



**OSU** Oregon State University

# The Linus Pauling Institute

R E S E A R C H N E W S L E T T E R



## From the Director

*Balz Frei, Ph.D.  
LPI Director and Endowed Chair  
OSU Distinguished Professor of  
Biochemistry and Biophysics*

It is my pleasure to introduce the latest addition to the Linus Pauling Institute—Dr. Kathy Magnusson, who joined the Institute's Healthy Aging Program as a Principal Investigator in March. She comes to us from the Department of Biomedical Sciences in the College of Veterinary Medicine at Oregon State University, where she is a tenured professor. Dr. Magnusson received both a Doctor of Veterinary Medicine (D.V.M.) and a Ph.D. degree from the University of Minnesota, with a major degree in veterinary anatomy and a minor degree in neuroscience. After holding faculty positions at Colorado State University and the University of Idaho, she joined Oregon State University in 2005.



*Dr. Magnusson*

Dr. Magnusson calls herself an “aging neuroscientist interested in how we can prevent or repair the declines that occur during aging in learning and memory ability.” She jokingly adds that she hopes “to figure this out before I forget what the question is.” Dr. Magnusson is particularly interested in how aging affects specific proteins in the brain called “N-methyl-D-aspartate (NMDA) receptors,” which play a dominant role in memory function. She also is investigating how dietary and lifestyle interventions may slow age-related cognitive decline, memory loss, and brain atrophy, the harbingers of Alzheimer's disease.

A few years ago, she was the recipient of an LPI Pilot Project grant—together with her colleague, Dr. Jane Ishmael—to investigate how dietary zinc levels may influence NMDA receptor properties in the elderly. She also has collaborated with several LPI Principal Investigators, including Dr. Tory Hagen, with whom she explored the role of lipoic acid in the aging brain. Since there is evidence

*continued on page 2*



## Dairy, Beans, and Health

*An interview with Gerd Bobe, Ph.D.  
Assistant Professor of Animal Sciences  
LPI Principal Investigator*

**Q. You were born and raised in Europe. What brought you to the United States?**

**A.** I was raised on a farm in western Germany. Originally, I wanted to study abroad for one year. When I talked to students who had studied abroad, they told me that one year wouldn't be enough to learn about American culture and research. So I applied for a Master's degree, met my wife, earned my Ph.D., and stayed here.

**Q. Is there much difference between the research environment in Europe and in the United States?**

**A.** There were many differences when I left Europe in the early 1990s. For example, less funding was available for research in agriculture and animal science.

**Q. You earned a Ph.D. in animal nutrition from Iowa State University. Do you think that your early exposure to farm life stimulated your interest in animal nutrition?**

**A:** Definitely. I have an older brother who did all the outside work, while I helped with the animals. Taking care of animals has always been very important to me.

**Q. Your initial research concerned the fatty acid and protein composition of milk in cows and dairy products. What did you learn about that relationship?**

**A.** In a series of studies, I showed that milk protein and fatty acid profiles can be altered by the cow's diet and breeding.

**Q. How does the cow's diet affect the quality of dairy products like milk and butter?**

**A.** I demonstrated in a series of experiments that the cow's

*continued on page 2*

*Continued from cover — From the Director*

that elevated vitamin D levels in the elderly are correlated with improved cognitive function, Dr. Magnusson is also collaborating with LPI's Dr. Fritz Gombart to investigate how vitamin D deficiency and vitamin D supplementation affect memory in young and old mice.

Coincidentally, Dr. Maret Traber and I were recently involved in a related study looking at diet and brain function in the elderly (summarized on page 6). In collaboration with Dr. Gene Bowman of Oregon Health & Science University in Portland, we found that old adults who had high plasma levels of B vitamins and vitamins C, D, and E performed better on memory and learning tests and had less brain shrinkage than old adults with lower plasma levels of these vitamins. High plasma levels of B vitamins and C and E reflect a Mediterranean-type diet rich in fruits and vegetables, whole grains, nuts, and vegetable oils. Vitamin D is formed in the skin upon sun exposure, and only a few foods like fish and fortified milk provide vitamin D in the diet.

A similar association was observed between increased plasma levels of omega-3 fatty acids and healthy brain aging. These omega-3 fatty acids, often called EPA and DHA, are primarily found in marine fish and fish oil supplements. Our findings are consistent with previous research suggesting that low DHA status is a risk factor for Alzheimer's disease and other types of dementia. In addition, the study with Dr. Bowman found that old people with high plasma levels of *trans* fats from highly processed, nutrient-poor foods, such as packaged, fried, or baked foods, were more likely to exhibit brain shrinkage and score lower on the cognitive function tests than old people with low plasma levels of *trans* fats.

Interestingly, all of these dietary patterns associated with poor or healthy brain aging are also associated with cardiovascular health. For example, people who eat diets high in fruits and vegetables have about a 20% lower risk of suffering a heart attack and a 30% lower risk of a stroke, while high intake of *trans* fats is associated with about a 20% increased risk of these cardiovascular events. In addition, clinical trials have shown that fish oil supplements significantly lower the risk of heart attacks and sudden cardiac death in people with heart disease. These parallels between dietary patterns and either brain or heart health suggest common underlying causes, such as chronic inflammation or high blood pressure. Indeed, it is known that inflammation is counteracted by fish oils, and a diet rich in low-fat dairy products and fruits and vegetables, as well as vitamin C supplementation, have beneficial effects on blood pressure.

While more studies are needed to demonstrate a causal link between brain health in the elderly and the beneficial or detrimental dietary patterns identified in our study with Dr. Bowman, these data certainly are intriguing and, well, food for thought! **LPI**

*Continued from cover — Interview with Gerd Bobe*

diet can improve the fatty acid profile and the textural properties of milk and dairy products.

**Q:** *How does changing the cow's diet by including certain grains or nuts influence things like butter?*

**A:** Feeding cows oil seeds that are rich in polyunsaturated fatty acids increases the proportion of unsaturated fatty acids and decreases the proportion of saturated fatty acids in dairy products.

**Q:** *Were you mainly interested in the health effects of the dairy products, not their palatability?*

**A:** The main focus was to improve the fatty acid profile and the nutritional properties of dairy products for human consumption.

**Q:** *Do you think that the routine use of hormones in dairy cows or cattle poses any serious threat to human health?*

**A:** I'm not aware of any detrimental effects on human health.

**Q:** *What about the use of antibiotics to spur growth and to protect cows and cattle from infection? Do you think that has any health consequence for people who consume those dairy or beef products?*

**A:** Again, I'm not aware of any detrimental effects on human health when antibiotics are used according to their labeled directions.

**Q:** *Does cow's milk contain partially hydrogenated or trans fat and, if so, does that have consequences for human health?*

**A:** The milk of dairy cows contains *trans* fatty acids; however, consumption of *trans* fatty acids from ruminant sources has not been associated with detrimental effects on human health, unlike *trans* fatty acids from the industrial partial hydrogenation of vegetable oils.

**Q:** *What is conjugated linoleic acid, or CLA? Does it have any special health benefit?*

**A:** Conjugated linoleic acid is a group of isomers of linoleic acid. Isomers are compounds that have the same chemical makeup but different structures. Most research has been done on *cis*-9, *trans*-11 linoleic acid and *trans*-10, *cis*-12 linoleic acid. I was involved in a study that examined the effect of these isomers on gene expression of the corpus luteum in the ovaries of cows and reported that both isomers downregulated the gene expression of cyclooxygenase 2 (COX-2). Inhibitors of COX-2 have been shown to inhibit inflammation and decrease the risk of many chronic diseases.

**Q:** *How does CLA occur in dietary sources?*

**A:** *Cis*-9, *trans*-11 linoleic acid is predominantly synthesized in tissues from *trans*-11 linoleic acids by *delta*-9 desaturases. *Trans*-10, *cis*-12 linoleic acid and the

remaining proportion of *cis*-9, *trans*-11 are synthesized by microorganisms in the cow's rumen from linolenic acid and linoleic acid.

**Q:** *You've also looked into the relationship between selenium status and immune function in sheep. Does that have relevance to people?*

**A:** The objective of the studies has been to examine the effect of selenium source (inorganic sodium selenite versus organic selenium yeast) and dosage (regular versus supranutritional—higher than what is usually consumed dietarily—dosage) on selenium status, performance, and health of ewes and their progeny. The studies are still ongoing.

**Q:** *A lot of your research has focused on the effects of flavonoids, which are polyphenolic pigments from plants, on intestinal cancer in mice, the risk of pancreatic cancer in human smokers, and the recurrence of colorectal polyps in the Polyp Prevention Trial. What led to your interest in flavonoids?*

**A:** In cell culture and animal models for chronic diseases, flavonoids exhibit biochemical properties beneficial for the prevention of multiple chronic diseases, including cancer. Looking at the effect of flavonoids on cancer risk in epidemiological studies was the logical next step.

**Q:** *What was the Polyp Prevention Trial?*

**A:** The Polyp Prevention Trial (PPT) was a large, multicenter, randomized four-year nutritional intervention trial in the early 1990s that evaluated the effects of promoting a high-fiber, high-fruit and -vegetable, low-fat diet on the recurrence of any or advanced colorectal adenoma.

**Q:** *What was the main outcome of that study?*

**A:** The main outcome was that the intervention and control group did not differ in recurrence of any or advanced adenoma. However, strict adherence to a low-fat ( $\leq 20\%$  of energy intake), high-fiber ( $\geq 18$  grams per 1,000 kcal of energy), high-fruit and -vegetable diet ( $\geq 3.5$  servings per 1,000 kcal) was associated with a 35% and 56% decrease of any and advanced colorectal adenoma recurrence, respectively.

**Q:** *Did they measure oxidative stress or inflammation in those participants?*

**A:** Several genetic and blood markers of metabolic syndrome and inflammation were measured. We identified several biomarkers that were modified by diet and/or predicted risk of adenoma recurrence.

**Q:** *Do we know that flavonoids in food help protect against polyps or colon cancer?*

**A:** In the PPT, a flavonol-rich diet was associated with a decreased risk of advanced colorectal adenoma recurrence. Flavonols are a subclass of flavonoids.

**Q:** *Since absorption of flavonoids into the blood stream is quite limited, and they are very quickly metabolized once absorbed, is their beneficial effect due, then, to a local effect in the colon?*

**A:** This is an area of active research—we did not examine that.

**Q:** *What compounds are synthesized by gut microbes that might have beneficial effects?*

**A:** Butyrate is one compound that has been proposed to have beneficial effects. There are probably many more compounds that have beneficial effects—this is a new, rapidly growing research area. We still have a lot to learn.

**Q:** *What is butyrate?*

**A:** Butyrate is a four-carbon, short-chain fatty acid produced by intestinal microorganisms.

**Q:** *How do flavonoids compare with other dietary factors in protecting against polyp formation or colon cancer?*

**A:** In the PPT, a high-dry bean diet and a flavonol-rich diet were associated with decreased advanced adenoma recurrence.

**Q:** *Do different types of flavonoids have different health effects?*

**A:** Based on results from cell culture studies and animal models of chronic diseases, individual flavonoids differ in their action on biochemical pathways. In the PPT, only the consumption of the flavonoid subgroups flavonols and, to a smaller extent, isoflavonoids was associated with decreased advanced adenoma recurrence.

*continued on page 4*





**Q: Is it possible to estimate total flavonoid intake from the diet?**

**A:** It is difficult to accurately estimate flavonoid intake from the diet because of limitations in flavonoid databases from foods, variations in the food quantities of recipes, and variability of flavonoid content due to the climatic, growing, soil, and harvesting conditions of plants, and storage conditions and preparation of foods.

**Q: Why are flavonoids synthesized in plants? What function do they perform?**

**A:** Flavonoids have multiple functions in plants. It has been proposed that flavonoids and their metabolites have roles in UV protection and signaling in symbiosis, as well as acting as chemical messengers to regulate physiological processes, as pigments to attract pollinator animals, and as defensive compounds against pathogens.

**Q: Flavonoids in tea have been found to inhibit lesions in the rat colon induced by dietary mutagens. Do flavonoids also protect against esophageal cancer?**

**A:** There are two histological types of esophageal cancer—esophageal adenocarcinoma (EAC) and esophageal squamous cell carcinoma (ESCC)—that differ in their etiology. EAC is associated strongly with gastro-esophageal reflux disease and obesity, while ESCC is associated strongly with tobacco and alcohol consumption. I was involved in a population-based, case-control study of white and black men in the U.S. that examined the effect of flavonoid consumption on the risk of EAC and ESCC. Overall, consumption of total flavonoids had little protective effect in this population of heavy smokers and drinkers; however, there was some suggestion that foods rich in the flavonoid subgroup anthocyanidins may be protective in EAC and that isoflavonoid-rich foods may be protective in ESCC.

**Q: You also investigated the role of lignans, legumes, beans, and sugar on colon cancer. What did you find?**

**A:** Lignans are diphenolic compounds present in the structural portion of plants, which are partially or fully converted by the intestinal microorganisms to enterolactone and enterodiol. In the PPT, individual and total lignan intake was not associated with colorectal adenoma recurrence; however, high-lignan intake was associated with the increased risk of any adenoma recurrence in women and in individuals with saturated fat intake below or equal to 18.3 grams per day.

**Q: What about legumes and beans?**

**A:** In the PPT, a high-dry bean diet was associated with a decreased risk of advanced colorectal adenoma recurrence. The results from the PPT were followed up by the Legume Inflammation Feeding Experiment (LIFE), a randomized, crossover feeding study of a legume-enriched (250 grams per day) diet among men under conditions of weight maintenance. The main study was followed by a third, optional four-week period, which encouraged weight loss. Participants lost on average 4.4% of their body weight during the weight-loss phase and improved biomarkers of metabolic syndrome and inflammation.

**Q: What about sucrose intake?**

**A:** Using a mouse model of colon cancer, we reported that sucrose compared to cornstarch consumption increased tumor number, serum glucose and insulin concentrations, and body weight in those mice.

**Q: Does a low glycemic diet that emphasizes legumes improve blood lipid profiles?**

**A:** During the four weeks on the high-legume, high-fiber, and low-glycemic index diet in the LIFE Study, total and low-density lipoprotein (LDL) cholesterol concentrations during the weight-maintenance phase decreased by 10% and 11%, respectively, and during the weight-loss phase by 13% and 16%, respectively. In addition, total triglyceride concentrations decreased on the high-legume diet by 15% and 28% during the weight-maintenance phase and the weight-loss phase, respectively.

**Q: How does that diet affect insulin resistance and inflammation?**

**A:** During the four-week weight-loss phase, glucose and insulin concentrations dropped by 6% and 14%, respectively. In addition, concentrations of the inflammatory markers, C-reactive protein and soluble TNF receptor 1, decreased during the weight-maintenance phase and the weight-loss phase.

**Q: What kinds of beans were used in that diet?**

**A:** The high-legume diet contained approximately 250 grams or 1.5 cups of legumes a day. The legumes were of the *Phaseolus vulgaris* species and included navy, pinto, kidney, lima, and black beans.



**Q:** *Based on your research in this area, would you make any special dietary recommendations for people who are trying to manage weight and help prevent age-related disease?*

**A:** The results of the PPT and the LIFE study are encouraging. Further research needs to be done to validate those findings before dietary recommendations can be made. Personally, I increased my consumption of beans, fiber, fruit, and vegetables over the last few years.

**Q:** *What are you currently working on?*

**A:** I work on identifying metabolic pathways and biomarkers that are modifiable by legume and flavonol intake and can predict cancer risk.

**Q:** *And that, of course, has relevance not only to cancer but also to cardiovascular disease and diabetes?*

**A:** Yes.

**Q:** *Where is your research headed?*

**A:** My research is headed toward personalized cancer and disease prevention. I will use an “omics” approach—

genomics, proteomics, metabolomics—to look at genes, proteins, metabolites, and other substances in human intervention trials to identify subpopulations that most likely benefit from a particular diet.

**Q:** *How do you like the Linus Pauling Institute's new building?*

**A:** It is a dream come true!

**Q:** *Does it meet all your research needs?*

**A:** Definitely! It is great to work in close proximity to a group of very talented and highly successful researchers, which makes your own work so much better.

**Q:** *Do you like living in Oregon?*

**A:** Yes. We are close to the coast and to the mountains, and the rain in the winter doesn't bother me. Corvallis reminds me of where I was raised in Germany.

**Q:** *What do you like to do in your free time?*

**A:** I love to spend time with my seven-year-old daughter. Family is very important to me. **LPI**

## RECENT PUBLICATIONS BY LPI SCIENTISTS

SUMMARIES OF SELECTED PUBLICATIONS BY STEPHEN LAWSON

*LPI scientists are identified in boldface.*

### Healthy Aging Program

**GOMBART AE.** The vitamin D-antimicrobial peptide pathway and its role in protection against infection. *Future Microbiol.* 4:1151-1165, 2009

In the early 19<sup>th</sup> century, exposure to sunlight was found to be beneficial for tuberculosis patients, although the mechanism was unknown. Sunlight is required for the endogenous synthesis of vitamin D in the skin. Recent research has found that vitamin D regulates the synthesis of antimicrobial peptides in the body, including cathelicidin and defensin, involved in innate immunity. Cathelicidin and defensin punch holes in bacterial membranes, leading to their death. A study in hemodialysis patients by the author showed that high cathelicidin levels in the blood were associated with decreased mortality from infections. Some phytochemicals and dietary fats, such as curcumin and polyunsaturated fatty acids, may also stimulate antimicrobial peptide activity by binding to the vitamin D receptor on cells. The quantitative relationship between vitamin D and these antimicrobial peptides hasn't yet been worked out.

**SHAY KP, MOREAU RF, SMITH EJ, SMITH AR, and HAGEN TM.** Alpha-lipoic acid as a dietary supplement: Molecular mechanisms and therapeutic potential. *Biochim. Biophys. Acta* 1790:1149-1160, 2009

In this review, the authors discuss the biochemical effects of supplemental lipoic acid, which is usually found as a racemic mixture of the S and R forms. The R form has

greater bioavailability. About 20-40% of a dose of lipoic acid is absorbed into the blood stream and then fairly rapidly metabolized and excreted. It accumulates in the liver, heart, skeletal muscle, and, possibly, in the brain. In humans, oral doses as high as 600 mg twice a day for six months and intravenous infusions of 600 mg daily have not resulted in any significant side effects or toxicity. Both the oxidized and reduced forms of lipoic acid scavenge reactive oxygen species and each selectively chelates reactive metals like copper, iron, lead, and mercury. Lipoic acid induces the synthesis of glutathione—an important endogenous antioxidant—and may increase the absorption of vitamin C into the blood stream. Lipoic acid influences the transcription factor Nrf2, resulting in increased glutathione synthesis and phase 2 detoxification enzyme levels. Lipoic acid improves glucose handling, enhances vasodilation, lowers blood pressure, and has anti-inflammatory properties. Oral and intravenous lipoic acid have also been used to significantly attenuate diabetic neuropathy.

**LI L, SMITH A, HAGEN TM, and FREI B.** Vascular oxidative stress and inflammation increase with age: Ameliorating effects of alpha-lipoic acid supplementation. *Ann. N. Y. Acad. Sci.* 1203:151-159, 2010

Age-related increases in oxidative stress and inflammation have been implicated in the development of cardiovascular diseases. In this study, the authors found that biomarkers of

*continued on page 6*



oxidative stress (e.g., superoxide radicals) and inflammation (e.g., NF- $\kappa$ B activation) were elevated in the aortas of old rats compared to young rats. The levels of superoxide dismutase—an important endogenous antioxidant enzyme—were decreased in old rats. Supplementing the diets of old rats with lipoic acid for two weeks reduced these biomarkers of oxidative stress and inflammation, increased levels of superoxide dismutase, and alleviated endothelial dysfunction.

**BARBEITO AG, MARTINEZ-PALMA L, VARGAS MR, PEHAR M, MAÑAY N, BECKMAN JS, BARBEITO L, and CASSINA P.** Lead exposure stimulates VEGF expression in the spinal cord and extends survival in a mouse model of ALS. *Neurobiol. Dis.* 37:574-580, 2010

Amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease, is a neurological disease in which the death of motor neurons leads inexorably to the patient's death. Functional mutations in the gene coding for the endogenous antioxidant enzyme copper-zinc superoxide dismutase (SOD) are associated with a significant number of ALS cases. Such mutations cause the enzyme to lose its affinity for zinc, and the zinc-deficient SOD then becomes very reactive—leading to the generation of reactive oxygen and nitrogen species in astrocytes that damage motor neurons—and contributes to the development of ALS. Although environmental exposure to lead is a risk factor for ALS, the authors found that, paradoxically, small amounts of lead added to cultured astrocytes expressing the defective SOD increased the amount of vascular endothelial growth factor, which, in turn, protected motor neurons from death. Mice with the SOD mutation given low, non-toxic levels of lead

lived longer than unsupplemented mice, suggesting that lead inhibits neuroinflammation. Recent studies have also associated low lead levels in ALS patients with longer survival.

**MONETTE JS, GOMEZ LA, MOREAU RF, DUNN KC, BUTLER JA, FINLAY LA, MICHELS AJ, SHAY KP, SMITH EJ, and HAGEN TM.** (R)- $\alpha$ -Lipoic acid treatment restores ceramide balance in aging rat cardiac mitochondria. *Pharmacol. Res.* 63:23-29, 2011

Ceramides are sphingolipids found in cell membranes that have structural and signaling functions in cells. Ceramides are also associated with oxidative stress and programmed cell death (apoptosis) and accumulate upon exposure of cells to inflammatory stimuli. Such accumulation may lead to altered function of mitochondria—cellular organelles that generate chemical energy. The authors found that ceramides increased by over 30% in the heart mitochondria from old rats compared to young rats. Supplementing old rats with lipoic acid for two weeks lowered ceramide levels to those observed in young rats and restored mitochondrial energy metabolism.

**BOWMAN GL, SILBERT LC, HOWIESON D, DODGE HH, TRABER MG, FREI B, KAYE JA, SHANNON J, and QUINN JF.** Nutrient biomarker patterns, cognitive function, and MRI measures of brain aging. *Neurology.* 78:241-249, 2012

The Oregon Brain Aging Study began in 1989 with nearly 300 men and women aged 65 years and older to investigate the link between diet and brain aging. Blood samples were obtained and various nutrients were measured, including vitamins, fatty acids, and carotenoids (beta-carotene, lycopene, lutein, etc.). Additionally, neuropsychological tests were administered, and the subjects' brain volumes were assessed by MRI. Several nutrient biomarker patterns emerged from the analysis that were associated with cognitive function and brain volume. In particular, those subjects who scored highest in plasma values for the B vitamins and vitamins C, D, and E performed best on cognitive function tests and had greater total cerebral brain volume. Subjects who had the highest levels of plasma *trans* fats (partially hydrogenated fats found in many processed foods) had worse cognitive function and less total cerebral brain volume. Omega-3 fatty acids and higher lutein plus HDL cholesterol scores were associated with better cognitive and memory function, respectively.

**GOMEZ LA, HEATH SH, and HAGEN TM.** Acetyl-L-carnitine supplementation reverses the age-related decline in carnitine palmitoyltransferase 1 (CPT1) activity in interfibrillar mitochondria without changing the L-carnitine content in the rat heart. *Mech. Ageing Dev.* 133:99-106, 2012

Research has shown that supplementation with the non-protein amino acid acetyl-L-carnitine (L-carnitine to which an acetyl chemical group has been added) improves memory performance and increases physical activity in old rats. In this study, the authors investigated the specific biochemical mechanisms that may explain these observations. There are two subpopulations of mitochondria—the organelles that produce chemical energy in cells. The authors found that acetyl-L-carnitine increases the activity of the enzyme carnitine palmitoyltransferase 1 (CPT1) in one mitochondrial



subpopulation in heart cells of old rats. CPT1 controls the oxidation of fatty acids, a crucial process in mitochondrial energy metabolism, and declines with age. While these relationships are complex and not fully understood, the authors propose that age-related oxidative modifications of CPT1 may be reversed by acetyl-L-carnitine supplementation, leading to improved cardiac function in old animals.

## Cardiovascular and Metabolic Diseases

**MICHEL AJ, HAGEN TM, and FREI B.** A new twist on an old vitamin: Human polymorphisms in the gene encoding the sodium-dependent vitamin C transporter 1. *Am. J. Clin. Nutr.* 92:271-272, 2010

In this commentary, the authors reflect on a paper by Timpson *et al.* discussing variations among humans in the gene coding for one of the vitamin C transporters (SVCT1) on cells. These transporters control the amount of vitamin C that gets into the blood stream and into cells. Analysis of a cohort of 15,000 people in the United Kingdom found that people with a single nucleotide polymorphism (SNP) in the SVCT1 gene have significantly reduced concentrations of vitamin C in blood. SVCT1 is especially important in the reabsorption of vitamin C in the kidneys, and alterations in its gene affect the level of vitamin C in the blood. The glucose transporter may compensate for the inefficient SNP in the affected SVCT1 gene since it takes up oxidized vitamin C, which may be increased by supplementation. Since the incidence of the SNP may be about 3% in Caucasians and over 9% in African-Americans, studies assessing the effect of vitamin C intake on health and disease outcomes should take SNPs among subjects into account.

**TRABER MG.** Regulation of xenobiotic metabolism, the only signaling function of alpha-tocopherol? *Mol. Nutr. Food Res.* 54:1-8, 2010

Studies on vitamin E supplementation and mortality have been conflicting. Vitamin E is a family of eight isomers, but only one—RRR-alpha-tocopherol (natural vitamin E)—is selectively recognized by transport mechanisms for distribution to the body's tissues. Vitamin E is metabolized by cytochrome P450s, the same enzymes that metabolize xenobiotics like drugs. Thus, the non-RRR-alpha-tocopherol isoforms are metabolized for excretion in the urine or bile

and do not accumulate in the body, unlike RRR-alpha-tocopherol, which does accumulate—but not excessively—due to its slower metabolism. Results from the Women's Health Study showing that vitamin E reduces the incidence of venous thromboembolism may be explained by vitamin E's interference with the conversion of active vitamin K, which is critical in blood clotting.



**KUIPER HC, BRUNO RS, TRABER MG, and STEVENS JF.** Vitamin C supplementation lowers urinary levels of 4-hydroperoxy-2-nonenal metabolites in humans. *Free Radic. Biol. Med.* 50:848-853, 2011

Oxidative stress has been implicated in age-related diseases, but intervention trials with antioxidants have had conflicting results for myriad reasons. It would be useful to validate biomarkers of oxidative stress that can help identify people who might benefit from antioxidant supplementation. The authors found that the levels of lipid peroxidation (LPO) products in urine can be affected by vitamin C intake. LPO products are derived from polyunsaturated fatty acids and can damage proteins and DNA; they are associated with Alzheimer's disease and cancer. Specifically, supplementation with 500 mg of vitamin C twice per day for 17 days in volunteers reduced levels of urinary LPO products by 20-30%. These LPO products may be more sensitive biomarkers of oxidative stress than the commonly used F<sub>2</sub>-isoprostanes, which are also products of lipid peroxidation.

**JUMP DB.** Fatty acid regulation of hepatic lipid metabolism. *Curr. Opin. Clin. Nutr. Metab. Care* 14:115-120, 2011

In this review, the author summarizes findings from studies on the role of dietary fatty acids in the metabolism of fats in the liver. People with diabetes or metabolic syndrome typically have low levels of polyunsaturated fatty acids (PUFA). In mice, high-fat diets lead to hyperglycemia, insulin resistance, and fatty liver—conditions that are associated with decreased levels of enzymes that synthesize PUFA in the liver. Fatty acid elongase is a liver enzyme involved in the synthesis of PUFA that regulates carbohydrate metabolism and liver lipid content.



*continued on page 8*

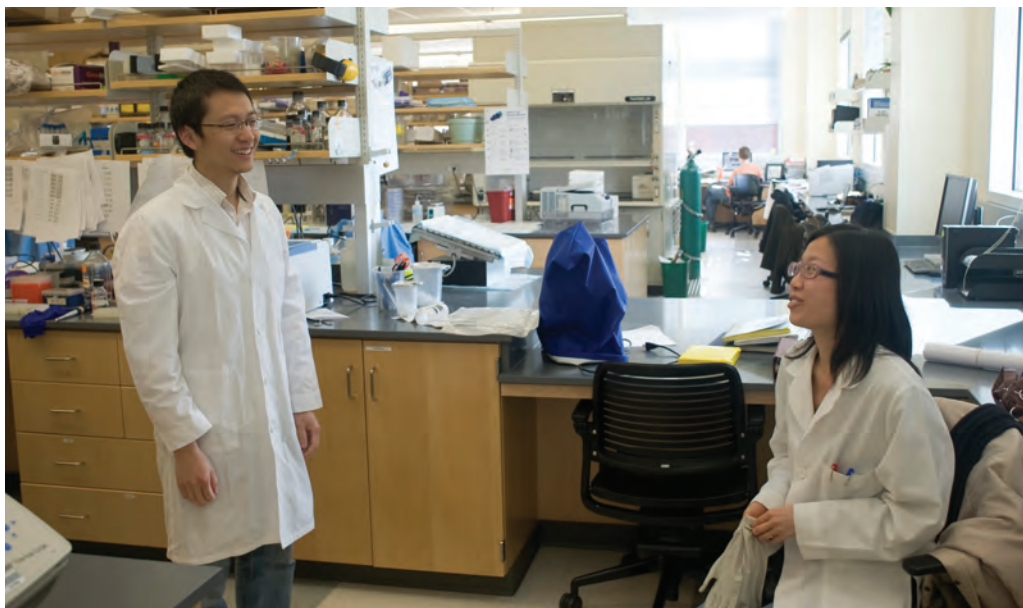
**LOTITO SB, ZHANG WJ, YANG CS, CROZIER A, and FREI B.** Metabolic conversion of dietary flavonoids alters their anti-inflammatory and antioxidant properties. *Free Radic. Biol. Med.* 51:454-463, 2011

Flavonoids are pigmented compounds found in fruits, vegetables, and tea that protect them from UV light and pathogens. They are believed to have health benefits in humans, but their mode of action has been unclear because they are poorly absorbed and then chemically modified before being rapidly excreted. The authors studied the anti-inflammatory and antioxidant activity of two flavonoids—quercetin (found in apples) and catechins (found in tea) and their metabolites—in human aortic endothelial cells in culture. The antioxidant and anti-inflammatory behavior of metabolites differed significantly from the parent compounds depending on the type of chemical modification, illustrating that the biological activity of metabolites of the dietary flavonoids cannot be predicted. Cell culture studies have limited utility in evaluating the activity of dietary flavonoids in the body.

Bioavailability correlated inversely with the dose; it was highest for the low dose and lowest for the high dose. The levels of metabolites peaked in plasma about 15-25 hours after initial xanthohumol dosing. Scaling from rats to humans on the basis of body weight suggests that the dietary intake of xanthohumol by humans is insufficient to achieve its postulated health benefits.

**TRABER MG and STEVENS JF.** Vitamins C and E: Beneficial effects from a mechanistic perspective. *Free Rad. Biol. Med.* 51:1000-1013, 2011

Vitamin C, required for collagen synthesis to prevent scurvy, plays a number of other crucial biochemical roles in the body. It regulates hypoxia-inducible factor-1 (HIF-1), which is involved in cell growth, metal transport, programmed cell death (apoptosis), blood vessel formation (angiogenesis), and energy metabolism. Vitamin C lowers levels of the HIF-1 $\alpha$  subunit, high levels of which have been associated with aggressive cancer. Vitamin C accumulates in immune cells called neutrophils when they attack bacteria, presumably to protect the neutrophils from damage by the reactive oxygen species they produce to



**LEGETTE L, MA L, REED RL, MIRANDA CL, CHRISTENSEN JM, RODRIGUEZ-PROTEAU R, and STEVENS JF.** Pharmacokinetics of xanthohumol and metabolites in rats after oral and intravenous administration. *Mol. Nutr. Food Res.* 55:1-9, 2011

*In vitro* and rodent studies have shown that xanthohumol, a flavonoid in hops used to make beer, has antioxidant, anti-inflammatory, antimicrobial, and cancer chemoprotective properties. However, not much is known about the uptake of xanthohumol into the blood stream from the gut, its distribution to tissues, or its metabolism *in vivo*. The authors gave low, medium, and high doses of xanthohumol to rats and determined that peak plasma concentrations were achieved about four hours after dosing and that half of the xanthohumol was gone from the plasma in 18-30 hours.

kill pathogens. The suppression of HIF-1 by vitamin C also regulates the death and removal of neutrophils when they have completed their function. Importantly, vitamin C is the premier water-soluble antioxidant in blood and protects against damaging free radicals and, with vitamin E, the formation of oxidized lipids. In cultured cells, vitamin C reacts with the lipid peroxidation product acrolein—a toxic and potentially carcinogenic substance primarily formed by heating food—assisting in its metabolic degradation and elimination. Vitamin C also exerts beneficial effects on blood pressure and vascular function by indirectly improving nitric oxide activity.

Vitamin E is a family of eight fat-soluble antioxidant molecules, only one of which, *RRR*- $\alpha$ -tocopherol, is selected for distribution to tissues. Deficiency of vitamin E causes hemolysis (rupture of red blood cells) and peripheral neuropathy. The degeneration of sensory neurons—leading



to ataxia—has been observed in infants deficient in vitamin E due to fat malabsorption problems. There also seems to be a role for vitamin E in preserving proper immune function in elderly people. Vitamin E terminates the chain reaction of lipid peroxidation and is regenerated from its oxidized form by vitamin C. In some populations studied, such as elderly women, supplemental vitamin E decreased cardiovascular mortality, heart attacks, and strokes. While adequate vitamin E intake over a lifetime may help protect against chronic diseases, about 95% of Americans did not meet the Estimated Average Requirement some years ago (12 mg/d [17.9 IU/d] for adult men and women). Vitamin E may also ameliorate abnormally high levels of oxidative stress. Furthermore, vitamin E interferes with the synthesis of vitamin K, which is involved in blood clotting, possibly preventing thrombosis.

## Cancer Chemoprotection Program

**HO E, CLARKE JD, and DASHWOOD RH.** Dietary sulforaphane, a histone deacetylase inhibitor for cancer prevention. *J. Nutr.* 139:2393-2396, 2009

In the cell's nucleus, DNA is wrapped around proteins called histones. Acetylation (addition of acetyl chemical groups) of histones results in genes being turned on, and the deacetylation of histones causes genes to be turned off. Histone deacetylase (HDAC) inhibitors, therefore, keep genes, including tumor suppressor genes, active. Cancer cells seem to be especially sensitive to acetylation, which triggers differentiation and apoptosis (programmed cell death). Sulforaphane—found in cruciferous vegetables like broccoli—is an isothiocyanate whose metabolites act as HDAC inhibitors. Sulforaphane also induces Phase 2 enzymes that detoxify carcinogens, which is important in the early stage of carcinogenesis. It has also been found to induce cell-cycle arrest in cultured human prostate cancer cells and to slow tumor growth in xenografts of human prostate cancer cells in mice. In a mouse model of colon cancer, sulforaphane inhibited the development of polyps. About 74% of sulforaphane from broccoli extracts are absorbed in the intestine and have a biological half-life of about two hours.

**HSU A, BRAY TM, and HO E.** Anti-inflammatory activity of soy and tea in prostate cancer prevention. *Exp. Biol. Med.* (Maywood) 235:659-667, 2010

Chronic inflammation has been implicated in prostate cancer, which is responsible for about 10% of cancer deaths in men. In this review, the authors focus on the effects of diet on prostate cancer, since environmental factors play an important role



in cancer development. Historically, the incidence of prostate cancer has been lower in Asian countries, where soy products and tea are commonly consumed, than in Western countries. Inflammation, as indicated by activation of the transcription factor NF- $\kappa$ B, is associated with benign prostatic hyperplasia, which often precedes prostate cancer. Epigallocatechin-3-gallate (EGCG), a catechin in green tea, attenuates NF- $\kappa$ B activity *in vitro* and inhibits carcinogen activation and tumor growth in mice.

Isoflavones are found in soy and act as phytoestrogens. Consumption of soy in Asia is associated with a low incidence of prostate cancer, presumably due to its isoflavone content. Through cell-signaling effects, isoflavones, especially genistein, inhibit angiogenesis (blood vessel formation) needed to support tumor growth and cancer cell proliferation. High dietary intakes of soy also inversely correlate with testosterone levels in Japanese men, illustrating the hormone-like effects of soy. In the authors' studies, only supplementation with both green tea and soy—but not with either alone—suppressed inflammation and inhibited prostatic hyperplasia in hormone-treated rats. The authors argue that a “whole foods” approach that relies on modest concentrations of these compounds lacking toxicity may be most effective against prostate cancer.

**BOBE G, MURPHY G, ALBERT PS, SANSBURY LB, LANZA E, SCHATZKIN A, and CROSS AJ.** Dietary lignan and proanthocyanidin consumption and colorectal adenoma recurrence in the Polyp Prevention Trial. *Int. J. Cancer* 130:1649-1659, 2012

Lignans and proanthocyanidins are polyphenols that have attracted interest because of their anti-inflammatory and anticancer properties. Lignans are found in the fibrous portion of plants, especially whole grains and flax, and are metabolized by gut bacteria to compounds that have estrogenic activity. Primary dietary sources of proanthocyanidins are tea, chocolate, and apples. The authors evaluated the association between lignan and proanthocyanidin intake—estimated from databases linked to a food frequency questionnaire—and adenoma recurrence

*continued on page 10*

in 1,859 participants in a four-year, randomized, nutritional intervention study that encouraged the consumption of a high-fiber, high-fruit, and vegetable-enriched diet. Overall, no association between lignan and proanthocyanidin intake and adenoma recurrence was observed; however, lignan intake was associated with adenoma recurrence in women, indicating that high lignan intake may increase the risk of adenoma recurrence in women.

CASTRO DJ, LÖHR CV, FISCHER KA, WATERS KM, WEBB-ROBERTSON BJ, DASHWOOD RH, BAILEY GS, and WILLIAMS DE. Identifying efficacious approaches to chemoprevention with chlorophyllin, purified chlorophylls, and freeze-dried spinach in a mouse model of transplacental carcinogenesis. *Carcinogenesis* 30:315-320, 2009

The authors previously reported that indole-3-carbinol—a phytochemical in cruciferous vegetables—green tea, or caffeine fed to pregnant mice exposed to a carcinogenic polycyclic aromatic hydrocarbon called dibenzo[a,l]pyrene (DBP) protected the offspring from mortality due to lymphomas and decreased the number of lung tumors per mouse. Exposure to DBP is widespread because it is formed from the combustion of coal, petroleum products, tobacco, and other organic material. The authors have also demonstrated that chlorophyll or its derivative chlorophyllin protected trout from liver cancer caused by exposure to aflatoxin B<sub>1</sub> formed by molds on grain and nuts. In the present study, oral co-administration of chlorophyllin and DBP to pregnant mice significantly protected their offspring from carcinogenesis, even though the offspring had no direct exposure to either compound. This provides another example of the utility of phytochemical chemoprotection against transplacental carcinogenesis.

CLARKE JD, HSU A, RIEDL K, BELLA D, SCHWARTZ SJ, STEVENS JF, and HO E. Bioavailability and inter-conversion of sulforaphane and erucin in human subjects consuming broccoli sprouts or broccoli supplement in a cross-over study design. *Pharmacol. Res.* 64:456-463, 2011

It has long been known that consumption of cruciferous vegetables like broccoli, Brussels sprouts, and cabbage confers some protection against cancer. Glucosinolates in these vegetables are converted by myrosinase—an enzyme in the vegetables released by chopping or chewing—into isothiocyanates like sulforaphane and erucin, as well as other compounds. Sulforaphane has demonstrated anti-cancer properties in cell culture and animal studies. The authors examined the bioavailability of sulforaphane in humans consuming broccoli sprouts or broccoli supplements by measuring sulforaphane and erucin in the blood. Both compounds were measured because sulforaphane can be converted to erucin and erucin to sulforaphane in the blood. The bioavailability of sulforaphane and erucin in the broccoli supplement was much lower than in fresh broccoli sprouts, probably because the supplements lack the enzyme myrosinase.

MCQUISTAN TJ, SIMONICH MT, PRATT MM, PEREIRA CB, HENDRICKS JD, DASHWOOD RH, WILLIAMS DE, and BAILEY GS. Cancer chemoprevention by dietary chlorophylls: A 12,000-animal dose-dose matrix biomarker and tumor study. *Food Chem. Toxic.* 50:341-352, 2012

Dibenzo(*def,p*)chrysene (DBC, formerly known as DBP), a polycyclic aromatic hydrocarbon formed by the combustion of organic substances like coal, wood, and oil, is a potent carcinogen in animals. Because people are unavoidably exposed to DBC in urban areas, they may be at increased risk for cancer. The authors exposed trout to DBC and observed a linear dose-response increase in the incidence and multiplicity of liver tumors up to the dose of maximum effect. Co-treatment of the trout with chlorophyll-enriched spinach extracts at human dietary intake levels significantly inhibited the incidence and multiplicity of tumors, except at the highest DBC doses. This suggests that chemoprevention studies in animals conducted with very high carcinogen doses may not have much relevance to people. Chlorophyll's likely protective mechanism is its binding to DBC in the gut, thereby preventing DBC uptake into the blood stream and delivery to target tissues.

WONG CP and HO E. Zinc and its role in age-related inflammation and immune dysfunction. *Mol. Nutr. Food Res.* 56:77-87, 2012

In this paper, the authors review the role of zinc deficiency in age-related immune dysfunction—leading to increased susceptibility to infections—and inflammation, which contributes to chronic diseases like heart disease and certain cancers. Over 40% of older Americans do not consume the daily Estimated Average Requirement for zinc (9.4 mg/d and 6.8 mg/d for men and women over 50, respectively), and there is an unexplained age-related decline in zinc levels that does not appear to be due to decreased dietary intake or absorption. Zinc inhibits the activation of NF- $\kappa$ B, a molecule that regulates the inflammatory response. Zinc supplementation has been shown to improve immune response and to lower inflammation.

Epigenetics refers to changes in gene expression without corresponding alterations in the underlying DNA. Zinc plays an epigenetic role in the methylation of DNA required for normal development and the suppression of carcinogenesis. Additionally, rodent experiments have shown that maternal zinc deficiency impairs immune function and glucose handling in offspring through epigenetic mechanisms. **LPI**

LPI is grateful for the bequests  
we have received from the  
following friends this past year:

Mr. John F. Holterhoff  
Mr. Gerald D. Carney  
Ms. Zella E. Mack





## LPI's Healthy Youth Program

Simone Frei, M.P.H., M.A.  
Program Coordinator  
Healthy Youth Program

Providing public education to promote optimum health and prevent disease has always been a major commitment of the Linus Pauling Institute. Our educational efforts have been mainly focused on adults. We recently decided to reach out to our youth as well, to make an impact on their health. Hence, we developed the Healthy Youth Program in 2009 in response to the declining emphasis on nutrition and physical education in our schools and the alarming increase of childhood weight problems in the United States. The goals of the Healthy Youth Program are to provide educational and activity programs to school children and their families to instill healthful diet and lifestyle habits in our youth, thereby helping them maintain a healthy body weight and prevent the chronic diseases of adulthood.

### Micronutrient Intake in Elementary School Children

Our micronutrient intake study assesses the dietary intake levels of all vitamins and essential minerals, as well as the vitamin D body status, in a cohort of elementary school children in Corvallis, Oregon. To date, 172 children have completed a validated food questionnaire (Block Kids Food Questionnaire), and a subset of 71 children completed a vitamin D blood spot test from ZRT Laboratories in Beaverton, Oregon. Preliminary data indicate that 70% of children had serum vitamin D levels between 21 and 30 ng/mL and 13% had levels below 20 ng/mL, considered insufficient and deficient, respectively. None of the children met the recommended intake levels for vitamin E and linoleic acid, and only one child met the Adequate Intake (AI) for potassium. Very few of the children met the AI for alpha-linolenic acid and the recommended intake level for fiber. Seventy-six percent of children aged 5-8 years and 92% of children aged 9-11 years, respectively, did not meet the recommended intake levels for calcium, 40% and 61% for magnesium, 40% and 54% for phosphorus, and 22% and 44% for vitamin A. Most children met the recommended intake levels for the B vitamins and vitamin C.

While we still need to collect and analyze more data, these preliminary results raise serious concerns about the nutrient

intake of children even in affluent and well-educated communities. The low dietary intakes of calcium and magnesium, together with low vitamin D status, may have detrimental consequences for bone health, both in the short term (failure to mineralize growing bones and achieve peak bone mass) and long term (osteoporosis). There is a critical need for tools that help parents and health professionals assess the nutritional status of children and provide guidance to improve their nutrient intakes, including improved diet and use of dietary supplements.

### Childhood Nutrition and Exercise in Elementary Schools

Our study, *Childhood Nutrition and Exercise in Elementary Schools*, examines elementary school teachers' needs, knowledge, concerns, and barriers regarding nutrition education and physical activity in elementary schools and also assesses school cafeteria staff's knowledge and attitudes towards childhood nutrition. Confidential and anonymous surveys have been administered to 227 elementary school teachers and 59 school cafeteria staff in public elementary schools in

Oregon. Results indicate that the majority of Oregon's classroom teachers see a need to provide nutrition education to elementary school children, but they expressed great concern about time and budget restrictions. Competing academic expectations and lack of a suitable curriculum limit the time that teachers can spend on nutrition education. Parents and school cafeterias were perceived as important to improve the efficacy of a revised nutrition curriculum. Most teachers were interested to learn a new nutrition curriculum; however, money was a potential limiting factor for training. Cafeteria staff also see a need to improve the eating habits of the students and want to get involved with nutrition education. However, time and training are limiting factors.

We also found that most teachers would welcome more physical activity breaks for children during the school day. The teachers are willing to be part of the solution and want to learn more about ways they can incorporate physical activity breaks into their daily classroom schedule.

### K-5 Nutrition Curriculum

Based on the results of the above described study, we are developing a K-5 nutrition curriculum, as well as an exercise DVD. Our curriculum will reflect the core tenets of LPI regarding healthful diet and lifestyle and will be divided into three age-appropriate segments: a) kindergarten and 1st

*continued on page 12*



grade, b) 2<sup>nd</sup> and 3<sup>rd</sup> grades, and c) 4<sup>th</sup> and 5<sup>th</sup> grades. We believe that a successful nutrition curriculum needs to be engaging and tied to other academic areas in school, making its content more meaningful and applicable. This will allow the teachers to incorporate the curriculum into their lesson plan as an academic enrichment. Therefore, our curriculum will include many hands-on activities that relate to math, science, and English language skills.

## Exercise DVD

With the help of a group of exercise and sports science students at Oregon State University, we are developing a DVD with different segments of physical activities that can be done in a classroom setting.

Since many classroom teachers are not trained in exercise instruction or may be uncomfortable demonstrating exercises to their students, they may prefer to use this DVD to provide physical activity breaks. The exercises demonstrated in the DVD will include stretching, yoga, strengthening, flexibility, and aerobic moves, such as jumping in place. Sports exercise students will demonstrate the exercises with music in an engaging and fun way, while media students are responsible for producing the DVD.

## Cooking Fun & Play

We have partnered with KidSpirit to offer *Cooking Fun & Play*, an after school program for elementary and middle school students. KidSpirit is a program in OSU's College of Public Health and Human Sciences aimed at improving the skills, lifestyle, and social development of children of all ages, abilities, and cultural backgrounds.

The main objective of *Cooking Fun & Play* is to teach children the importance of a healthful diet, familiarize them with preparing healthful meals, and increase their level of physical activity. Since many experts agree that health-related behaviors are developed during childhood, we believe our program will have a lasting impact on these children's health into adulthood.

On two afternoons per week, students learn about the importance of healthful eating, such as the benefits of eating plenty of fruits and vegetables and substituting whole-grain foods for refined-grain foods. Students also learn to identify which foods are healthful and which foods should be consumed in moderation or avoided, especially highly processed, calorie-dense, nutrient-poor foods.

Through hands-on teaching, the students learn to follow a recipe and cook their own meal, develop cooking skills, plan a menu, and put together a grocery shopping list. We teach the children how to cook meals that are not only affordable but also healthful and nutritious. Parents and guardians are encouraged to participate in the cooking sessions so that these skills can be implemented into the family's daily routine to improve the dietary habits of the entire family.

On the other two afternoons per week, students participate in physical activity games that are non-competitive, don't require athletic skills, and are designed to attract those children who typically avoid competitive or recreational sports. Students also participate in weekly swim lessons and learn about water safety.

## To Grow Box

We have partnered with the Corvallis Environmental Center to expand their gardening education program for low-income families, the *To Grow Box*, to include an interactive and engaging nutrition education component. Participation in this program is free. The expanded *To Grow Box* will educate families on how to grow their own vegetables, the importance of eating a healthful diet with plenty of fruits and vegetables, how to cook nutritious and healthful meals with fresh produce, and how dietary habits affect health and well-being.

The *To Grow Box* is a six-week program that is offered in the summer at the SAGE Community Garden in Corvallis. The program will provide families with the knowledge and skills to plant their own vegetable garden and to incorporate fresh produce into their meal planning. Families will be provided with recipes that are not only healthful and nutritious but also affordable and tasty. Every week, families will take home a box full of fresh produce harvested right from the garden. Childcare will be provided and children will be encouraged to participate in the gardening and cooking. In each class, families will work in the garden, harvest the produce, prepare and cook a meal, and end the day eating dinner together in the garden.

Nutrition education will be provided in an informal and interactive way while the families are preparing dinner. Families will be encouraged to ask questions and will be given the opportunity to meet individually with our nutrition



educator to discuss their family's health behaviors. Families will also receive a binder with nutrition information, resources, and recipes, including the ones prepared in class. After the completion of the program, participants will be provided with a box filled with gardening supplies to start their own vegetable garden. Follow-up for technical garden support will be available to participating families for up to one year.





# The Spartan Garden

Candace Russo, M.S.  
Garden Manager  
Healthy Youth Program



## The Spartan Garden: Soil to Seed to Plate

The Healthy Youth Program (HYP) has partnered with Corvallis High School (CHS) to develop a school garden (named the *Spartan Garden*, after the CHS mascot) that includes an outdoor classroom, as well as produce preparation and cooking spaces. The *Spartan Garden* provides place-based learning, where students explore where their food comes from, how to grow their own food, the value of eating healthful foods, and the link between a healthy environment and a healthy lifestyle.

Following a unique model, the *Spartan Garden* is primarily student-run, as high-school youth are capable of engaging in all aspects of the garden, from “soil to seed to plate.” Innovative design features allow multiple disciplines to use the garden for science, health, nutrition, cooking, environmental sustainability, art, woodworking, and more. The garden design includes a compost observatory, vegetable washing station with water catchment, cooking tables, cob oven, rain garden, living fence, and culinary herb spiral.

Students in each of the three horticulture classes at CHS are committed to preparing and maintaining the garden throughout the school year. This is a natural fit, as all garden activities provide “real-world” experiences directly related to learning objectives for this discipline. So far, students have prepared the soil by removing debris, adding compost, forming raised mounds, spreading leaves, and planting cover-crops to protect the soil from winter rains. The horticulture students have determined their garden’s soil type, tested for earthworm abundance, measured soil pH and nutrient levels, and started seeds for nutritious cool-season crops, including kale, greens, leeks, and broccoli.

Beyond the horticulture classes, many other disciplines are incorporating the *Spartan Garden* into their curricula. Foods and culinary arts students plan to harvest produce to use in their spring cooking classes; they will also be working with the Corvallis Environmental Center (CEC), a community partner, to offer “tasting tables” for their peers and teachers, as part of the Edible Corvallis Initiative. Spearheaded by the CEC, the “Tasting Tables” project

encourages healthful eating by showcasing seasonal food from local farms and provides tastings to schools throughout the Corvallis School District. “Tasting Tables” will be brought to CHS (currently they are only offered at the elementary and middle schools), and the *Spartan Garden* will become one of the highlighted “farms.”

Additionally, woodworking students have built a garden tool shed, which will also serve as a canvas for art students to create a garden mural. Work has also started on the vegetable washing station, which will allow food harvested from the garden to be cleaned on-site and made available to the school cafeteria, as well as for students to cook and eat themselves. Woodworking students are building the washing station, and ceramics students plan to create tiles for the surface of the table tops. Ceramics students will also create plates and bowls for the cooking area, host a clothesline art show in the garden, and make pots for “Thank You Herbs,” a donation project to build community support around the school.

The possibilities for curricular connections are endless, as is evidenced by the diversity of teachers that have expressed interest in the *Spartan Garden* project. I will be working with these teachers to help deliver lessons and develop and implement further ideas.

## Chefs in the Garden

The HYP is offering Chefs in the Garden, a month of summer day camps in August. Third through fifth graders will participate in gardening, nutrition, outdoor healthful cooking, environmental science, and physical fitness activities, using the *Spartan Garden* as the venue for these explorations. Themes for each of the four weeks are “Secrets of the Soil,” “Garden Creatures,” “Backyard Science,” and “Adventurous Artists.” Each day, camp goers will harvest food from the garden to cook and eat lunch together, participate in engaging activities surrounding the weekly theme, and help with fun garden tasks, which will, in turn, keep the *Spartan Garden* vibrant throughout the summer. **LPI**

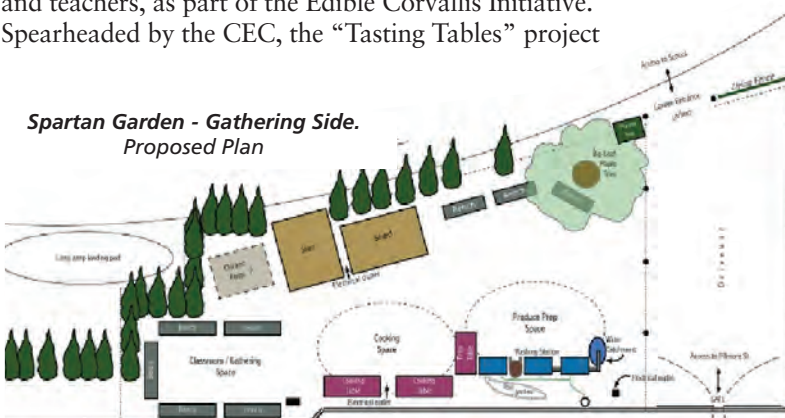
*Special thanks to the following donors who made the Healthy Youth Program possible:*

**Title Sponsor:** USANA Health Sciences, Inc., Salt Lake City, UT  
**Other Sponsors:** Joan Facey, Atlanta, GA  
Starker Forests, Corvallis, OR  
Tim and Starleen Wood Foundation

**Spartan Garden - Growing Side.**  
Proposed Plan



**Spartan Garden - Gathering Side.**  
Proposed Plan





## Briefly. . .

Giana Angelo, Ph.D.  
LPI Research Associate  
Micronutrient Information Center

### What's Good About Chocolate?

Most of the health benefits ascribed to chocolate are likely due to their flavonoids, dietary factors that belong to the general class of compounds known as phytochemicals, or plant chemicals. More than 5,000 varieties of flavonoids have been identified, and hundreds of flavonoids can exist in a single food. All flavonoids have the same basic polyphenol chemical ring structure, hence the occasional reference to flavonoids as polyphenols. Different flavonoids possess varying numbers of rings and chemical attachments, thus imparting different properties to the specific compound.

Due to their unique chemical structures, flavonoids may exert antioxidant, anti-inflammatory, and cytoprotective (cell protective) effects in humans. Consuming flavonoid-rich foods has been associated with a reduced risk of certain chronic diseases, particularly cardiovascular diseases (CVD).

Chocolate contains flavonoids belonging to the subclass called flavanols. The specific flavanols present in chocolate are catechins and procyanidins. Catechins are also present in tea, grapes, and berries; procyanidins are also present in grapes, berries, and red wine.

Flavanols in chocolate come from the cocoa. Dark chocolate contains approximately 43-63 mg flavanols per 100 grams (about 3 oz). However, differences in processing can greatly affect the amount of flavanols present in commercial cocoa-containing products.

A common and early event in CVD occurs when the endothelium—the inner lining of blood vessels—is damaged. Therefore, protecting endothelial function helps minimize the risk for atherosclerosis, heart attack, and stroke. Several small-scale randomized, placebo-controlled trials have been conducted to help determine what quantity of consumed flavanols benefits vascular health. Researchers found that ingesting a cocoa powder drink (containing 375 mg flavanols) twice daily for 30 days improved endothelial dysfunction and blood pressure in patients with coronary artery disease. In healthy adults, ingestion of 46 grams of dark chocolate (containing 250 mg flavanols) daily for 2 weeks improved endothelial function. Even as little as 6.3 grams of dark chocolate (containing approximately 30 mg of flavanols) consumed daily for 18 weeks lowered blood pressure in healthy adults with above-optimal blood pressure.

These studies demonstrate that the amount of flavanols associated with beneficial effects is achievable through dietary consumption of cocoa or cocoa-containing products. It is important to note that flavanols in dark

chocolate are found with other substances, such as fat, sugar, caffeine, and various additional phytochemicals.

### Calcium and Cardiovascular Diseases

A recent meta-analysis reported in the *British Medical Journal* has raised concern about the safety of calcium supplements, either alone or with vitamin D, on the risk of cardiovascular events like strokes and heart attacks. Specifically, the meta-analysis reported an increased risk for myocardial infarction—heart attack—in women taking calcium supplements. A “meta-analysis” is a statistical method that combines the results from several randomized controlled intervention trials that address similar questions. Although the meta-analysis raises an issue that needs further attention, there is insufficient evidence available at this time to definitively refute or support the claims that calcium supplementation increases the risk of cardiovascular diseases (CVD).

CVD is a broad term that encompasses many diseases affecting the heart and blood vessels. In the meta-analysis, the slight negative effect of calcium supplementation was seen with myocardial infarction in particular (approximately 25% increase in risk over five years of supplementation). In an earlier intervention trial by the same researchers, calcium supplementation had variable effects on other cardiovascular endpoints, including a beneficial effect on angina, which is chest pain caused by reduced blood flow to the heart and a common symptom of coronary artery disease. Why the authors removed angina from the recent meta-analysis was not explained and raises concerns.

The risk of myocardial infarction was statistically significant only at low to moderate calcium intakes, not at high levels of calcium intake. Moreover, those subjects with the highest intakes of calcium (>1,000 mg/day) had the lowest rates of death from all causes. This suggests that high calcium intake is protective overall. Why only a moderate dose of calcium would increase the risk of myocardial infarction is unknown.





CVD is a complicated disease with many risk factors. There are other clinical markers of cardiovascular health that can be measured in order to make the most informed decision about your calcium needs. However, the potential risk associated with calcium supplementation on cardiovascular events requires further research.

The Recommended Dietary Allowance (RDA) for calcium is 1,000 mg/day for women 19-50 years of age and 1,200 mg/day for women 51 years of age and older. It's advisable to meet this level of calcium intake from food sources. Good dietary sources of calcium and the amount of calcium per serving can be found online on the LPI Micronutrient Information Center in the section on calcium.

Calcium supplements may contain calcium in the form of calcium carbonate, calcium citrate, calcium citrate malate, calcium lactate, or calcium phosphate. Our intestines can absorb the calcium from these supplemental forms with the same efficiency as calcium from food, except for calcium citrate malate (found in fortified juices), which is very slightly more absorbable.

Importantly, our intestines can only absorb a maximum of 500 mg of calcium at a time. Therefore, if calcium is supplemented, it's best to consume it in small doses throughout the day and to take supplements with meals. **LPI**



## Developments

Michele Erickson  
LPI Director of Development

### Graduate Fellowships at LPI Supporting knowledge, discovery, and a passion for learning

**T**hey are innovators and idea generators: men and women filled with passion and questions, eager to experiment, ponder, and explore.

Tomorrow they will be professors, principal investigators, policy makers, and physicians. They will drive our society's future through scientific discovery, lending new understanding to the vital "protect and prevent" role of micronutrients and other dietary factors central to our ability to avert disease and improve human health.

Today they are graduate students. And with your support, the most promising of these future researchers will come to Oregon State University to study at the Linus Pauling Institute.

In a fiercely competitive academic environment, fellowships help LPI recruit the best and brightest graduate students. These talented scholars power the Institute's research engine, performing much of the daily lab work and tackling problems with fresh energy and perspectives. As they work closely with the Linus Pauling Institute's world-class faculty, they activate the kind of creative synergy that makes breakthroughs happen. Graduate students also shape the experience of many undergraduate students, whom they mentor, guide in the lab, and teach in the classroom.

Supporting graduate students at the Linus Pauling Institute is a meaningful way to invest in our research to determine the role of vitamins and essential minerals, phytochemicals, and dietary supplements in extending healthy lifespan and preventing or treating age-associated diseases.



OSU student Caitlin Crimp (left) with LPI Research Assistant Professor Dr. Debbie Mustacich (right)

Photo by Karl Maasdam

*"My colleagues and I really enjoy our graduate students. They are the heart and soul of our labs at OSU, and it's rewarding to see these bright, eager young people develop their talents. Even as they help us make scientific discoveries today, they are becoming the leading scientists of tomorrow."*

— Dr. Balz Frei, Director and Endowed Chair,  
Linus Pauling Institute

Even modest awards can make a great difference in enabling LPI to attract the finest students and to allow them to focus on their research, teaching, and learning. To recipients, your fellowship gift is extremely valuable at a pivotal moment in their lives.

Your gift supporting graduate fellowships is an investment to build LPI's future as a leading international research institute working to improve human health and wellness, today and for decades to come.

To make a gift designated to support LPI graduate students or to learn more, please contact:

Michele Erickson, Director of Development  
Linus Pauling Institute  
Oregon State University Foundation  
(800) 354-7281, [Michele.erickson@oregonstate.edu](mailto:Michele.erickson@oregonstate.edu)

# Linus Pauling Institute

*Stephen Lawson, Research Newsletter Editor*

Oregon State University  
307 Linus Pauling Science Center  
Corvallis, Oregon 97331

phone: 541-737-5075  
fax: 541-737-5077  
email: [lpi@oregonstate.edu](mailto:lpi@oregonstate.edu)  
Internet Web site: <http://lpi.oregonstate.edu>



Non-Profit Org.  
U.S. Postage  
**PAID**  
Portland, OR  
Permit No. 1006



## GIVING to the Linus Pauling Institute

Gifts in support of research efforts can be made at any time. Checks should be payable to *OSU Foundation for Linus Pauling Institute*. Information on giving is available through the OSU Foundation, 1-800-354-7281, or by writing to the Institute.

**Micronutrient  
Research for  
Optimum Health**

The Linus Pauling  
Science Center



Photo by Karl Maasdam

## *Look for these informative articles inside!*

Page 1 ..... *From the Director*

Page 1 ..... *Dairy, Beans, and Health  
Interview with Gerd Bobe*

Page 5 .... *Recent Publications by  
LPI Scientists*

Page 11 ..... *LPI's Healthy Youth Program*

Page 14 .... *Briefly. . .*

Page 15 ..... *Developments*

*Special thanks to Barbara McVicar for editorial assistance and photographs, authors of signed articles, and Dick Willoughby for the logo photograph of Linus Pauling.*



Printed on recyclable paper  
using soy inks