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Foundation Update Winter 2012

Selenium Science 2012: It's Time to Get Your Selenium Level Right

"Supplementation of people who already have adequate intake with additional selenium might increase their risk of type-2 diabetes. The crucial factor that needs to be emphasized with regard to the health effects of selenium is the inextricable U-shaped link with status; whereas additional selenium intake may benefit people with low status, those with adequate-to-high status might be affected adversely and should not take selenium supplements."

Rayman, Lancet 2012

Building a More Exceptional U



"It may be a U-shaped relation in which higher selenium concentration confers an increased risk of prostate cancer compared with an optimal moderate concentration. ...A U-shaped relation is supported by evidence from ... dogs, the only other animal that naturally develops prostate cancer."

Am J Clin Nutr, 2012

Selenium and human health
 Margaret P. Rayman

14692-2012-293-1284-8
 Selenium is incorporated into selenoproteins that have a wide range of pleiotropic effects, including antioxidant, anti-inflammatory, and thyroid hormone effects. In the past 10 years, associated polymorphisms in selenoprotein genes have drawn attention to the relevance of selenium status to human health. Low selenium status has been associated with increased risk of mortality, poor immune function, and increased risk of cardiovascular disease. Higher selenium status or selenium supplementation have beneficial effects, including improved thyroid function and reduced risk of autoimmune thyroid disease. Prospective studies have shown that higher selenium status is associated with a lower risk of prostate, colorectal, and bladder cancer. However, the results of these studies have been mixed, which probably emphasizes the fact that supplementation will only benefit those with low selenium status.

Editorial
 See corresponding article on page 111.

Selenium and prostate cancer: the puzzle isn't finished yet¹⁻³
 Eric L. Richman and Jane M. Chan

Selenium is an essential trace element and antioxidant whose pleiotropic effects have excited the field of cancer prevention. In a recent review of the National Prevention of Cancer trial (NPC), 200 µg selenium was associated with a 24% reduction in the risk of prostate cancer (1). These results...

Bone Turnover and Bone Mineral Density Are Independently Related to Selenium Status in Healthy Euthyroid Postmenopausal Women
 Antonia Hoeg, Apostolos Gogkios, Elaine Murphy, Sandra Mueller, Josef Kohrle, David M. Reid, Claus C. Gluer, Dieter Felsenberg, Christian Roux, Richard Eastell, Lutz Schoenberg, and Graham R. Williams

Institute for Experimental Endocrinology (A.H., S.M., J.K., L.S.), Charité-Universitätsmedizin Berlin, Campus Virchow Klinikum, D-13352 Berlin, Germany; Molecular Endocrinology Group (A.G., E.M., G.R.W.), Department of Medicine, Imperial College London, London W12 0BZ, United Kingdom; Biometrisches Laboratorium (C.C.G.), Diabetologische Endokrinologie, Universitätsklinikum Schleswig-Holstein, D-26111Ratzeburg, Germany; School of Medicine...

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Prostatic Response to Supranutritional Selenium Supplementation: Comparison of the Target Tissue Potency of Selenomethionine vs. Selenium-Yeast on Markers of Prostatic Homeostasis
 David J. Waters^{1,2,3}, Sharon Shen¹, Sreeta S. Kengeri¹, Emily C. Chiang¹, Gerald F. Combs, Jr.¹, J. Steven Morris^{1,2} and David G. Bostwick¹

¹ Department of Veterinary Clinical Sciences, Purdue University, West Lafayette, IN 47907, USA; ² The Center on Aging and the Life Course, Purdue University, West Lafayette, IN 47907, USA; ³ Gerald P. Murphy Cancer Foundation, West Lafayette, IN 47906, USA.

"[In 1144 women] higher selenium levels [in the optimal bottom part of the U curve] were associated with higher hip bone mineral density ..."

The Osteoporosis and Ultrasound Study (OPUS) from Europe, 2012

Live to Perform.

"Based on the significant anticancer efficacy of Se-yeast in men with low baseline selenium in the NPC Trial together with the equipotent effects of the two forms of selenium reported here, we speculate that subgroup analysis of prostate cancer risk in SELECT will show that men with low baseline selenium concentration can achieve prostate cancer risk reduction from selenium supplementation."

Waters et al, Nutrients 2012

The year 2012 witnessed a compelling convergence of new scientific evidence (4 studies are highlighted above) that further supports the Murphy Foundation's stance on selenium and your health. **In a U-shaped world, dose matters because more of a "good thing" like selenium is not necessarily better.** If successful aging and personalized cancer prevention is your goal, then it pays to get your selenium level right. In 2010, scientists at the Murphy Foundation published convincing scientific evidence for this sort of U-shaped thinking about selenium and lowering your cancer risk. We issued the following statements: **"Not everyone should take selenium supplements.** You should use the SeleniumHealth™ toenail test to know your selenium level so we can guide you to achieve the optimal level for reducing your cancer risk." **Summarizing the science of 2012: Getting your selenium level right is an important facet of a healthy lifestyle.** For more information on the selenium toenail test and getting your selenium level right, you can contact **Cheri Suckow, RN**, at the Murphy Foundation or go to www.seleniumhealthtest.org.

Inside This Issue

Achieving excellence in research and education is a creative process that requires stamina and openmindedness to new ideas. But which new ideas signal the truest direction for the surest progress? Progress prevails when we fine-tune our process of discovering. The psychologist **William James** wrote: "The truth of an idea is not a stagnant property inherent in it. Truth *happens* to an idea." In this issue of **Foundation Update**, you will encounter stories about some of the new ideas in aging and cancer research and education that we are pursuing. It is our invitation to you *to experience truth happening*.

Updates

Trailblazing Research on Aging Continues: The Old Grey Muzzle Tour II —

Experts agree that discovering the secrets to successful aging will demand a sustained effort using innovative scientific approaches. Accepting this challenge, the Murphy Foundation



has placed its bet on man's best friend to track down some of the answers to the really tough questions about why we age. In 2010, our research on aging and healthy longevity broke out of the ivory tower and headed into the living room, capitalizing on the opportunity to study first-hand some of the oldest-living dogs in the U.S. in their homes. Dr. Waters' 22 day cross-country scientific expedition from Boston to Seattle – *The Old Grey Muzzle Tour* – captured the imagination of scientists and the public, and was featured on **Good Morning America** and in **USA Today**. Now, the Murphy Foundation is proud to announce that Dr. Waters will be hitting the road again in Spring 2013 on *The Old Grey Muzzle Tour II*.

This time the expedition will be broadened to include not only

Scientific Stops – where Dr. Waters studies the oldest dogs in their homes – but also **Celebration Stops** where he will meet with groups inspired by our work, to recognize their support. As our research continues to be published in scientific journals, *The Old Grey Muzzle Tour II* will not only extend the research but also raise public awareness of the true heroes of cancer prevention we are studying: **the cancer-resistant exceptionally long-lived Rottweiler dogs who are teaching us and furthering the pet-person partnership to beat cancer**. "We see the Muzzle Tour as a key element to building the momentum we need to sustain healthy research progress on what it takes to achieve the all-important goal of cancer avoidance," said **Seema Kengeri, MPH, Data Base Coordinator at the Murphy Foundation's Center for Exceptional Longevity Studies**. Stay tuned for more details of the Tour slated for March 2013.

Message to Health Professionals: Find Your Intellectual Heroes — Solving the cancer problem will demand tip-top performance. Sustained performance requires renewal. But where will our researchers and other health professionals find renewal? Rather than believing that medical progress is inextricably linked to the next technological breakthrough, Murphy Foundation scientists are proposing an innovative alternative: **There is no better cure for cancer than optimizing the performance of all hands on deck**. In March, **Dr. Waters delivered the keynote address** to open an **International Symposium on Interdisciplinary Research, Education, and Communication (IDREC)** in Orlando, FL. His talk entitled "**The Paradox of Tethering: Key to Creative Excellence in the Research-Education Space**" sketched out a strategy for sustained self-renewal and creative excellence: **Each person assembling a gallery of intellectual heroes to serve as their life-long teachers**. He argued that tethering ourselves to intellectual heroes does not limit our creative potential but instead achieves exactly the opposite effect — enabling us to see and reach our own greatest potential. By strengthening the habit of strategic tethering, we place an active, partially guided search for self-renewal and a heightened receptivity to new ideas at the very heart of achieving excellence. In early 2013, Dr. Waters' talk will be published in **Informing Science**, a scientific journal read

by investigators interested in the goal of enhancing the fidelity of communication in science and medicine, as well as in business and everyday life. The Murphy Foundation is growing to see 3 domains – the biology of successful aging, the science of cancer prevention, and the skills and attitudes of peak personal performance – as increasingly integrated, representing a fruitful yet underexplored intersection of inquiry. The merging together of the goals of optimizing health and promoting peak mental performance is captured in our axiom: **“Live to Perform”**. To learn more, contact us to receive a copy of Dr. Waters’ published keynote address.

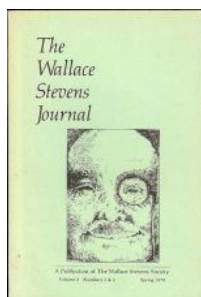
What Do Old Worn Out Cells Have to Do with Aging and Disease? — From laboratory studies, scientists have known for a long time that cells aging in a petri dish naturally



undergo a process called **cellular senescence**. Senescent cells completely lose their ability to divide and they switch on the production of inflammatory proteins. What remains shrouded in uncertainty is whether senescent cells – so carefully characterized in the laboratory – actually accumulate in aging animals and people. Moreover, do senescent cells significantly contribute to the diseases and disability we see as a consequence of aging? A landmark paper published in *Nature* in late 2011 tackled this question head-on. Researchers at Mayo Clinic

and their collaborators genetically engineered rodents so they could identify senescent cells and trigger their removal. They showed that **eliminating senescent cells from these aging mice was beneficial** — the procedure significantly delayed the onset of aging-related chronic diseases. In November 2012, Murphy scientists travelled to Mayo Clinic to participate in a scientific conference entitled **“Senescence and Healthspan”**, which focused on the prospect of using senescence-targeted approaches to promote successful aging. “The paper published by the Mayo group signaled a notable inflection point in aging research”, said **Emily Chiang, PhD, Director of the Murphy Foundation’s Aging Biorepository**, and one of 125 scientists from around the world who attended the conference. Moving forward, a high priority will be to go beyond engineered rodents to define what role senescent cells play in driving human aging and specific aging-related diseases. And that is where Murphy Foundation scientists will be investing their effort — by putting their expertise with highly successfully aging dogs to work to drive a deeper understanding of cell senescence and aging.

Innovating Science Education : The Wisdom of Wallace Stevens — In May,

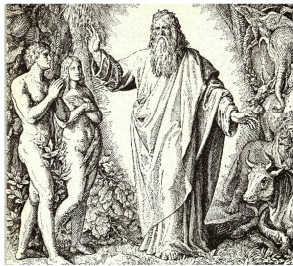


Dr. Waters delivered a paper at the **23rd Annual Conference of the American Literature Association in San Francisco, CA**. What could possibly lure an aging-cancer scientist to hang out with a bunch of the best and brightest literary scholars and students of the humanities? Dr. Waters’ paper entitled “Researching by Rabbit Light: Situating Wallace Stevens and Science Education” introduced a fresh idea: **Exposing young scientists-in-training to the versatile imagination of the poet Wallace Stevens is precisely what science education needs**. Waters argued that we need more

Poet-Scientists – not discoverers with a knack for rhyme but discoverers who care more deeply about language, so they come to realize how the process of naming things limits the scientific method. The truth is that our thinking is severely limited by our words, the categories we use. Categories can cripple understanding, block medical progress. An example is when we assume that taking a dietary supplement is either good or bad for us instead of seeing all interventions as good and bad, depending on the situation. This process of artificially oversimplifying the way things are makes us more likely to *impose* our preconceived biases rather than *discover* new connections. Dr. Waters’ talk was enthusiastically received and a manuscript describing the opportunities to innovate science education through Stevens is currently under review. Our idea is to teach young scientists to combine analytical reasoning with intuitive imagination **so they may become hyphenated, imagino-analytical discoverers** best positioned to solve the enigmas of aging, the mysteries of cancer. We urge our scientific colleagues to spread the word: **It pays to be hyphenated.**

Training the Next Generation of Cancer Prevention Scientists — The Murphy Foundation has a strong commitment to cross-training scientists-in-training in 3 specific areas: cancer, aging, and the communication of health-related research. In August, Dr. Waters

And On the 6th Day, God Created *The Critical Molecular Target of Selenium*



participated as one of 15 faculty educating 75 young trainees from 25 countries at the **National Cancer Institute's 2012 Summer Curriculum in Cancer Prevention Course**. Dr. Waters' talk on animal models to advance cancer prevention travelled beyond typical boundaries to challenge students about their process of scientific discovery. He challenged them to ponder what he calls "**The Myth of the Single Solution**" — how the idea that there is a single solution to the problem of complex diseases, such as cancer, can intimidate young trainees. *If there is only one solution, how will each of them possibly find*

it? Dr. Waters encouraged the students to escape The Myth of the Single Solution and to regain confidence by re-imagining their research question – their pursuit of one of the multiple useful avenues of discovery – as being perfectly matched to the unique skill set they are so diligently working to acquire. Written evaluations of the talk by attendees suggested that Dr. Waters' presentation was on the mark: "He was extremely motivating and thought-provoking ... I was renewed by his talk. I really liked the combination of science and professional development." Another student remarked: "Clearly a great public speaker able to convey information in an infectious way. The lecture was an inspiring mix of scientific findings and philosophy." The bottom line is this: **The world's progress in preventing cancer hinges on shaping, provoking, and inspiring the next generation of scientists.** That is why the Murphy Foundation will continue its tireless efforts to innovate education.

Murphy Foundation Website Promotes Peak Personal Performance —

The Murphy Foundation has updated its website to provide visitors with new perspectives on professional and personal development. "**Dr. Waters' Choice**" features brief descriptions of books which readers may find as valuable sources of useful ideas. Examples include: R.G. Collingwood's **Speculum Mentis: The Map of Knowledge** (1924) which encourages each of us to adopt a more holistic, multi-angled orientation as we try to make sense of the world, steering us away from the ruts of specialization; Zander and Zander's **The Art of Possibility** (2000), published by Harvard Business School and written by a husband and wife team, offers insights on how we might re-orient ourselves in a universe of possibilities — positioning ourselves for a life of ongoing transformation and satisfying purpose.

In Memorium — We are honored to recognize the passing of a special individual with close ties to the Murphy Foundation. **Pat Jones** of Federal Way, WA was instrumental in forging a lasting relationship between the Murphy Foundation's research team and the **Gamma Delta Chapter of the Phi Beta Psi Sorority**, an organization dedicated to supporting innovative cancer research. Each February, Dr. Waters would travel to Seattle to deliver the keynote talk at Gamma Delta's Sweetheart Dinner, updating attendees on what questions scientists were wrestling with at the frontiers of cancer and aging research. Pat's optimism, generosity, and love of life will continue to be an inspiration to all who knew her.

Kudos

Big Recognition for Research Achievement in the Biology of Aging —

The Gerontological Society of America (GSA) annually hosts the world's largest gathering of scientists to exchange ideas in the field of aging. Each year, a special group of distinguished scientists are inducted as GSA Fellows. In 2012, **Dr. Waters was inducted as a Fellow in the Biology of Aging**, joining an elite group of 62 scientists world-wide who have achieved this prestigious designation. Clearly, our work is seen as illuminating a new research path — harnessing pet dogs as biogerontology's new workhorses to innovate progress and shed light on what it takes to promote healthy longevity. And it is through the process of searching and re-searching the biology behind successful aging that this prize will be realized.

Gerald P. Murphy  Cancer Foundation

INNOVATIVE RESEARCH FOR PERSONALIZED CANCER PREVENTION

Dear Friends,

December 2012

This year marks 12 years that the Murphy Foundation has been advancing under my leadership. Over this time, many of you have appreciated the scope of our accomplishments: moving our basic research on selenium and cancer prevention into developing the **SeleniumHealth™** toenail test that men are using to get their selenium level right; telling the world in *Scientific American* about the unique opportunities to gather **Cancer Clues from Pet Dogs** that will help both people and pets fight cancer; developing a **Personalized Cancer Prevention Program** that is cross-training the next generation of researchers in cancer, aging, and communicating health research to the public; and my cross-country trek **The Old Grey Muzzle Tour** putting the Murphy Foundation on the map as leaders of a whole new way of thinking about how aging research is done. Today, as we look to the horizon, **our process of discovering and reporting shows no signs of slowing down.**

Your unwavering faith in Murphy Foundation scientists to perform at the highest possible level inspires us. Each year at this time, my team and I appraise our accomplishments by asking the question framed by the famed philosopher and father of modern psychology William James: **“Does the world, with our additions, rise or fall in value?”** It is these high expectations that stretch our imaginations and motivate us to succeed.

This issue of **Foundation Update** highlights the considerable progress that we have made in 2012. This body of work is the product of dedicated investment in specific areas of research and education that we believe hold great promise. While grants and contracts fund the majority of our work, **our needs cannot be met without the individual gifts that you make to support us.** You make our ideas come to life. ***You make our discovering-reporting process happen.*** With each dollar that you generously invest in the Murphy Foundation, we move ahead – ever closer to the goal of living the longest and healthiest that we can. To each of you, let me say how grateful we are to serve you in this pursuit.

Best Holiday Wishes,
David J. Waters, DVM, PhD

Please detach and return in the envelope enclosed, with checks payable to “GPMCF”

Please accept my enclosed tax-deductible gift in support of the Murphy Cancer Foundation:

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