FUNGAL POLYSACCHARIDES FROM *INONOTUS OBLIQUUS* INDUCE MACROPHAGE ANTI-CANCER ACTIVITY

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Plant and fungal polysaccharides have been reported to interact with the immune system in multiple ways and the effects on macrophages have been studied extensively. The polysaccharides can bind pattern recognition receptors (PRRs) on the surface of macrophages and initiate an immune response [1,2]. Within cancer immunotherapy there is an increasing awareness on the role of macrophages, and the therapeutic potential of switching tumor-associated macrophages (TAMs) from a pro-tumor to an anti-tumor state [2,3]. When properly activated, macrophages can kill cancer cells directly, secrete cytokines for immune cell recruitment to tumors, and stimulate T cells to fight metastases [4]. As such, macrophages are attractive targets for novel anti-tumor immunotherapy drugs. We have evaluated six polysaccharides isolated from the medicinal fungus *Inonotus obliquus* for their ability to activate mouse and human macrophages. Of these, two water-soluble polysaccharides, AcF1 and AcF3, were able to trigger anti-tumor functions of macrophages [5]. Macrophages were activated by AcF1 and AcF3 to secrete nitric oxide and the pro-inflammatory cytokines tumor necrosis factor-α (TNF-α) and interleukin (IL)-6. The polysaccharides also triggered production of IL-12p70 when combined with interferon-γ, a central cytokine for anti-tumor immunity, and induced macrophage-mediated inhibition of cancer cell growth *in vitro* and *in vivo*. AcF1 and AcF3 were shown to interact with the PRRs Toll-like receptor 2 (TLR2) and TLR4, and dectin-1a. The polysaccharides were complex and highly branched, consisting of a (1,3/1,6)-β-glucose (Glc) region, in addition to monomers such as (1,6)-α-galactose (Gal) and (1,4)-α-galacturonic acid (GalA) [6]. We have shown in this study that the polysaccharides AcF1 and AcF3 from *I. obliquus* have a strong potential for cancer immunotherapy by binding to multiple PRRs and by inducing potent anti-cancer activity of macrophages.

References:

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