AICR Research Grants Program

We fund and analyze the science that investigates the links between lifestyle and cancer.

For over three decades, we have dedicated ourselves to understanding how our weight, activity, and diet play a role in cancer risk. This knowledge has revolutionized the understanding of cancer prevention. It’s now transforming the medical and scientific community’s approach to cancer treatment and survival.

* We have shown that foods, activity and weight influence the cancer process.
* We have identified over 60 specific foods and other lifestyle factors that modify the risk of cancer.
* We systematically collect and analyze this evidence in our Continuous Update Project.
* We turn the evidence into clear, authoritative recommendations for lowering cancer risk.

Our research clearly shows we can make cancer less likely to happen. Thanks to your support we continue to make scientific advances. The following pages showcase the 2015 AICR funded projects.

The Grantees

**BRAIN CANCER**

**Kenneth Schwartz, MD**
Michigan State University
East Lansing, Michigan

*Pilot study of a metabolic nutritional therapy for the management of primary brain tumors*

Patients who are diagnosed with a certain kind of brain cancer (glioblastoma) have an average life expectancy of only 12 to 15 months. Dr. Schwartz will conduct a 12-week pilot study to test the use of nutritional therapy in brain cancer patients. The therapy will use an energy restricted ketogenic diet, which has been shown to decrease tumor growth in mice.

*continued on next page*
**BREAST CANCER**

**Heather Baer, ScD**  
Brigham and Women’s Hospital  
Boston, Massachusetts  
*Body size at young ages and novel biomarkers of breast cancer risk*

Dr. Baer is looking at data from girls to see whether body fatness in childhood and adolescence has effects on breast density or on levels of an ovarian hormone called MIS (Mullerian inhibiting substance) later in life.

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**Rowan Chlebowski, MD, PhD**  
Harbor-UCLA Medical Center  
Los Angeles, CA  
*Women’s Interventional Nutrition Study (WINS) long-term survival analysis*

Results from the initial WINS study suggested that a lifestyle intervention targeting dietary fat intake and weight loss could improve overall survival in breast cancer patients. Dr. Chlebowski’s group will examine long-term survival information for this group of 2,180 WINS participants. This update of long-term survival of WINS study participants will provide more information regarding the influence of lifestyle on breast cancer.

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**Joanne F. Dorgan, PhD**  
University of Maryland, Baltimore  
Baltimore, Maryland  
*Prospective study of diet in youth and adult breast density*

Heavier girls are at a decreased risk of breast cancer throughout life, but the underlying mechanism is not understood. Women with dense breasts are at an increased risk of breast cancer. Girls who are heavier have lower breast density as adults, which could contribute to lower breast cancer risk in women who were heavier as children and adolescents. The objective of this study is to identify dietary factors in youth that influence breast density.

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**David Feldman, MD**  
Stanford University  
Palo Alto, California  
*Diet induced obesity and breast cancer: Protective role of vitamin D*

Dr. Feldman is using a mouse model of breast cancer to investigate how vitamin D deficiency and obesity may increase breast cancer risk. His study aims to develop vitamin D as a therapy to protect against obesity-related breast cancer and will examine the effects of vitamin D added to the diet.

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**Leena Hilakivi-Clarke, PhD**  
Georgetown University  
Washington, District of Columbia  
*Role of genistein in reversing tamoxifen resistance by acting as HDAC and DNMT inhibitor*

Over 50% of estrogen receptor positive (ER+) breast cancer patients who receive anti-estrogen therapy such as tamoxifen either never respond to the treatment or eventually develop resistance to it. Reversible epigenetic changes are associated with the development of anti-estrogen resistant breast cancer. However, reversal seems to occur only in individuals who acquired epigenetic change before breast cancer is detected. This study will investigate whether tamoxifen resistance in female rats exposed to a high-fat diet in utero can be prevented by life-long or adult dietary intake of genistein, or genistein intake that starts during tamoxifen treatment.

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**Melinda L. Irwin, PhD, MPH**  
Yale University  
New Haven, Connecticut  
*A mail- and video-based weight loss trial in breast cancer survivors*

Building on the Lifestyle, Exercise and Nutrition (LEAN) Study, Dr. Irwin will conduct a randomized controlled trial examining changes in body weight, diet, physical activity, and quality of life in overweight breast cancer survivors randomized to receiving the LEAN book and videos mailed to them compared to overweight breast cancer survivors randomized to wait-list control. Body weight 6 months after the study will be assessed to determine maintenance of weight loss, and predictors of weight loss at 6 and 12 months. Results from this study will provide evidence-based findings on how much weight loss is feasible when intervening via the LEAN book and videos, as well as predictors of weight loss success.

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**Greg Kucera, PhD**  
Wake Forest University Health Sciences  
Winston-Salem, North Carolina  
*Effects of fish oil on lipid metabolites in breast cancer*

By studying women who were recently diagnosed with metastatic breast cancer, Dr. Kucera hopes to determine whether fish oil protects against breast cancer and if so, how he proposes that omega-3 fatty acids may be safe and inexpensive tools in the arsenal of agents to combat breast cancer.
**BREAST CANCER cont’d**

**Jennifer Ligibel, MD**  
Dana-Farber Cancer Institute  
Boston, Massachusetts  
*Impact of physical activity on tumor gene expression in women with newly diagnosed breast cancer*

This study evaluates the impact of exercise on human breast cancer cells. The study enrolls women as they are diagnosed with breast cancer and assigns them to an exercise group or a control group. Breast tumor tissue is collected at the time of enrollment and again at the time of breast surgery. The effect of exercise on tumor tissue is assessed by comparing changes in tissue markers over time in patients assigned to the exercise group vs. the control group. Dr. Ligibel’s project will provide information about the cellular pathways that exercise affects in breast cancer cells, providing insight into how exercise could affect cancer formation and prognosis.

**Henry Thompson, PhD**  
Colorado State University  
Fort Collins, Colorado  
*Diet composition and weight loss: effect on long term prognosis in breast cancer survivors*

This study is based on the successful completion of the clinical phase of a 6-month weight loss intervention, referred to as CHOICE, in post-menopausal breast cancer survivors. This project will use the CHOICE menus and recipes, comparing a low fat/high carbohydrate diet to a high fat/low carbohydrate diet, to induce weight loss in a post-menopausal rat model of obesity and breast cancer, with cancer endpoints as the primary outcome. The investigators hypothesize that weight loss using these diets will improve breast cancer outcomes and the magnitude of benefit will be affected by dietary pattern.

**Trygve Tollefsbol, PhD, DO**  
The University of Alabama at Birmingham  
Birmingham, Alabama  
*Epigenetics of early life exposure to cancer preventive cruciferous vegetables*

Dr. Tollefsbol’s group will use a mouse model to determine when in early life sulforaphane-rich cruciferous vegetables are most effective in preventing epigenetic alterations that can lead to breast cancer. Although the sulforaphane in foods such as broccoli sprouts has epigenetic effects that can help prevent breast cancer at concentrations, it’s not known how it works or when the best life course exposure is for optimal cancer protection. This study aims to pinpoint the optimal stages of early life that ample cruciferous vegetable exposure most effectively prevents epigenetic changes that lead to cancer and the mechanisms responsible for these effects.

**COLON CANCER**

**Leonard H. Augenlicht, PhD**  
Albert Einstein College of Medicine of Yeshiva University  
New York, New York  
*Mechanism establishing dietary induced relative risk for intestinal tumors*

Dr. Augenlicht’s lab will study how vitamin D levels influence stem cells to give rise to tumors. These experiments may establish a new understanding how risk of cancer is caused by long-term dietary exposures. This may lead to new ways of detecting individuals at higher risk, which is a key to cost effective methods to detect tumors early and remove them before they can spread, and to nutritional interventions that may lower the risk of these tumors from ever developing in the first place.

**Robert Chapkin, PhD**  
Texas A&M University  
College Station, Texas  
*Interactive chemoprotective effects of dietary fat and fiber on adult intestinal stem cells*

Colorectal cancer continues to pose a serious health problem in the U.S. In view of safety concerns surrounding the use of pharmaceutical agents as cancer preventive agents, potentially innocuous dietary preventive agents are now considered attractive alternatives. Dr. Chapkin will study the interactive effects of fish oil-derived n-3 polyunsaturated fatty acids and fiber with respect to colon tumor development.

**Derek Huffman, PhD**  
Albert Einstein College of Medicine  
New York, New York  
*Walnuts as a dietary strategy to break the obesity-colon cancer link*

Whole walnuts are uniquely rich in many bioactive compounds that may help to oppose many of the harmful side-effects of obesity on cells and tissues. Dr. Huffman’s group will examine this by supplementing the diet of mice either kept to a normal weight with a healthy diet or made obese with a cafeteria diet with walnuts, and determine whether walnuts are able to improve several outcomes in healthy mice and/or prevent detrimental effects to occur in obese mice.

**Sabrina Peterson Trudo, PhD, RD**  
University of Minnesota – Twin Cities  
St. Paul, Minnesota  
*Effect of vegetable intake on heterocyclic amine metabolism in humans*

A diet high in red meat increases colon cancer risk, possibly due to the meat compounds called heterocyclic amines (HCAs). Lab research has found that carrots, broccoli and other plant foods may reduce or “deactivate” the levels of HCAs and other carcinogens. Dr. Trudo is studying whether eating carrots, broccoli and other plant foods after eating grilled hamburger meat reduces the levels of harmful HCAs formed by grilled meat.
**COLON CANCER cont’d**

**Daniel Rosenberg, PhD**
University of Connecticut Health Center
Farmington, Connecticut

*Beneficial effects of walnut consumption on colon cancer and inflammation*

Dr. Rosenberg’s research aim is to examine the chemo-preventive efficacy of walnuts for reducing the incidence of colon cancer. His study will evaluate the effectiveness of walnuts in inhibiting the formation of precancerous lesions and tumors in three different mouse models. One of the goals of Dr. Rosenberg’s laboratory is to develop and implement effective approaches for colon cancer prevention.

**Kana Wu, MD, MPH, PhD**
Harvard University School of Public Health
Boston, Massachusetts

*Sugar sweetened beverages, fructose and sucrose, genetic susceptibility, molecular subtypes and colorectal cancer survival*

Dr. Wu’s study will examine whether higher intake of sugar-sweetened beverages, refined carbohydrates, fructose, sucrose, and glycemic load after a diagnosis of colon cancer is associated with worse prognosis; and whether these associations differ by form or source of sugar, molecular subtypes of colon cancer, or genetic susceptibility to obesity or increased insulin secretion. This project will provide a better understanding of the biological mechanisms that play a role in progression to fatal tumors and help to optimize dietary guidelines for colorectal cancer patients.

**ESOPHAGEAL CANCER**

**David Christiani, MD, PhD**
Harvard University
Boston, Massachusetts

*Gene-environment interactions among circulating vitamin D levels, vitamin D pathway gene polymorphisms, BMI and esophageal adenocarcinoma prognosis*

Esophageal cancer incidence is rapidly increasing in the United States. Dr. Christiani will look at DNA, serum vitamin D and other data from approximately 700 esophageal cancer patients. The findings will provide information on how multiple factors may affect survival.

**LEUKEMIA CANCER**

**James DeGregori, PhD**
University of Colorado Denver
Aurora, Colorado

*Linking dietary folate, tissue fitness and cancer*

Dr. DeGregori is examining why diets both high in folate and low in folate are associated with increased cancer risk. He hypothesizes that both high and low folate diets impair metabolism and result in reduced cell fitness.

**Emily Tonorezos, MD**
Sloan-Kettering Institute for Cancer Research
New York, New York

*Diet and insulin resistance in survivors of childhood leukemia*

Many adult survivors of acute lymphoblastic leukemia (ALL) become obese and develop insulin resistance, but it is not clear why. Dr. Tonorezos will compare the diets, eating behaviors and activity of long-term ALL survivors to people without a history of cancer. This study may lead to dietary recommendations for ALL survivors that would improve their health and longevity.

**LIVER CANCER**

**Bryan Fuchs, PhD**
Massachusetts General Hospital
Boston, Massachusetts

*Prevention of hepatocellular carcinoma by EGCG*

Dr. Fuchs is using an animal model of chronic liver disease to determine whether EGCG (a phytochemical in green tea) inhibits the development of liver cancer by inhibiting cirrhosis. He is testing EGCG alone and in combination with erlotinib, a common treatment for the disease, to determine if it slows tumor progression.

**LUNG CANCER**

**Piyali Dasgupta, PhD**
Marshall University
Huntington, West Virginia

*Anti-metastatic activity of capsaicin in human small cell lung cancer*

Small cell lung cancer accounts for about 15 percent of lung cancers and has a 5-year survival rate of only 5 percent. Emerging evidence shows that capsaicin, found in chili peppers, can suppress the growth of small cell lung cancer and other cancers. This study will examine whether or not capsaicin can inhibit the spread of small cell lung cancer to distant organs, as well as how it works. Results could lead to the development of a new nutrition-based treatment for this cancer.

**MULTIPLE SITES**

**Kirstin Ness, PhD**
St. Jude Children’s Research Hospital
Memphis, Tennessee

*Impact of resistance training and protein supplementation on lean muscle mass among childhood cancer survivors*

Young adults who were treated for cancer during childhood have less overall lean muscle mass than expected for their age. Dr. Ness’s study tests the effects of a weight lifting intervention and dietary protein supplementation on muscle mass, physical well-being and blood markers of overall health. Before and after the 6 month intervention participants will have a body scan to look at lean muscle mass, be evaluated for their muscle strength and physical abilities and have their blood tested for markers of overall health.
MULTIPLE SITES cont’d

**William Redmond, PhD**
Providence Portland Medical Center
Portland, Oregon

*Vitamin E analog-induced tumor autophagy to enhance tumor immunity*

Dr. Redmond’s study will examine a drug derived from vitamin E that selectively kills cancer cells while not harming normal cells. The study aims to better understand how this vitamin E derived drug works and will provide important information on its use as a supplement for treating metastatic cancer. The supplement is non-toxic and can be given to cancer patients either in the diet or in pill form.

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**Susan Steck, PhD, MPH, RD**
South Carolina Research Foundation
Columbia, South Carolina

*Inflammatory potential of diet and risk of cancer mortality in women*

Dr. Steck’s group developed a dietary inflammatory index to assess the overall quality of diet with regard to its inflammation potential. People who reported a high pro-inflammatory diet prior to cancer diagnosis were at increased risk of gastrointestinal tract cancer death. They will now examine diet after diagnosis and risk of dying from cancer or from all-causes in the Women’s Health Initiative cohort. This work will provide insights into translatable opportunities for health promotion and cancer control.

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**Robin Wilson, PhD**
Penn State College of Medicine
Hershey, Pennsylvania

*Genetic, dietary and environmental influences on vitamin D metabolism*

Although there is not yet conclusive evidence linking vitamin D to cancer prevention, the inconsistent results may be due to how individuals metabolize vitamin D. Dr. Wilson’s new study is investigating genetic differences in vitamin D metabolism.

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**Louise Fong, PhD**
Thomas Jefferson University
Philadelphia, Pennsylvania

*Dietary zinc deficiency and modulation of gene expression in oral preneoplasia in p53-deficient mice*

Oral cancer is a major cause of cancer deaths worldwide. Population studies have shown that zinc deficiency may be a contributing factor in this disease, but its role is unclear. This study will examine the relationship between zinc and genetic factors that are thought to be important in the development of this cancer. The aim of the study is to advance our understanding about how this cancer can be prevented.

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**Barbara Gower, PhD**
The University of Alabama at Birmingham
Birmingham, Alabama

*Targeted disruption of cancer cell metabolism and growth through modification of diet quality*

Cancer cells rely primarily on the use of glucose as fuel. Growth of cancer cells is inhibited by substances called ketone bodies that are produced by healthy cells when fat is burned. It is possible that diets that promote use of fat as fuel could block cancer growth. Studies in mice have shown that ketogenic diets are able to slow cancer growth and decrease death from cancer. This study will investigate the effects of a ketogenic diet on cancer markers, tumor size, and metabolic variables in women with recurrent ovarian cancer.

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**Rosemarie Schmandt, PhD**
University of Texas M.D. Anderson Cancer Center
Austin, Texas

*Do-it-yourself chemoprevention: can exercise increase circulating omentin levels to inhibit ovarian tumor recurrence and metastasis?*

Dr. Schmandt’s group will study omentin, a protein produced by belly fat and whose production is inhibited in the presence of tumor cells. Laboratory studies have shown that omentin slows the growth of ovarian cancer cells and prevents metastasis. If omentin production is blocked by tumor cells, then the re-induction of omentin synthesis by exercise may inhibit ovarian cancer progression and improve patient outcomes.

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**Steven K. Clinton, MD, PhD**
The Ohio State University
Columbus, Ohio

*Maximizing the impact of tomatoes for prostate cancer prevention: the impact of tomato variety and carotenoid profiles*

Laboratory studies have found that lycopene-containing tomato foods reduce prostate cancer in animal models. Work from Dr. Clinton’s lab has shown that bioactive phytochemicals are more readily absorbed if the chemical structure of lycopene is in a particular configuration. Tangerine tomatoes are a rich source of this type of lycopene and will be compared with standard red tomatoes. The goal is to use this information to better design tomato juices for future clinical trials.
MULTIPLE SITES cont’d

Jay H. Fowke, PhD
Vanderbilt University Medical Center
Nashville, Tennessee
A prospective analysis of obesity and progression from HGPIN to prostate cancer
This study will examine the role of centralized obesity and inflammation in prostate cancer progression. Men with high-grade prostatic intraepithelial neoplasia (HGPIN), which is a marker of prostate cancer susceptibility, will be identified and followed for conversion from HGPIN to prostate cancer. Body composition measurements and blood inflammatory markers will be collected. Study results will provide a comprehensive assessment of immune system regulation associated with centralized fat deposition and conversion from HGPIN to prostate cancer.

Dominic Smiraglia, PhD
Roswell Park Cancer Institute
Buffalo, New York
Dietary folate interventions in a mouse model of castration recurrent prostate cancer
In Dr. Smiraglia’s study, he is comparing the development of prostate cancer in mice fed a folate-restricted diet to mice that are fed a diet that is supplemented with folate. He hopes to show that dietary folate restriction, when combined with androgen deprivation therapy, will result in decreased cancer recurrence.

Stephanie Smith-Warner, PhD
Harvard University School of Public Health
Boston, Massachusetts
Carbohydrate quantity and quality and advanced prostate cancer risk: of mice and men
Dr. Smith-Warner will examine whether men who eat foods that elevate insulin and glucose levels have a higher risk of advanced prostate cancer risk in the Pooling Project of Prospective Studies of Diet and Cancer. In a companion study, mice will be injected with prostate cancer cells and randomized to a diet with either no carbohydrates, a low-glycemic index Western diet, or a high-glycemic index Western diet. Biomarkers and prostate cancer growth will then be compared. This proposal will investigate mechanisms that link foods or dietary constituents to risk of advanced prostate cancer.

Our Vision
We want to live in a world where no one develops a preventable cancer.

Our Mission
We champion the latest and most authoritative scientific research from around the world on cancer prevention and survival through diet, weight and physical activity, so that we can help people make informed lifestyle choices to reduce their cancer risk.