

NATURALLY DERIVED POLYSACCHARIDES INTERACTING WITH PATTERN RECOGNITION RECEPTORS

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Naturally derived polysaccharides have the potential to trigger pattern recognition receptors (PRRs) on the surface of immune cells, thereby initiating an immune response [1]. Therefore, polysaccharides could represent an attractive alternative for novel immunotherapeutic drugs. In this study, water-soluble polysaccharides isolated from selected medicinal plants and a fungus from Norway and Brazil were screened for their ability to activate an immune response by interacting with PRRs. The polysaccharides included, among others, pectins and arabinogalactan-proteins, and their structures are previously characterized. To identify polysaccharides of potential interest for immunotherapy, human embryonic kidney (HEK293) blue reporter cell lines transfected with specific human PRRs (TLR2-TLR1, TLR2-TLR6, TLR3, TLR4, TLR5 and Dectin-1a) were utilized. Additionally, THP1-Blue™ cells were used to monitor NF-κB activation in a monocyte-like environment. Several of the polysaccharides showed the ability to activate both TLR2-TLR6 and TLR4, while some also activated TLR2-TLR1 and the classical β-glucan receptor Dectin-1a. Furthermore, the same polysaccharides activating multiple PRRs showed a potent activation of THP1-Blue™ cells, comparable to the known immunogenic crude Zymosan [2]. The most active polysaccharides were pectins isolated from *Opuntia ficus-indica* (L.) Mill. and *Daphne mezereum* L., as well as arabinogalactan proteins isolated from *Persea americana* Mill. Interestingly, of the most potent stimulants of THP1-Blue™ cells, only the pectic polysaccharide from *D. mezereum* showed interaction with Dectin-1a. This indicates a lesser importance of this receptor for immune stimulation in THP1-Blue™ cells. In conclusion, this research shows the ability of purified water-soluble polysaccharides to stimulate multiple PRRs, possibly contributing to a synergistic effect on stimulation of immune cells.

References:

1. Yin M., Zhang Y., Li H., *Front. Immunol.* **2019**, *10*, 145
2. Gantner B. N., Simmons R. M., Canavera S. J., Akira S., Underhill D. M., *J. Exp. Med.* **2003**, *197*(9), 1107-17