Dear Colleague,

Welcome to the Spring 2014 issue of the Nutrition Frontiers, a quarterly newsletter from the Nutritional Science Research Group (NSRG), Division of Cancer Prevention, NCI. In this issue, we cover modulation of natural killer cells, and the role of omega-3 fatty acid exposure and consumption in relation to colon and prostate cancer. Plus, learn about our spotlight investigator, announcements and more.

RESEARCH UPDATE: ON THE CLINICAL FRONT
Low-Fat Fish Oil Diet and Prostate Cancer

In a post hoc analysis, Galet and colleagues examined if lowering the dietary n-6:n-3 fatty acid ratio with a low-fat diet (15% kcal fat) supplemented with 5 g fish oil/day correlated with anti-tumorigenic effects in prostatectomy patients. Surrogate endpoints included changes in circulating levels of Leukotriene B4 (LTB4) and 15-S-hydroxyeicosatetraenoic acid [15(S)-HETE], and cell-cycle progression score (CCP), which predicts cancer recurrence after prostatectomy; they also assessed the expression of the LTB4 receptor BLT1 in human prostate cancer specimens. Serum 15(S)-HETE levels and the CCP score were significantly lower in the treated group. For the first time, expression of the LTB4 receptor BLT1 in human prostate cancer specimens was demonstrated. These results suggest a potential role for the 15-lipoxygenase pathways in the anticancer effect of a low-fat fish oil diet. Further studies may determine if dietary modulation of pro-inflammatory eicosanoids impacts prostate cancer cell proliferation through the LTB4/BLT1 and 15(S)-HETE pathways.

July 17-18, 2014
Fourth Public Meeting of the 2015 Dietary Guidelines Advisory Committee
Bethesda, MD

September 16-17, 2014
Fifth Public Meeting of the 2015 Dietary Guidelines Advisory Committee
Bethesda, MD

September 28-October 01, 2014
Frontiers in Cancer Prevention Research, American Association for Cancer Research
New Orleans, LA

October 16-18, 2014
West Lafayette, IN

October 18-21, 2014
Food & Nutrition Conference & Expo, Academy of Nutrition and Dietetics
Atlanta, GA

October 29-31, 2014
AICR Annual Research Conference, American Institute of Cancer Research

RESEARCH UPDATE: WHAT'S NEW IN BASIC SCIENCE

Effects of n-3 Fatty Acid Metabolite on Colonic Stem Cells

While it is well known that diet plays an important role in colon cancer development, the effect of a very high n-6 to n-3 fatty acid ratio, commonly observed in Western diet, is unknown. Recently, Fan and colleagues documented ex vivo responses of Lgr5+ colonic stem cells to exogenous n-6 fatty acid-derived prostaglandin E2 (PGE2) and n-3 fatty acids-derived PGE3. Colonic crypts were isolated from Lgr5+-EGFP-IRES-creERT2 transgenic mice and cultured in a three-dimensional platform. PGE2, compared with PGE3 and control, significantly promoted stem cell expansion and modulated its ability to differentiate into goblet cells. Furthermore, there was no difference between PGE3-treated group and control. These results suggest that chemopreventive n-3 fatty acid-derived PGE3 does not increase intestinal stem cell expansion or influence mucus secretion.

Modulation of Natural Killer Cell Activity by AhR

Variation in natural killer (NK) cell cytotoxicity may be influenced by exogenous factors, including the diet. Shin and colleagues recently described the critical role of the aryl hydro-carbon receptor (AhR) in modulating NK cell antitumor activity. AhR, upon ligand binding, translocates from the cytosol to the nucleus where it binds with ARNT (aryl hydrocarbon receptor nuclear translocator). This complex of AhR and ARNT regulates the expression of specific genes containing xenobiotic-response element DNA sequences. Shin et al. showed that the activation of AhR with agonistic ligands potentiates NK cell cytopytic activity and that activation of this receptor is a critical modulator of NK cell antitumor effector functions. The implications of AhR modulating NK cell effector functions are particularly relevant because natural AhR ligands, such as indole-3-carbinol in cruciferous vegetables, can be commonly found in the diet.

SPOTLIGHT: TRYGVIE TOLLEFSBOL

Trygve Tollefsbol, PhD, DO is a Professor of Biology, Director of the
Dr. Tollefsbol earned doctorate degrees in molecular biology and osteopathic medicine at the University of North Texas Health Sciences Center and postdoctoral training at Duke University and the University of North Carolina. He serves as Associate Editor for *Frontiers in Epigenomics*, contributing Editor of *Lewin’s GENES* classic textbook on molecular biology and Series Editor for *Translational Epigenetics*. His research focuses on the epigenetics of cancer prevention and aging as well as telomerase gene regulation in response to nutrients. Dr. Tollefsbol and his colleagues invented chromatin immunoprecipitation-genomic bisulfite sequencing for studying the epigenetic effects of nutrients. He was recently awarded a R01 entitled, *Combinatorial Epigenetic-Based Prevention of Breast Cancer*.

**DID YOU KNOW?**

**Strawberry - A Real Berry?**

For centuries, the heart-shaped berry has been the symbol of Venus, the Goddess of Love. Historically, strawberries have been appreciated for their medicinal value from root to leaf and their sweet taste. The Native Indians crushed fleshy red strawberries into cornmeal to make strawberry bread and inspired the Colonists to create their own version - hence, Strawberry Shortcake was born. Yet, they are not a “true berry” because they belong to the genus (*Fragaria x ananassa*) a member of the rose family and are considered a “false” fruit. The hundreds of brownish/white specks, commonly considered the seeds, are the actual tiny individual fruits embedded in a fleshy scarlet receptacle.

Strawberries are particularly rich in ellagic acid and contain vitamin C, folate, and potassium. Only 55 calories are in a cup of strawberries, so eat up. Store them in the crisper drawer of your refrigerator, up to 7 days, depending on the ripeness when purchased or picked. And don’t wash until just before eating. Happy pickings!

**References**

- [http://www.pickyourown.org/strawberries/Strawberry_guide_from_the_University_of_California.pdf](http://www.pickyourown.org/strawberries/Strawberry_guide_from_the_University_of_California.pdf)
- [http://www.pickyourown.org/strawberryfacts.htm](http://www.pickyourown.org/strawberryfacts.htm)
- [http://www.aicr.org/foods-that-fight-cancer/foodsthatfightcancer_berries.html](http://www.aicr.org/foods-that-fight-cancer/foodsthatfightcancer_berries.html)
Sincerely,

*Your friends at the Nutritional Science Research Group*

Division of Cancer Prevention
National Cancer Institute
National Institutes of Health
U.S. Department of Health & Human Services