Dear Colleague,

Welcome to the fall issue of the *Nutrition Frontiers*, a quarterly newsletter from the Nutritional Science Research Group (NSRG), Division of Cancer Prevention, NCI. This issue showcases the anti-inflammatory properties in black raspberries, retinoic acid's role in the differentiation process, and kava in lung tumorigenesis. Plus, learn about our spotlight investigator, Robert Turesky, upcoming announcements and more.

**RESEARCH UPDATE: WHAT'S NEW IN BASIC SCIENCE**

**Black Raspberries’ Modulate Inflammatory and DNA Methylation Properties**

Wang and colleagues investigated whether the anti-inflammatory activities of black raspberries (BRBs) are able to modulate DNA methylation in the colon, spleen and bone marrow and whether BRBs prevent colonic ulceration in mice given dextran sodium sulfate (DSS), a colitis-inducing substance. Colons were collected on days 7, 14, and 28 from mice given either: 1) drinking water and control diet; 2) 1% DSS in the drinking water and control diet; or 3) 1% DSS in drinking water and a 5% BRB diet. The 5% BRB diet decreased DSS-induced ulceration on day 28. At day 7, the berry diet inhibited the nuclear localization of NF-κB p65, a potent proinflammatory transcription factor, and the suppression continued through days 14 and 28. Also at day 7, the berry diet exerted its protective effects on DNA methylation processes, including decreased promoter methylation of tumor suppressor genes in the Wnt pathway. These findings support the possibility that BRBs may reduce or prevent DSS-induced colon tumorigenesis in mice.
Retinoic Acid-Induced Leukemic Cell Differentiation

Retinoic acid (RA), a metabolite of vitamin A, plays a role in the differentiation processes of multiple cell types. Acting as a chemo-therapeutic agent, RA induces myeloid differentiation in acute promyelocytic leukemia. In a recent study, Geil and Yen report a novel, although not exclusive, mechanism of transcriptional regulation by Raf-1 which is phosphorylated and translocated to the cell nucleus. Once there, it causes transformed cells to undergo terminal differentiation and G0 cell cycle arrest. They have recently demonstrated a novel RA-induced differentiation activity in a patient-derived leukemic cell line, HL-60. RA stimulates interaction of phosphorylated Raf-1 with the nuclear transcription factor NFATc3 to activate CXCR5 gene. Thus Raf-1 has a role in driving the nuclear signaling of RA-induced differentiation of leukemic progenitor cells. This new regulatory role for gene transcription augments the understanding of the function of Raf-1.

Kava Blocks Lung Tumorigenesis in A/J Mice

Following up on research that a commercial kava product blocks lung tumorigenesis in A/J mice, Narayanapillai and colleagues recently identified the active ingredient in kava as dihydro-methysticin (DHM). DHM demonstrated chemopreventive activity against the tobacco-specific pulmonary carcinogen 4-(methylnitrosamo)-1-(3-pyridyl)-1-butanone (NNK)-induced lung tumorigenesis in A/J mice. They found a 97% reduction of adenoma multiplicity at a DHM dose of 0.05 mg/g of diet (equivalent to a human dose of 47 mg/day). NNAL, the active metabolite of NNK, can generate two reactive species, leading to DNA modifications. DHM selectively reduced DNA adducts in lung tissues derived from NNAL. Safety studies revealed no adverse effects, including hepatotoxicity, from DHM over 17 weeks at a dose of 0.5 mg/g of diet. Further studies are needed to determine the role of DHM as a chemopreventive agent in lung cancer for humans.

SPOTLIGHT: ROBERT TURESKY

Robert Turesky, PhD, is a Professor in the Department of Medicinal Chemistry, and Director of the Masonic Cancer
Center’s Analytical Biochemistry shared resource, a mass spectrometry facility devoted to the cancer and chemoprevention programs at the University of Minnesota. Dr. Turesky received his BSc in biochemistry from the University of Massachusetts, and PhD in nutrition and food science from MIT. He has held various positions, including Group Leader at the Biomarkers Unit, Nestlé Research Center, Switzerland; Division Director at the National Center for Toxicological Research, USDA; and PI at the Wadsworth Center, NY State Department of Health. His research focuses on the biochemical toxicology of dietary and environmental genotoxicants. He is developing novel mass spec techniques to measure biomarkers, such as urinary metabolites, and protein and DNA adducts, in molecular epidemiological studies to understand the role of chemical carcinogen exposures.

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DID YOU KNOW?

Walnut: The Royal Nut Can Be A Smart Choice

What we know as English walnuts are not English at all, they are Persian and they were reserved for royalty. The Persian walnut tree dates back to central Asia 17,000 years ago, making it one of the oldest food trees known to humanity. They became known as English walnuts when English merchant marines traded and transported them to ports around the world, despite never being grown commercially in England. The black walnut is another variety that is native to America, although it is the English walnuts that are grown in California and have been since they were first cultivated by the Franciscan Fathers in the late 1700s.

Walnuts are versatile in the kitchen and on your plate, they can be used in cooking or added to salads, cereals, and yogurts. Click here for a sampling of the delicious ways to add walnuts to weekday meals, holiday menus, and simple snacks

References

• http://www.walnuts.org/cooking-with-walnuts/recipe-collections
• http://www.foodreference.com/html/fwalnuts.html

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Your friends at the Nutritional Science Research Group

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