Biological Activities of *Lactobacillus casei* through the Regulation of Host Immune Function

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*Lactobacillus casei* strain Shirota (LcS) has been demonstrated to have beneficial effects in numerous disease models, especially murine autoimmune disease and carcinogenesis models, via host immune modulation. It has also been reported that LcS induced recovery of the host immune responses that were decreased by treatment with carcinogens, and that augmented the natural killer activity and T cell functions of host immune cells. After LcS is ingested by the host, it is incorporated into M cells in Peyer's patches (PP) and digested to form active components. In PP, macrophages or dendritic cells that phagocytosed LcS gained ability to produce tumor necrosis factor-α. The components of LcS digested in PP were then recognized through toll-like receptor 2 in macrophages, resulting in the production of several cytokines which elicit varied responses in host immune cells. Also, it was observed by 2D-PAGE analyses that the expression level and/or the phosphorylation of some proteins in PP and mesenteric lymph nodes were definitely altered after the ingestion of LcS, providing more evidence of cellular responses.

Screening and Development of Unique Microbial Functions and Their Industrial Applications

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Over the past decade, the industrial use of microbial functions, such as their unique enzyme systems, catalysis and so on, has developed rapidly and is gathering increasing attention, particularly their use in solving environmental problems. Here, several unique microbial enzymes or reactions recently discovered in our laboratory and now used industrially are introduced, through which I will emphasize importance of screening for potential microorganisms and mutual collaboration between academia and industries.

Screening is a key step in process development, because, in many cases, the substrates in industrial processes are artificial compounds, and enzymes known to catalyze suitable reactions for such processes are still unknown. Therefore, screening for novel enzymes that are capable of catalyzing new reactions is constantly needed. In addition, the discovery of new enzymes sometimes provides clues for designing new enzymatic processes. One of the most efficient and successful means of finding new enzymes is to screen a large number of microorganisms, because of their characteristic diversity and versatility. However, it is obviously very difficult to propose rational method of screening for novel enzymes; it is something like midnight-walk without moonlight. There are three important stages in a general strategy: (1) designing the process and deciding the type of enzymatic activity desired; (2) deciding which groups of microorganisms are to be selected and screened; and (3) designing an appropriate, convenient and sensitive assay that will allow as many microorganisms as possible to be screened. It is also important, during the course of screening, to observe the functions of microorganisms carefully in order to obtain the desired (but serendipitous or random) result.

Single Cell Oil Production by *Mortierella alpina*

A filamentous fungus, *Mortierella alpina* 1S-4, was isolated as an potential producer of triacylglycerol containing C20 polyunsaturated fatty acids (PUFAs) such as arachidonic acid. With this discovery as a starting point, we conducted employing methods from metabolic engineering and molecular biology for controlling cultures and breeding mutant strains. These parental and mutant strains are now used for large-scale production of a variety of PUFAs.