Review
InvivoGen

β-Glucans: bittersweet ligands of Dectin-1

β-Glucans have been consumed for many centuries for their healing properties. Since the discovery of their immunomodulating capabilities, about five decades ago, β-glucans have attracted a great deal of attention in the biomedical arena. Numerous articles have reported the biological activities of β-glucans including anti-infective, anticancer and wound repair activities. Unfortunately, many inconsistencies and contradictions remain unresolved.

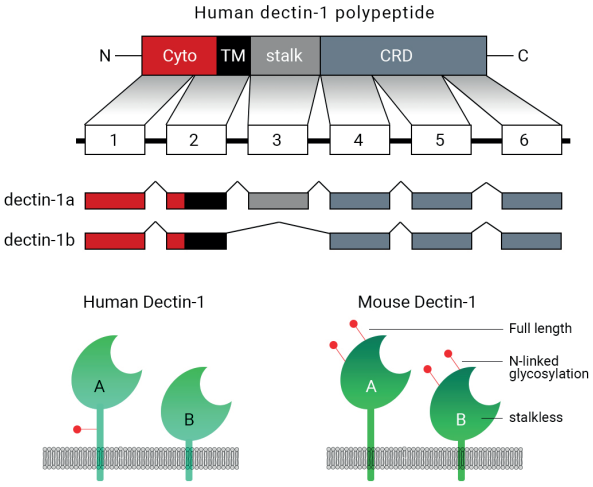
FUNGAL PAMPS

β-Glucans are carbohydrates consisting of a backbone of glucose residues joined by β-(1->3) linkages with β(1->6) linked glucose side-chain residues. These polysaccharides are major cell wall structural components in fungi and are also found in plants and some bacteria. Depending on the source, β-glucans vary in the type of linkage, the degree of branching, molecular weight and tertiary structure.

β-Glucans are not synthesized by animals and thus are recognized by the innate immune system as pathogen-associated molecular patterns. This recognition is mediated by pattern recognition receptors and, among them, Dectin-1 has emerged as the primary receptor for these carbohydrates [1].

RECOGNITION BY CLRS

Dectin-1 is a C-type lectin receptor expressed primarily by cells of myeloid origin, including macrophages, dendritic cells and neutrophils. In human and mouse, Dectin-1 is alternatively spliced into two major isoforms, a full-length A isoform and a 'stalkless' B isoform. Human Dectin-1 (hDectin-1) is structurally similar to mouse Dectin-1 (mDectin-1) with 60% identity in amino acid sequence, but display differences in the number and position of

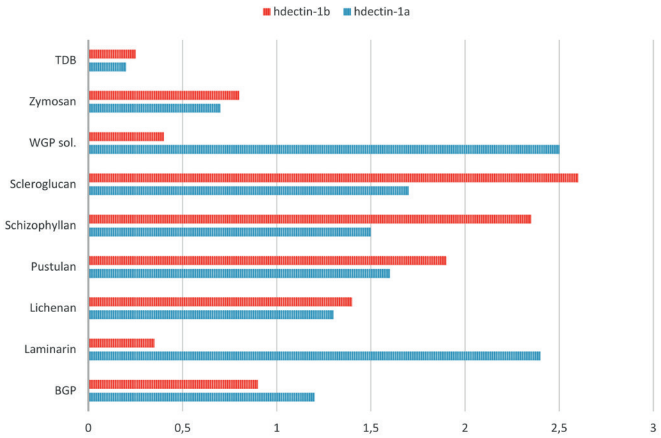


N-linked glycosylation. N-linked glycosylation has been shown to affect the cell surface expression and ligand binding of Dectin-1 [2] and may explain some of the contradictory results published in the literature.

DECTIN-1 SIGNALING

Binding of β-glucans to Dectin-1 triggers a variety of cellular responses via the Syk/CARD9 signaling pathway, including phagocytosis, respiratory burst and secretion of cytokines. Although not yet fully understood, the ability of β-glucans to induce these cellular responses is influenced by their macromolecular structure. Dectin-1 is usually described as a β(1-3)-linked glucan specific receptor.

Stimulatory activity of Dectin-1 ligandsHowever, we along with others [3] have found that linear β(1-6)-linked glucans, such as the lichen β-glucan pustulan, also bind and activate Dectin-1. It is well accepted that particulate β-glucans, such as the widely used yeast cell-wall fraction zymosan, bind to and activate Dectin-1 inducing cellular responses. In contrast, the interaction of soluble β-glucans with Dectin-1 is subject to debate.



Stimulatory activity of Dectin-1 ligands:
HEK-Blue™ hDectin-1a and HEK-Blue™ h Dectin-1b cells wre stimulated with 1µg/ml or 10µg/ml Dectin-1 ligands, respectively, and 10 µg/ml TDB. After 24h incubation, Dectin-1 induced NF-κB activation was assessed by measuring the levels of SEAP using the QUANTI-Blue™ assay.

The general consensus, though, is that soluble β-glucans, such as laminarin, bind to Dectin-1 but are unable to initiate signaling [4]. In accordance with published studies on mDectin-1, we found that a soluble mDectin-1 receptor was able to bind particulate as well as soluble β-glucans and that cells expressing the murine dectin-1 gene could respond to particulate but not soluble β-glucans.

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However, we obtained different responses with hDectin-1. Cells expressing the human stalkless dectin-1b isoform behaved similarly to mDectin-1-expressing cells, whereas cells expressing the human full-length dectin-1a isoform responded to both particulate and soluble β-glucans. We found no data in the literature confirming or contradicting this latter result.

Most published studies focus exclusively on the responses of mDectin-1 to β-glucans, which may differ considerably from the response mediated by hDectin-1. In addition to discrepancies between mDectin-1 and hDectin-1, many inconsistencies exist due to the use of very different, and often impure, β-glucans, and the analysis of different cell types and model systems. Recognition of β-glucans by the immune system appears very complex and further studies are required to fully understand the immunomodulating properties of these molecules.

INVIVOGEN'S PRODUCTS

PRODUCT	DESCRIPTION	UNIT SIZE	CAT.CODE	PRICE
Pustulan	Dectin-1 Agonist - Beta-glucan from Lasallia pustulata	100 mg	tlrl-pst	More info
Zymosan	Cell wall preparation of S. cerevisiae	100 mg	tlrl-zyn	More info
Laminarin	Dectin-1 ligand - Soluble beta-glucan from Laminaria digitata	100 mg	tlrl-lam	More info
Fc-mDectin-1a	Soluble murine Dectin-1 receptor	50 µg	fc-mdec1a	More info

For more information, please visit : **www.invivogen.com**

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