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学 位 論 文 要 旨
Dissertation Abstract

氏名： Ika Dyah Kumalasari
Name

学位論文題目： Evaluation of Immunological Functions of Indonesian Local Crops
Title of Dissertation （インドネシアの農産品の免疫機能解明に関する研究）

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Functional food is defined as a food that satisfactorily demonstrates beneficial effects on one or more target functions in our body. Some of the functional foods improve the physical function and reduce the risk of specific pathologies by modulating the immune, secretion, nerve, circulating, or digestive system. Activation of the immune response contributes to reduction of the risks of diseases caused by pathogens.

Indonesia has many local crops that can be potentially developed as functional foods. At first we screened some of Indonesian local products especially tubers that are commonly used as the carbohydrate and fiber sources.

Arrowroot (*Maranta arundinacea* L.) extracts stimulated IgM production by HB4C5 cells and Ig (IgG, IgA, and IgM) production by mouse primary splenocytes *in vitro*. In addition, arrowroot extracts strongly enhanced IFN-γ production by splenocytes *in vitro*. Oral administration of arrowroot extracts to mice for 14 days increased the Ig levels in serum. These results suggest that arrowroot extracts contain Ig production-stimulating factors.

Bengkoang (*Pachyrhizus erosus* L.) fiber extracts (BFE) facilitated IgM production by HB4C5 cells. In addition, production of IgM, IgG, and IgA by mouse primary splenocytes was facilitated by BFE in a dose-dependent manner. BFE also significantly facilitated production of both IL-5 and IL-10 by splenocytes. Ig production activity of lymphocytes from the spleen, Peyer's patch (PP), and mesenteric

lymph node was significantly activated by oral administration of BFE to mice for 14 days. BFE significantly enhanced Ig production by PP lymphocytes, especially IgA production. The levels of IgG, IgM, and IgA in serum were also significantly enhanced by intake of BFE. Furthermore, the cytokine (IL-6, IL-10, TNF-α, TGF-β, and IFN-γ) production activity of lymphocytes was also facilitated by oral administration of BFE. It is suggested from these results that BFE activates both B cells and T cells.

On the other hand, BFE stimulated the phagocytotic activity of macrophage cell line J774.1 cells. In addition, BFE significantly facilitated production of TNF-α and IL-6 by J774.1 cells and mouse primary peritoneal macrophage (P-Mac) *in vitro*. The phagocytotic activity of P-Mac from the BFE-administrated BALB/c mice was also significantly enhanced. BFE also increased the production of nitric oxide by J774.1 cells and facilitated the gene expression level of inducible nitric oxide synthase (iNOS). The effect of BFE on cytokine production was investigated under the co-existence of Toll-like receptor 4 (TLR4) inhibitor to evaluate the molecular mechanism of BFE. Treatment of J774.1 cells with a TLR4 inhibitor significantly inhibited the stimulatory effect of BFE on IL-6 and TNF-α production, suggesting that BFE induces TLR4 signaling. BFE also facilitated gene expression of adaptor protein MyD88, IL-1 receptor associated kinase 1 (IRAK1) and TNF-receptor associated factor 6 (TRAF6). The major molecules involved in TLR4 signaling such as JNK, P38, ERK and translocation of NF-κB were activated by BFE. These results suggest that BFE activates J774.1 cells via activation of signaling pathways of TLR4.