-
3	β-1.3-glucan with challenge	100 g/T

Table 1. Experimental design.

Immune modulation and β-glucans

Natural immune-modulators are gaining traction in animal production. β-glucans are known immune modulators, which have been demonstrated to stimulate specific and non-specific immune responses and as such increase resistance to infections and diseases.

Several immune cells in the animal's body, like the antigen presenting cells such as macrophages and dendritic cells, can recognise β-(1,3)-glucan carbohydrate structures by specific receptors on their surface (such as the dectin-1 receptor).

In response to binding β-(1,3) glucan, the immune cells will become more active in engulfing, killing and digesting invading pathogens and will initiate a signalling cascade stimulating the attraction, formation and activation of other immune cells.

Mode of action of algae β-(1.3)-glucans

Linear β-(1,3)-glucans are derived from algae, Euglena gracilis, as this organism stores the molecule as a polysaccharide storage product, located in its cytoplasm.

β-glucan is known because of its immune modulating properties. It is commercially used to be supplemented via the feed to food producing animals in order to enhance performance and resistance to diseases by supporting the immune system. In order to have immunomodulatory effects, the molecule has to be taken up by immune cells.

A study has been done to test if the algae derived β-(1,3)-glucan is taken up by immune cells and if other immune signalling pathways are induced.

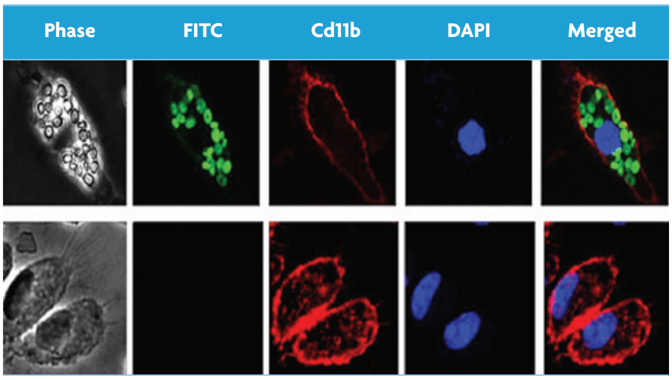
Mouse macrophages were collected from mouse intestine and spleen and distributed into chamber slides (5×10^5 cells/chamber).

Triplicate wells were incubated with Fluorescein Isothiocyanate (FITC)-linked β-(1,3)-glucan preparations (5μg/ml) for two hours.

Unbound particles were washed away, and cells were incubated for 72 hours longer and then stained for macrophages marker (CD11b) and nucleus marker (4',6-diamidino-2-phenylindole, DAPI). Cells were imaged using confocal microscopy.

The results of the confocal imaging showed that β-(1,3)-glucan was readily phagocytosed by mice macrophages (Fig. 1), as the image shows a clear presence of the FITC-labelled β-(1,3)-glucan in the cytoplasm of the macrophage).

Fig. 1. Mouse macrophages stained for surface (CD11b, red) and nucleus (DAPI, blue) marker, supplemented with FITC-labelled β-(1,3)-glucan (row 1) and non-supplemented macrophages (row 2). Merged picture of FITC, DAPI and CD11b staining shows uptake of β-(1,3)-glucan by mouse macrophages.



Help the animals to resist diseases

Coccidiosis continues to be the most frequently diagnosed disease and is consequently perceived as the most important economical disease in the poultry industry.

This disease is caused by protozoan parasites developing

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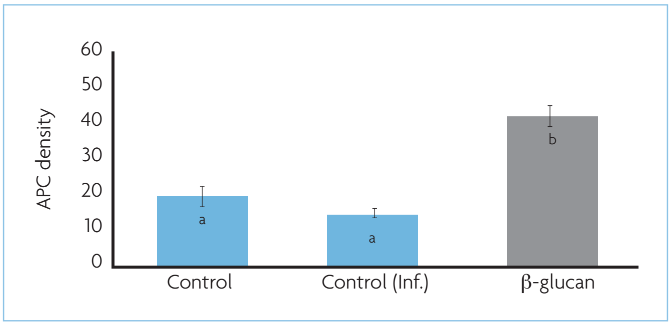

Fig. 2. Antigen presenting cells (APCs) density.

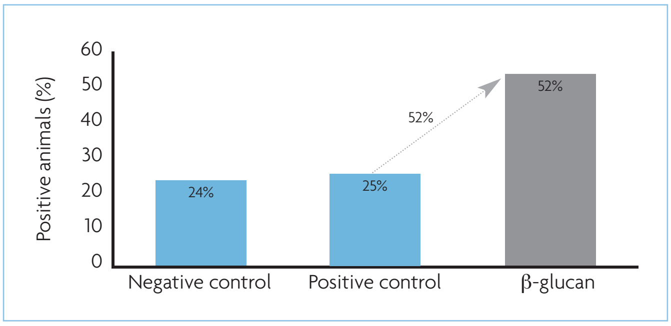

Fig. 3. Positive animals after vaccination.

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within the intestine of poultry. Natural immune stimulants like β-glucans are perceived as being a suitable alternative and help in anticoccidial programmes.

Therefore, a scientific trial was conducted to test the effects of a dietary β-(1.3)-glucan (Aleta, Kemin) supplementation on the intestinal lesions and immunity of broilers undergoing a coccidiosis challenge.

This trial lasted for 20 days and consisted of 240 birds divided over three treatments, with eight replicates per treatment.

The experimental design is shown in Table 1 focusing on the recommended dose of β-(1.3)-glucans.

Chicks were challenged with E. acervulina (75,000 oocysts/bird), E. maxima (40,000 oocysts/bird), and E. tenella (50,000 oocysts/bird) by oral gavage on day 14 of the study.

On day 20 lesion scoring was performed. Samples of the jejunum were evaluated by immuno-histochemistry to measure antigen presenting cell (APC) density.

Results show the β-(1.3)-glucan treated group had lower lesion scores across all three regions of the gut regardless of Eimeria species. β-(1.3)-glucan enhanced recruitment and activation of immune cells in the intestinal tissue, as the group receiving algae β-glucan showed significant elevated levels of APCs, which explain the reduction in intestinal lesions.

β-(1,3)-glucans for better vaccination

One of the most common viral infections in chickens, infectious bursal disease (IBD), is caused by the IBD virus which destroys B-lymphocytes leading to immunosuppression, and consequently poor performance. Vaccination is most important in IBD prevention and control.

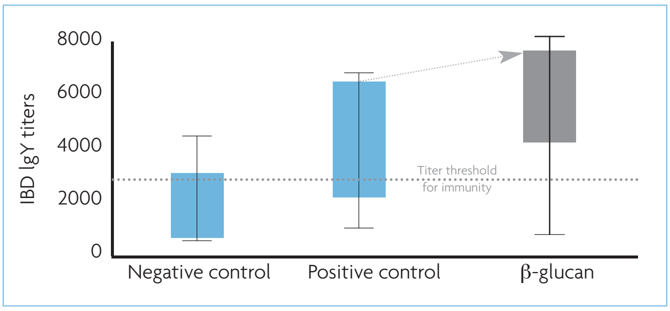
The efficient vaccine helps to prevent the disease by boosting the animals' immune system to produce antibodies that in turn fight the invading virus.

A new tool in improving vaccination efficiency is the use of an in-feed supplementation modulating the immune system. The aim of this trial was to test if the use of β-(1,3)-glucans (Aleta) in feed could enhance Gumboro vaccination efficacy in poultry, where a broiler was taken as a model. 96 male Ross 308 broilers were divided over three treatments: a negative control group, a positive control group and an algal β-glucan group.

The broilers were orally vaccinated on day 18 with a live freeze-dried IBD vaccine. To monitor vaccination efficiency, blood samples were taken at day 18 and 35 to measure antibody titers (IgY) against IBD.

During this trial we observed a 16% higher IBD specific antibody titer (IgY), and 52% more seroconverted birds, in the algal β-glucan supplemented group compared to the non-supplemented, vaccinated group (positive control),

Fig. 4.IBD IgY titers (ELISA units) per treatment at day 35 in relation to the titer threshold protective immunity.



Conclusion

Immune modulation and support can be a useful tool to reduce the need for antimicrobials. Supporting the immune system by in feed supplementation of algae β-glucan showed that not only the number of animals that react to the vaccination doubled, but those that react develop higher antibody titers. ■