Oral  $\beta$ -glucans modulate systemic antigen responses in dogs and pigs

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The cell wall glucans of yeasts and fungi consist of a linear backbone of  $\beta$ -1,3-linked glucosylunits with  $\beta$ -1,6-linked side chains (1, 2). Although a lot is already known about the mechanism of action of  $\beta$ -1,3/1,6-glucans on the innate immune system (3, 4), there is still a lot to be learned about their effects on the adaptive immune system in mammals. We aimed to determine if oral supplementation could modulate a systemic immune response. The latter was examined in pigs using a model antigen, but also in dogs analyzing the response against a parenteral vaccine. In three experiments using newly weaned pigs, Macrogard, a  $\beta$ -1,3/1,6-glucan from Saccharomyces cerevisiae, was administered in the feed during three different time periods (one, two and three weeks) and the adjuvant effect of this  $\beta$ -glucan was determined on a systemic immunisation with thyroglobulin. A first immunisation occurred during  $\beta$ -glucan supplementation, while the second one occurred after ceasing the administration. Macrogard exerted significantly higher thyroglobulin-specific primary immunoglobulin (Ig) M and secondary IgA antibody responses in serum. However, Macrogard suppressed the thyroglobulinspecific proliferation of peripheral blood mononuclear cells. A higher dose of Macrogard significantly increased thyroglobulin-specific IgM but not IgA responses, and the animals itself showed hyperaemia. Suppression of the T-lymphocyte proliferation might account for the absence of the switch from IgM to IgA. Weight gain and feed conversion were also determined, without significant differences between groups.

In another study, also dogs were orally given Macrogard in tablets, daily for four weeks. At the end of this period, the total serum IgA level decreased significantly in the group treated with the glucan compared to that in the control group as well as compared to the concentrations before supplementation. In contrast, the total serum IgM level rose significantly, whereas no effect on the IgG level occurred. Similar changes were seen in *Bordetella*-specific IgA and IgM titres following vaccination during the supplementation period. The IgA concentration also became significantly lower in the saliva and tears of the glucan group than in the placebo group. The effects disappeared one week after the cessation of the supplementation. There seems to be a temporary decrease in the switch from IgM to IgA due to oral Macrogard supplementation in dogs probably by its suppression of T-lymphocyte proliferation as seen in pigs.

In conclusion, oral  $\beta$ -glucans are able to modulate the humoral as well as the cellular immunity against a systemically administered antigen.

- 1. Manners et al. 1973. The structure of a beta-(1--6)-D-glucan from yeast cell walls. Biochem J 135, 31-36.
- 2. Zekovic et al. 2005. Natural and modified (1-->3)-beta-D-glucans in health promotion and disease alleviation. Crit Rev Biotechnol 25, 205-230.
- 3. Brown and Gordon, 2003. Fungal beta-glucans and mammalian immunity. Immunity 19, 311-315.
- 4. Kataoka et al. 2002. Activation of macrophages by linear (1 -> 3)-beta-D-glucans Implications for the recognition of fungi by innate immunity. Journal of Biological Chemistry 277, 36825-36831