Immunopotentiation by oral intake of liposomal β-sitosterol

Naoto Oku, Hiromichi Imanaka, Kosuke Shimizu and Tomohiro Asai
Global COE Program, Department of Medical Biochemistry, Graduate School of Pharmaceutical Sciences, University of Shizuoka

A number of plant components are known to have immunopotentiaion activity. In this study, we investigated the activity of phytosterol through determining chemopreventive activity against experimental tumor metastasis. Tumor metastasis occurs through various steps and the level of host defense is one factor affecting tumor metastatic potential. We previously demonstrated that intravenous injection of lower number of metastatic tumor cells could be failed to form metastatic colony in target organ, whereas larger number of them could complete tumor metastasis. This finding indicates that immune surveillance in the host plays an important role in the initial phase of tumor metastasis. Thus, increase in host defense may prevent the tumor cells from occurring metastasis.

At first, liposomal β-sitotosterol, or liposomal cholesterol were orally administered into mice, and the absorption and distribution of β-sitosterol and cholesterol of these mice were examined. As a result, uptake quantities of cholesterol in plasma and small intestine of mice was increased after liposomal cholresterol had been administered. On the contrary, β-sitosterol was merely detected in the plasma post-administration of liposomal β-sitosterol, suggesting that β-sitosterol was poorly absorbed into plasma. Next, using DiI labeled liposomes, the mucoadhesive behavior of these liposomes were examined. As a result, liposomes containing β-sitosterol and cholesterol showed same adhesive and penetrative behavior. DiI in β-sitosterol liposomes and cholesterol liposomes penetrated into the intestinal mucosa of ileum in the same manner. Interestingly, IL-18 production in the small intestinal epithelial cells were intensely observed by the administration of liposomal β-sitosterol. Finally, oral administration of phytosterol liposomes showed chemopreventive effect on tumor metastasis due to upregulation of host defense from metastatic tumor cells. The results of present study suggest that oral administration of liposomal β-sitosterol may enhance mucosal immunity, especially NK cell activity. Therefore, liposomal β-sitosterol might serve as effective means for preventing metastasis and intestinal immunopotentiation.