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Foundation UpdateFall 2007

Straight Talk about Selenium and Your Health
by David J. Waters, PhD, DVM, Director, Murphy Cancer Foundation

Genetic Damage in the Prostate

There are 17,000 men out there whose lives could be radically changed this year. I'm talking about the choice between being diagnosed with an aggressive prostate cancer this year and never developing that cancer at all. The proactive plan of action is a simple one — you've got to get your selenium status ship-shape. All it takes is measuring your selenium level. A simple clip of your toenails provides us with a reliable picture of how much of the cancer-fighting nutrient you are getting from your diet and supplements over the last three months. With this knowledge, you can adjust your selenium intake into the optimal range for lowering your prostate cancer risk.

Why get tested? If, when it comes to cancer protection and selenium, more is always better there would be no need to measure your selenium level. Our advice would be: Go right ahead and supplement all you want. But our research and the work of others has delivered a solid blow to this thinking. **We made an important discovery — there is a U-shaped dose response between selenium intake and genetic damage in the prostate.** Too much selenium may be as bad for you as too little. You want to be in the middle. Hence, we don't recommend taking selenium supplements until you find out where you are exactly on the curve. The staff at the Murphy Cancer Foundation can provide the nutritional guidance to get you where you need to be.

The SeleniumHealth™ toenail test takes away the guesswork. Your physician doesn't "guess" your cholesterol level. He measures it with a blood test and if it is out of whack, he personalizes a strategy of diet and medication to bring your cholesterol to within the desired range. If this seems smart for your heart, then why not personalize your prostate protection?

Prostate cancer is a process that takes 20-30 years to develop so it's not too early for men in their 30s and 40s to think about selenium and their own personalized prostate protection. Therefore, SeleniumHealth™ is a test for men of all ages because effective prevention begins now. This year alone, we estimate up to 17,000 men in the United States will develop the aggressive form of prostate cancer because their selenium levels are too low. Among these men, the sobering statistic is that approximately 1/3 will succumb to their cancers despite state-of-the-art care, exercising all available treatment options. Now, with SeleniumHealth™, it doesn't have to be you. Or your father, brother, son, uncle, grandson . . .

SeleniumHealth™
"Get your selenium level right."

To learn more about getting the test:
www.seleniumhealthtest.org

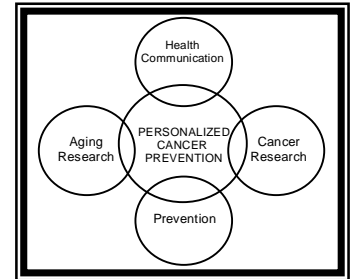
Murphy Foundation: Leaders in Personalized Cancer Prevention

Selenium Intake

What is personalized cancer prevention? We define personalized cancer prevention as a strategy that will enable each person to reduce his or her risk for lethal cancer by matching the *dose, duration, and timing* of an intervention with their own cancer risk profile. Personalized cancer prevention requires a unique constellation of expertise, including an understanding of cancer and aging, a passion for prevention, and proven health communication skills (**Figure**).

Is personalized cancer prevention really a new idea?

Cardiologists and firefighters already recognize the power of prevention. But the sobering reality is that until now most cancer research has been focused on treatment, rather than prevention. Go ahead – Google it – there’s not much out there.



How many researchers have combined expertise in both cancer and aging?

Surprisingly, few scientists are cross-trained in the fields of cancer and aging. The sights of most have been set on *killing cancer cells*, with little attention paid to the biology of aging.

But as more cancer scientists turn their attention toward *prevention*, we will need a more complete understanding of what exactly happens in old tissues – the tissues in which most cancers arise.

So the Murphy Foundation is cross-training young scientists in both cancer and aging to make them better prepared.

As the Murphy Foundation develops the science at the cancer-aging intersection, do you see other obstacles to achieving the goal of personalized cancer prevention? Yes. A major obstacle is that *the public is bombarded by health news, but seldom hears the real story in context*. We are committed to helping scientists *and* the public improve this communication by: (1) holding town meetings that enable people to become savvy consumers of health-related news; and (2) hosting a summit between media and scientists that will encourage scientists to take responsibility for accurately communicating their work to the public. People need access to health news they can use – that means cutting-edge research communicated in the correct context.

What accomplishments are positioning the Murphy Foundation as leaders in personalized cancer prevention?

As you read further in this newsletter, you will see a wide range of accomplishments. All of these highlights fit firmly under the umbrella of personalized cancer prevention – from investigating the health benefits of antioxidant supplements, to training programs in the biology of aging, to focusing on the differences in how to optimize health in men and women. Moreover, our innovative “cells to dogs to humans” research approach clearly shows how the Murphy Foundation is bringing to bear its unique constellation of expertise to achieve the goal of personalized cancer prevention.

UPDATES

Murphy Foundation Investigating Whether Antioxidant Supplements Can Reduce Your Cancer Risk.

In April 2007, we announced the launch of the first-ever cancer prevention trial in pet dogs, which will rigorously evaluate the health benefits of dietary antioxidant supplements. The study is supported by P&G Pet Care and the Rottweiler Health Foundation. "The intervention we're testing is a potent antioxidant combination that significantly reduces the sensitivity of cells to oxidative stress," said **Michael Hayek, PhD, associate director of Research and Development, P&G Pet Care**. "In a pilot study, we teamed up with Murphy Foundation scientists to show that daily treatment with these supplements rendered the blood cells of dogs more resistant to oxidative stress challenge in the laboratory", said Hayek. Previous work with Rottweiler's conducted by Murphy Foundation scientists confirmed this breed's strong predisposition to bone cancer. "Rottweiler owners stand strongly committed to helping us figure out just how to reduce the number of dogs that succumb to cancer," said **lead investigator David J. Waters, PhD, DVM**. This trial takes an important first step toward that goal. Our end goal is to help not only dogs, but their human owners as well, by preventing this devastating disease. We are testing whether a change in diet that heightens your defenses against oxidative stress translates into reduced cancer risk or increased longevity. Enrollment of 700 dogs into the trial is expected to be completed during the next 30 months. By exploiting the compressed life span of pet dogs, this landmark study is equivalent to enrolling 30-year old people and monitoring the results of a 60-year life-long intervention — an unprecedented feat. **Read about it in Redorbit.com/news/health.**

Murphy Foundation Recognized for Innovative Impact on Prostate Cancer. In September 2007, Murphy Foundation scientists were recognized by the Department of Defense Prostate Cancer Research Program (DoDPCR) as “**Innovative Minds in Prostate Cancer Today (IMPACT)**”. Over the last 10 years, the congressionally

directed Department of Defense program has funded more than 1600 prostate cancer research projects totaling more than \$700 million dollars. Our work on the cancer-preventive effects of selenium was recognized as one of 120 funded projects that had the most impact on the prostate cancer field. Dr. Waters delivered a lecture entitled **“More is Not Always Better: Using the Dog Model to Identify What Dose of Selenium Provides the Best Protection Against Prostate Cancer”** to 600 scientists and prostate cancer survivors attending the IMPACT meeting in Atlanta. The meeting marked the 10th anniversary of the DoDPCR and the first public forum to showcase its efforts to conquer prostate cancer. Receiving this recognition highlights the innovation of the Murphy Foundation’s work that is collaboration **with Bostwick Laboratories and joint research with Purdue University.**

Keck-National Academies Think-tank: Can We Extend Healthy Human Lifespan?

In November 2007, Dr. Waters was one of 100 scientists summoned to Irvine, California to participate in the National Academies Keck Futures Initiative. This year’s conference was entitled *The Future of Human Healthspan : Demography, Evolution, Medicine and Bioengineering* — an intensive 2-day discussion of various longevity initiatives from around the world. The idea was to engage outstanding researchers in an intellectually rich discussion of a cross-disciplinary theme — shifting the focus from how long we live to how healthy we live. Each year since 2003, the Futures Initiative has selected a theme where the intersection of science, engineering, and medical research has the greatest potential to spark discovery. Previous conferences have focused on molecular signaling, nanotechnology, genomics, and smart prosthetics. This year, not only did this elite group grapple with thorny issues about the biology of aging, and just how best to push healthy human longevity, these scientists are now eligible to apply for *Futures* grants totaling over \$1,000,000 that will provide seed funding to pursue important new ideas and collaborations. Dr. Waters’ selection to this one-of-a-kind scientific think-tank is further evidence of the growing respect by the scientific community for the Murphy Foundation’s effort to unleash pet dogs to find aging and cancer clues. There is growing recognition that our continuing studies on exceptionally old Rottweiler’s, together with exploiting the profound differences in lifespan between small and large dog breeds, can provide a testing ground to explore just what mechanisms Mother Nature uses to construct long-lived humans.

SHORTS

Great News: Research Happening at the Cancer-Aging Interface. In February 2007, the American Association for Cancer Research organized **“Translational Research at the Aging and Cancer Interface”**, its first attempt to bring together scientists from these two disciplines. Dr. Waters was one of 35 invited speakers from around the world who participated in the 3-day conference. His lecture, **“Looking for Windows to the Aged Prostatic Microenvironment: Non-Invasive Predictors of Genetic Damage within the Prostate”**, emphasized the high priority that the Murphy Foundation is putting on risk stratification. “We are developing accurate, non-invasive methods for men to determine their risk for prostatic DNA damage and cancer”, said **Seema Kengeri, MPH, Murphy Foundation Research Associate** and co-author of the work. “This means assays using blood and toenails, not something invasive like a prostate biopsy.”

Destination Sweden: International Graduate Student Training on Biology of Aging

In June 2007, Dr. Waters joined the world’s top researchers in Biogerontology to teach a 2-week graduate training program in Jonkoping, Sweden. This first **International Program in Aging Research** offered a multidisciplinary training experience on the use of mammalian models to study the complex mechanisms of aging. The program was co-directed by **Roger McCarter, PhD and Gerald McLearn, PhD of Penn State University** and Stig Berg, PhD of Jönköping University.

First Gerontology Training Program for DVMs designed by Murphy Foundation and Purdue Center on Aging and the Life Course.

Veterinarians everywhere are missing out on something — they receive no formal training in the biology of aging and longevity. "Veterinarians who graduated last spring or 30 years ago are in the same boat", said Dr. Waters. We are training a select group of veterinarians to be the go-to experts on companion animal gerontology in their communities, and who will form a care-provider network for further clinical studies on aging and cancer prevention conducted by the Murphy Foundation. By studying the aging process in pet dogs,

we hope to determine the genetic and environmental determinants of exceptional longevity. The Murphy Foundation is home

to the unique **Exceptional Longevity Database**, systematically tracking the oldest pet dogs in the nation, which directly complements ongoing studies of human centenarians.

Tell Me, Is the Average Person a Man or a Woman? In May 2007, Foundation scientists presented their research at the first **Annual Meeting of the Organization for Study of Sex Differences**. The work, entitled “Sex Differences in the Anticancer Effects of Selenium”, was one of 60 scientific posters on display. The central tenet of the Murphy Foundation’s personalized cancer, prevention initiative is that we give too much advice designed for “the average person”. We ask: when it comes to selenium and cancer prevention, is the average person a man or a woman? “Our research on selenium supports a growing consensus that preventing cancer requires sex-specific approaches”, said **Emily Chiang, Research Associate at the Murphy Foundation**. This scientific conference, supported by the Society for Women’s Health Research and Eli Lilly will reconvene in New Orleans in 2008 ... and Murphy scientists will be there.

Coming Full Circle at MD Anderson Cancer Center. In October 2007, Dr. Waters participated in the MD Anderson Cancer Center’s **60th Annual Symposium on Cancer Research: Personalized Risk Assessment and Management** focused on recent progress in selecting treatments that are best for you on the basis of your tumor. The keynote address “Integrated Molecular Markers in the Era of Personalized Cancer Treatment” was delivered by **David Sidransky of Johns Hopkins University**. Though the symposium focused mainly on treatment and prognosis, Dr. Waters presented work championing the importance of personalized prevention. But this wasn’t the first time that the Foundation was recognized at this meeting. It was there in 1978, that **Dr. Murphy received the Heath Memorial Award**, an honor given annually to a scientist for outstanding contributions to cancer patient care through clinical application of basic cancer knowledge. It looks like we’ve come full circle — Dr. Murphy’s legacy of moving basic science toward helping people is very much alive today in the Foundation’s innovative cancer prevention research.

SELECT Prostate Cancer Prevention Trial Reaches Halfway Mark and Still Going Strong. Since 2001, more than 32,000 men have been enrolled in this study designed to test whether daily supplementation with vitamin E or selenium can reduce the risk of prostate cancer. “SELECT is focused on prostate cancer and when the study is finished, we will know for sure whether these supplements can prevent the disease”, said **Inna Savikhin, R.N., Clinical Trials Coordinator** at the Murphy Foundation. Chosen as one of 400 study sites, the Murphy Foundation is proud to participate in the largest prostate cancer prevention trial ever conducted. The Foundation is conducting the trial under the supervision of the **Northern Indiana Cancer Research Consortium**, a cooperative oncology group with an impressive track record in cancer control research. The Foundation’s activities in SELECT, supported in part by the **Olin Looker Memorial Fund**, provide a vivid example of our commitment to saving lives through prevention. You’ll have to stay tuned because prevention research is “the long haul” — expected completion date for SELECT is 2012!

KUDOS

The Far-reaching Effects of Scientific American. It was one year ago that “Cancer Clues from Pet Dogs” hit newsstands across the country in the December 2006 issue of *Scientific American*. Today, the article stands as Dr. Waters’ guided tour of comparative oncology, the field of inquiry that explores the striking similarities between cancers of humans and animals. The scientific community and other media sources were quick to take positive notice. Several new doors opened including: the production by **ScienCentral** of New York City of a video clip called “**Anti-Cancer Dogs**”, distributed to ABC TV affiliates which aired to more than 20 million people nationwide; an invitation for Dr. Waters to deliver keynote addresses at the Sigma Xi Honorary Society, and the 38th Annual Scientific Meeting of the **Environmental Mutagen Society**; and an invitation to submit an invited perspective on cancer prevention research to the scientific journal, *Nutrition and Cancer*. *Scientific American* is a monthly science magazine that has been informing the public since the Civil War. Dr. Waters joins a select company of scientists including Nobel laureates who have contributed work that is scientifically provocative, yet accessible to non-experts, such as the nature of chemical bonds by Linus Pauling (1954), the structure of DNA by James Crick (1957), and the fossil evidence of prehistoric man by Mary Leakey (1982).