P - 5

Modulation of gene expression by green tea and its constituents

Mamoru Isemura, Koichi Abe and Naohide Kinae
Global COE Program, Graduate School of Nutritional and Environmental Sciences, University of Shizuoka

Green tea is known to have beneficial effects on several diseases including cancer, obesity and cardiovascular diseases. In order to understand the molecular basis for such effects, we have examined modulation of gene expression by green tea and its constituents.

Previously, we reported that dietary supplementation of powdered green tea for 1 week reduced gene expression of gluconeogenic enzymes, glucose-6-phosphatase (G6Pase) and phosphoenolpyruvate carboxykinase (PEPCK), in the mouse liver, suggesting its anti-diabetic effect. The results from the DNA microarray analysis showed that administration of green tea with a high catechin content for 4 weeks resulted in reduced G6Pase gene expression in the rat liver, suggesting its chronic effect. Reduction in gene expression of PEPCK was not found after 4 weeks, suggesting that the reducing effect on PEPCK gene expression is rather acute. It was also shown that administration of epigallocatechin gallate (EGCG) in mice for 4 weeks gave the results similar to those from the experiment in the rats as examined by reverse transcription-polymerase chain reaction (RT-PCR). Thus, the effect on G6Pase gene expression of green tea appears to be attributable, at least in part, to EGCG.

When the liver of the galactosamine-treated rats, an experimental model of hepatitis, was examined by the DNA microarray technique, green tea with a high catechin content was shown to attenuate galactosamine-induced up-regulation of the expression of inflammatory cytokines, confirming our previous results from the RT-PCR analysis. These findings suggest protective effects of green tea on hepatitis.

Green tea and EGCG are known to have apoptosis-inducing activity on a variety of tumor cells, providing an explanation for its anti-cancer effects. It was found that gene expression of 67kDa laminin receptor in differentiated HL-60 cells after treatment with 1α,25-dihydroxyvitamin D3 and *all-trans*-retinoic acid was down-regulated, providing one explanation for the lower sensitivity to EGCG-mediated apoptosis as compared with untreated HL-60 cells. The finding supports the view that EGCG induces apoptosis preferentially in cancer cells as compared with normal counterparts.