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Benefits of β-glucans

β-glucans are cell wall polysaccharides that are composed of D-glucose monomers linked through β-glycosidic bonds, which are abundant in fungi/yeast, bacteria and plants. β-glucans from microorganisms are mainly comprised of β-(1→3) links and some β-(1→6) linked branches, while plant β-glucans are typically β-(1→3) and β-(1→4) linked without branching (Jin et al., 2018). A bacterial β-glucan (curdlan) is composed of only β-(1→3) links without any branches. The structure and molecular characteristics of individual β-glucans are considered to be important for their specific biological responses.

There has been much focus on β-glucans for their potential health benefits, from prebiotics for microbiota modification to vaccine adjuvants and cancer immunotherapy.

Prebiotic

Recently, the definition of a prebiotic was updated and expanded to "a substrate that is selectively utilized by host microorganisms conferring a health benefit" (Gibson et al., 2017). The prebiotic potential of (oat-derived) β-glucans has been demonstrated *in-vitro* (Fehlbaum et al., 2018) and has been reported *in-vivo* for different host species (Jayachandran et al., 2018).

Immunomodulation

β-glucans are probably best known for their immunomodulatory potential, although such effects may arise from a prebiotic effect through modification of the intestinal microbiota and/or its activity and resultant metabolites (e.g. short-chain fatty acids). However, β-glucans can also be recognised by pattern recognition receptors (PRRs) of the innate immune system, which are expressed by host, particularly immune, cells. Dectin-1 (a C-type lectin receptor) is a principle receptor involved in the recognition of β-glucans and is expressed on the surface of monocytes, macrophages, neutrophils, dendritic, T and intestinal epithelial cells, with evidence of expression by chicken immune cells (e.g. heterophil and peripheral blood mononuclear cells) (Nerren and Kogut, 2009). Other PRRs are also believed to be involved in the recognition of β-glucans, such as complement receptor 3, TLR2, mannose, scavenger or lactosylceramide receptors (de Graaff et al., 2018). Activation of dectin-1 and/or other PRRs

by β-glucans leads to signalling pathways within the respective cells, involving nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) and interferon regulatory factors (IRFs), and the production of an array of cytokines, including pro-inflammatory, and chemokines. These signalling proteins shape the nature of the immune response, including cell types and functional activity. Studies have shown that β-glucans from various sources can influence innate and adaptive immune cell responses (Jin et al., 2018) and, interestingly, it has been suggested that β-glucans may induce anti-inflammatory immune responses under normal/homeostatic circumstances but enhance pro-inflammatory responses when pathogen challenged (Teng and Kim, 2018). Certainly, in production animals (broiler chickens), Cox et al. (2010) reported that yeast β-glucan dietary supplementation altered intestinal cytokine and chemokine expression but did not induce a strong immune response or impair growth performance in an experiment devoid of (specific) pathogen challenge.

Conclusions and applications

The immunomodulatory effects of β-glucans are widely accepted and there is renewed interest in their potential for cancer immunotherapy and as vaccine adjuvants. β-glucans have been reported to be taken up by intestinal epithelial and/or M cells and subsequently detected in splenic, lymph node and bone marrow macrophages, suggesting migration of intestinal immune cells and carriage of β-glucans (de Graaff et al., 2018). This implies β-glucans can be translocated to tumour sites, can activate innate immune cells and counteract the typically immunosuppressive nature of the tumour microenvironment. Similarly, β-glucans administered via various routes have been shown to be good adjuvants, enhancing vaccinal immune responses in various animal models (Jin et al., 2018). The potential and immunomodulatory capability of β-glucans continues to be explored and employed in food animal production species, particularly in the context of antibiotic reduction strategies and disease management (Teng and Kim, 2018; Vetvicka et al., 2014; Meena et al., 2013).

The specific characteristics of the β-glucan needs to be considered for its potential effects. Dectin-1 has been reported to be highly specific for β-glucans with a pure (1→3) backbone (with at least seven glucose units and one β-(1→6) branch) and that mixed backbones of β-(1→3) and β-(1→4) linkage (e.g. plant-derived β-glucans) are not recognised by this receptor (Stier et al., 2014). However, cereal β-glucans have been demonstrated to have immunomodulatory capacity, implicating the involvement of the other (PR) receptors, with higher cellotriosyl:cellotetraosyl ratio β-glucans possessing greater activity (Mikkelsen et al., 2014). Of course, cereal β-glucans are associated with negative performance consequences in farm animals, which may limit their use/investigation for immunomodulation. Further research is, however, needed to better understand the structure-receptor-immune response relationship of β-glucans to refine the application of these effective immunomodulators.

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