TH1-Oriented Immunomodulating Activity of Gel-Forming (1→3)-β-Glucan

Yoshiyuki Adachi, Yoko Suzuki, Takafurri Jinushi, Toshiro Yadomae, and Naohito Ohno

Laboratory of Immunopharmacology of Microbial Products, Tokyo University of Pharmacy and Life Science, 1432-1 Horinouchi, Hachioji, Tokyo 192-0392, Japan

Several (1→3)-branched (1→3)-β-D-glucans (β-glucans) from mushrooms are known to enhance various immunopharmacological activities such as antitumor activity. Some of them, including lentianan and sonifilan (SFG), have been used clinically for cancer therapy in Japan. We have been investigating various immunopharmacological effects of β-glucans, such as grifolan (GRN) from Grifola frondosa (Dicks.: Fr.) S. F. Gray and sclerotinia sclerotiorum glucan (SSG) from Sclerotinia sclerotiorum IFO 9395, which were isolated originally by our group. GRN has a similar primary structure to SFG, but SSG consists of β-(1→3)-polyglucose backbone with every second residue substituted with monoglucosyl branches. The ultrastructures of GRN and SSG are distinct from that of SFG. Namely, GRN and SSG contain a mixture of single and triple helix conformers, whereas SFG is composed of triple helices only. Using SFG and SFG-OH, which is a single helical conformer prepared by alkaline treatment of SFG, we also found previously that the biological activities of β-glucans, that is, blood clearance, reactivity of limulus factor G activation, and nitric oxide (NO) synthesis in vivo and in vitro, are strongly associated with their conformation. However, we do not yet know the details of activities of various β-glucans on helper T-cell modulation.

The immunomodulating effects of various gel-forming (1→3)-β-glucans on balancing helper T-cell activity were examined in a murine model. Plasma from mice that were injected with GRN or SFG-OH and trinitrophenyl ovalbumin (TNP-OVA) contained TNP-specific antibodies of both IgG1 (Th2-mediated) and IgG2a (Th1-mediated) isotypes. Administration of SSG and TNP-OVA significantly augmented the synthesis of IgG2a antibodies, while the synthesis of IgG1 was reduced. However, SFG did not enhance the antibody response. Furthermore, it was shown by intracellular cytokine staining that the proportion of interferon-γ (IFN-γ)^+CD4^+ double-positive cells among the CD4^+ T cells from mice administered with SSG was most strongly increased by addition of PMA and A23187. On the other hand, the expression of IL-12 p40 mRNA was more markedly elevated in splenocytes after combined administration of TNP-OVA plus SSG than after administration of TNP-OVA alone. The highest IFN-γ production was observed when adherent cells of mice administered TNP-OVA and SSG were cultured with TNP-primed lymphocytes. This effect of administration of SSG on IFN-γ production was completely inhibited by addition of anti-IL-12 mAb. In conclusion, our study showed that β-glucans have various effects on the Th1- or Th2-dependent antibody subclasses; in particular, SSG induces the development of Th1 cells via the interleukin-12 (IL-12) pathway.