

[S-13]

**Cell Signaling Cascades as Prime Targets for
Chemoprevention with Dietary Phytochemicals**

Young-Joon Surh, Ph.D.

Seoul National University

Chemoprevention refers to the use of agents to inhibit, reverse, or retard tumorigenesis. Numerous phytochemicals present in edible plants have been reported to interfere with a specific stage of the carcinogenic process. Some antioxidative and anti-inflammatory substances derived from dietary or medicinal plants exert chemopreventive properties by targeting intracellular signaling molecules or events. Curcumin, a yellow colouring agent contained in turmeric (*Curcuma longa* L., Zingiberaceae), has been reported to possess strong anti-tumor promotional as well as anti-inflammatory and antioxidant activities. Recent studies from this laboratory have revealed that curcumin inhibits expression of cyclooxygenase-2 (COX-2) in mouse skin treated with the tumor promoter 12-*O*-tetradecanoylphorbol-13-acetate (TPA) through inactivation of the redox-sensitive eukaryotic transcription factor NF- κ B. Inhibition of NF- κ B by curcumin appears to be mediated by blocking ERK1/2 and p38 MAP kinases. [6]-Gingerol, a pungent ingredient present in ginger (*Zingiber officinale* Roscoe, Zingiberaceae), inhibited TPA-induced tumor necrosis factor- α production, ornithine decarboxylase activity, and skin tumor promotion in female ICR mice. Its anti-tumor promoting effects appears to be associated with inhibition of p38 MAP kinase and of subsequent NF- κ B activation. Capsaicin, a major pungent principle of hot chili pepper (*Capsicum annuum* L., Solanaceae) with potential anti-inflammatory and anti-tumor promoting properties, also suppressed TPA-induced activation of NF- κ B and AP-1, in mouse skin *in vivo*. The soy isoflavone genistein inhibits COX-2 induction in TPA- and TNF- α -stimulated human mammary epithelial cells by inactivating ERK1/2 and NF- κ B. Resveratrol, a phytoalexin present in grapes and red wine, attenuated TPA-induced expression of COX-2 and activation of AP-1 in mouse skin. The green tea polyphenol epigallocatechin 3-gallate (EGCG) inhibited activation of NF- κ B and AP-1 in the TPA-stimulated human mammary epithelial cell line. Under the same experimental

conditions, EGCG suppressed COX-2 induction, while it upregulated heme oxygenase-1 (HO-1). The molecular basis of reciprocal regulation of COX-2 and HO-1 by EGCG is under investigation.