S-IV-3

CHEMOPREVENTIVE FOOD PHYTOCEHMICALS: SCREENING, ACTION MECHANISMS, AND METABOLISM

Akira Murakami, Koichi Koshimizu, and Hajime Ohigashi[1]

Department of Biotechnological Science, Faculty of Biology-Oriented Science and Technology, Kinki University, Wakayama 649-6493. [1]Division of Food Science and Biotechnology, Graduate School of Agriculture, Kyoto University, Kyoto 606-8502, Japan
E-mail: murakami@bio.waka.kindai.ac.jp Fax: +81-736-77-4754

Cancer chemoprevention Chemoprevention with strategies using food phytochemicals is currently regarded ascompose one of the noticeable most visible and promising scientific fields for cancer control. A large body of data from both epidemiologic and rodent studies has demonstrated that the ingestion of various vegetables and fruits is occasionally beneficial for cancer risk reduction of cancer risks in humans. One of the goals of our research is to discover prominent chemopreventive agents from in edible plants by highlighting focusing on the molecular mechanisms of multistage carcinogenesis. We have so far screened more than 400 extracts from vegetables and fruits of found in Japan, Thailand, Indonesia, and Malaysia for their inhibitory activity toward the tumor promoter-induced Epstein-Barr virus (EBV) activation for as a means to evaluate their evaluation of cancer preventive prevention activityactivities. As the We have foundresults, that edible plants from Southeast Asian countries showed demonstrated a markedly higher potential to prevent carcinogenesis as compared to than those of from Japan. More than 40 active constituents, including acetoxychavicol acetate (ACA, *Languas galanga*) (1), auraptene (AUR, *Citrus natsudaidai*) (2), nobiletin (NOB, *C. unshiu*) (3), and zerumbone (ZER, *Zingiber zerumbet*), have been isolated and identified by activity-guiding fractionation of the active extarctsextracts. These food factors showed marked cancer preventive activity in various rodent models model organs such as the skin, tongue, esophagus, colon, or and liver. It is notable that ACA was found to significantly suppressed suppress superoxide anion generation from NADPH oxidase and as well as that of nitric oxide (NO) from inducible NO synthase

(iNOS) present in inflammatory leukocytes. InterestinglyFurther, ACA notablymarkedly attenuated an endotoxin-induced I κ-B protein degradation, leading to a blockade of the transcriptional activity of NF-κB being responsible for *iNOS* gene expression, while. Free free radical generation inhibitors, including ACA, indeed suppressed thewere found to suppress activated leukocyte-induced mutagenesis as detected by co-culturing differentiated HL-60 cells and AS52 cells. On the other hand, AUR selectively induced phase-2 enzyme activity in mouse livers, and whereas ZER induced apoptosis in a human adenocarcinoma cell line, colo205, and yet suppressed TPA- or azoxymethane-induced expression of cyclooxygenase-2 (COX-2) in rats or and mice. Moreover, we have recently found that both AUR and NOB havepossess intriguing characteristics of high localizability to and delayed clearance from digestive organs. These results suggest that our approach investigation may lead to the discovery of novel and promising cancer preventivespreventive agents in vegetables and fruits.

References:

(1) Y. Nakamura et al., *Cancer Res.*, 58, 4832-4839, 1998.
(2) A. Murakami et al., *Carcinogenesis*, 21, 1843-1850, 2000.
(3) A. Murakami et al., *Cancer Res.*, 60, 5059-5066, 2000.