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AS WE SEE IT

A Revolutionary Concept Slowly Gains Recognition

When Saul Kent and I established the Life Extension Foundation in 1980, we had no idea what we were in for. As young men, our objective was to raise public awareness about the fact that pathological aging need not be an inevitable consequence of human maturation. We were convinced that if the public could be enlightened about the importance of anti-aging research, greater resources would be devoted to finding ways to significantly extend the healthy human life span.



Back in 1980, few scientists believed that anything could be done to prevent the degenerative effects inflicted by aging. To counter this misconception, Saul and I pointed to then-current scientific studies showing that it was possible to prevent some age-related diseases and to slow the aging process itself, at least in animals. We argued that if enough funds were committed to research, therapies to retard human aging could be developed that would result in the greatest revolution in medical history.

Few people in 1980 thought that intervention into biological aging was possible, and many questioned why we would want to interfere with nature. We argued that aging was the greatest scourge afflicting humanity and that if people had the opportunity to live longer, many of society's problems would disappear.

We based our philosophical arguments on theories that people with limited life spans are not particularly motivated to protect society's long-term interests, since they themselves have only a relatively short time to live. Longer life spans, we asserted, would result in people behaving in a manner that would make the world a better place, since they themselves would have to exist in the environment they create.

COSTS OF CHALLENGING CONVENTIONAL WISDOM

Being controversial carries a heavy price. The news media viciously attacked our position and had no problem finding academic scientists to denigrate us in every way possible. The federal government raided our facilities twice, initiated an 11-year criminal investigation, and threw us in jail in 1991.

We retaliated by filing multiple lawsuits against the federal government, which resulted in the return of all the property it had seized from us. We rallied health freedom activists to keep the FDA from turning vitamins into drugs. We enlightened Americans about the availability of lower-cost prescription drugs in other countries. And we eventually convinced the US Attorneys' Office to dismiss the criminal indictments brought against us by the FDA.

One benefit of all this controversy was that even though the news media did not treat us well, it did report what we were doing. Because of this media coverage, many enlightened people found out about us, joined as members, and even made substantial donations to support us.

When the FDA conducted its first armed raid in 1987, we had only 4,000 members. Thanks to publicity generated by the FDA's actions, this number grew to 25,000 members by the time our criminal indictments were dismissed in 1995. We now have over 100,000 members and each month mail 250,000 copies of *Life Extension* magazine to newsstands, subscribers, and members.

SLOWING AGING: NO LONGER THOUGHT "IMPOSSIBLE"

What we were ridiculed for in 1980 is now accepted as scientific fact—that is, humans can take steps to significantly reduce the deleterious effects of normal aging.¹ Dozens of companies have raised billions of dollars to develop validated anti-aging drugs. Anti-aging doctors have formed and joined their own medical associations. The federal government now recommends some of the



by William Faloon



healthy lifestyle changes, supplements, and drugs that we were vilified for advocating in the 1980s.² Perhaps most notably, the news media has recognized the science behind our revolutionary objectives, and prestigious publications such as *Scientific American* have dedicated special issues to reporting what people can do to stave off aging.

When reporting on so-called “new” anti-aging breakthroughs, the news media continues to make some technical mistakes. To ensure so-called “balanced” reporting, the media finds scientists who criticize the concept of anti-aging medicine, even though these scientists often do not know what they are attacking. For instance, while all scientists now appear to acknowledge the devastating effects of free radicals, *Scientific American* quoted a prominent researcher as stating:

“Free radicals can’t be the bottom line when it comes to aging . . . Mice and men live in the same toxic world.”³

What this scientist overlooked is that humans have many more DNA repair genes than mice and many more endogenous antioxidants like glutathione and superoxide dismutase. While free radicals burn up a typical mouse in less than two years, some humans can withstand attack by free radicals for over 100 years. The fact that mice and men live in the same world is not relevant to the issue of free radicals and aging.

A good deal of the time, however, the news media reports solid facts that should encourage people to take practical steps to extend their healthy life span. While there is a lot more to slowing aging than suppressing toxic free radicals, the good news is that we can now quench these reactive oxygen species more effectively than ever before!

HOW TO LIVE TO BE 100

In a recent issue devoted to the subject of human longevity, *TIME* magazine brought out some interesting facts that are worth repeating. In investigating statistics relating to centenarians, *TIME* found that a whopping 90% of these people were functionally independent until they were 92 years of age, and 30% were in good shape at 100 years old and beyond.⁴

TIME interviewed scientists who stated that while the genes you are born with have some influence on your longevity, the dominant determinant of how long you will live is your lifestyle. *TIME* cited a Swedish study that examined identical twins who were separated at birth, whose results showed that lifestyle accounts for 70-80% of the determining factors that predict longevity.^{5,6}



WHY DO THE JAPANESE LIVE THE LONGEST?

TIME magazine reporters traveled to Okinawa to ascertain why this particular group of Japanese lives such long, healthy lives. Eating a diet low in salt and fat—but high in fruits and vegetables packed with antioxidants—was cited as one reason why Okinawans have such low rates of heart disease, cancer, and stroke.⁴

The most notable fact about Okinawans is that they “consume more soy than any other population on earth.” *TIME* noted that while Okinawans consume 60-120 grams of soy per day (compared to 30-50 grams for the average Japanese), Americans on average consume virtually no soy. According to *TIME*, consumption of antioxidant-rich soy “may be one of many reasons why deaths from cancer in Okinawa are far below the US rate.”⁴

Compared to Americans and Europeans, aging Okinawans also have very low rates of Alzheimer’s disease and other forms of senility. *TIME* attributed this phenomenon in part to Okinawans’ consumption of foods that are high in vitamin E and may protect the brain. Food sources of vitamin E provide the full spectrum of tocopherols (including gamma tocopherol), unlike common dietary supplements that contain only alpha tocopherol.⁷⁻¹¹

SCIENTIFIC AMERICAN CITES ENCOURAGING STUDIES

In a special issue titled “**The Science of Staying Young,**” *Scientific American* reports on exciting anti-aging research projects, including many that address the role of antioxidants in slowing age-related disease.¹²

In the opening narrative, *Scientific American* states that by 2050, there will be five times more people in the world over the age of 80 than there were in 2000. The United Nations predicts that people over 80 will be the fastest-growing segment of the world’s population.¹³ While some economists view this trend with alarm, *Scientific American* optimistically predicts that medical advances will reduce the “degradation that time imposes on our bodies and minds.”¹²

The role of free radicals in accelerating aging processes is discussed throughout this special issue of *Scientific American*. One of the articles sought to determine why certain people reach the advanced age of 95 and older while maintaining good health. One explanation is that these healthy oldest humans appear to have longevity genes that combat free radical damage, and thus

slow aging by reducing oxygen damage to cellular DNA.

While growing numbers of Americans are taking antioxidant supplements, the fact is that nothing has worked as well to date as the natural antioxidants—such as glutathione and superoxide dismutase—that are produced in our cells. While some of us have genes that continue producing natural antioxidants in advanced age, most people need help. The good news is that science is developing “super antioxidants” that quench destructive free radicals much more effectively than common supplements like alpha tocopherol.

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DEADLY ROLE OF OXYGEN RADICALS

Scientific American's special issue provides abundant information on the destructive force of free radicals and how this relates to aging. The magazine described how oxygen radicals damage almost every critical component of cells, including DNA, proteins, and membranes.

Researchers interviewed by *Scientific American* describe how they were able to double the life span of insects by programming their genes to produce more natural antioxidants such as superoxide dismutase.¹⁴ They note that pigeons live 35 years, or about 12 times longer than rats of approximately the same weight—with the difference being that pigeons produce half as many free radicals as rodents do.

According to *Scientific American*, oxidants bombard the DNA inside our cells roughly 10,000 times each day, but many of the free radicals generated are intercepted and neutralized by antioxidants. They note, however, that free radical damage adds up over time and “the result just may be an older, frailer you.”

Encouragingly, researchers interviewed by *Scientific American* describe studies in which old rats looked and functioned like younger rats following oral administration of antioxidants.¹² The researchers cautioned, however, that humans cannot expect the same benefits from most conventional supplements, as these do not supply the full spectrum of nutrients found in fruits and vegetables, and their nutrients may not be adequately disseminated throughout the body. Exceptions were nutrients like lipoic acid, which is uniquely able to boost antioxidant activity within the cell and protect against mitochondrial decay.

CRITICAL NEED TO KEEP SUGAR OUT

Of the various approaches to slowing aging, calorie restriction is considered the gold standard.¹⁵⁻³¹ The problem, of course, is that few people can adhere to a lifelong low-calorie diet.

Scientific American considered the beneficial bodily effects induced by calorie restriction, such as increased levels of the hormone DHEA and reduced blood levels of insulin and artery-clogging lipids.³²⁻³⁶ But one of the magazine's most profound findings concerns calorie restriction's effect of lowering glucose, which results in diminished cellular metabolic activity and fewer free radicals being generated.³⁷ *Scientific American* produced a brilliant molecular drawing of how excess glucose may accelerate aging and how calorie-restriction mimetics could slow aging by blocking the ability of cells to use excess glucose.¹²



As members know, the Life Extension Foundation has been a pioneer in investigating compounds to mimic the beneficial effects of calorie restriction. Our research has uncovered the calorie restriction-mimicking effects of the drug metformin.³⁸⁻⁴² Based on widely publicized findings about resveratrol, we are now seeking to ascertain whether this flavonoid can favorably alter genes that cause our bodies to degenerate with age.⁴³⁻⁷⁴

In reading *Scientific American's* report on the broad-spectrum benefits of calorie restriction, the importance of keeping excess sugar out of one's bloodstream becomes abundantly clear. People can now do this by taking relatively small amounts of super-soluble fiber before meals.

**Life Extension Is Not A
"Fad"**

REASONS FOR OPTIMISM

For those who think there is a limit to life span, *Scientific American* cites studies showing how the manipulation of genes in worms increased their life span to the human



I will never forget a cynical newspaper reporter asking Saul Kent in 1983 whether the concept of life extension was just a “fad” like the hula-hoop. Saul responded that good health and long life are not fads, and that once people derive the benefits of living a healthier lifestyle, they will not return to habits that induce illness, depression, and premature death.

To quote Victor Hugo, “There is nothing more powerful than an idea whose time has come.” The concept of using scientific methods to extend the healthy life span may have been a radical new idea back in 1980, but based on the high level of interest in personal health issues, life extension’s time has come.

equivalent of 500 years.⁷⁵⁻⁷⁷ *Scientific American* goes on to point out how researchers can now make normal human cells live forever in a petri dish—something that scientists have long ridiculed as an impossibility.

If gene manipulation can be done in worms and human cell lines, how long will it be before it enables people to live for hundreds of healthy years? While pessimists reply “never” because human genomic structure is too complicated, groundbreaking research funded by Life Extension has already identified ways to measure the effects of anti-aging compounds on gene expression.⁷⁸⁻⁸¹ This enables scientists to identify and validate ways to manipulate old cells to behave more like younger cells.

As the Life Extension Foundation enters its twenty-fifth year, the scientific community, the government, and even the news media are slowly recognizing that our concept of extending life is in fact technically feasible. This change in perception represents an enormous transformation in how humans view their role in the universe.

MORE RESEARCH IS URGENTLY NEEDED

As the New Year begins, we have reason to be optimistic about the prospect of living much longer than what is predicted by the mortality tables. We at Life Extension, however, are very much aware that time is not on our side. If our older members are to benefit from spectacular advances that may be only a few years away, the pace of scientific research must be accelerated.

The encouraging news is that new antioxidants have been discovered that significantly suppress damaging free radical and inflammatory reactions that are linked to underlying aging processes. These more potent antioxidants were introduced to Life Extension members less than two months ago, and several articles in this month’s issue elaborate on the science backing these enhanced formulations.

Every time you purchase a product designed to counteract age-related disease, you directly support our pioneering research. In 2004, the results of our work were published in several prestigious scientific journals, including the *Proceedings of the National Academy of Sciences USA*.⁸²⁻⁸⁴ Equally important to our research programs is that the

proceeds from our supplement sales help us to educate greater numbers of people about the need to prioritize research that would lead to cures for today’s killer diseases, while at the same time discovering validated methods to eradicate biological aging.

Because of our intensive work last year, Life Extension members can now obtain superior formulations that are priced lower and require swallowing fewer capsules than before. At this time of year, long-time members traditionally stock up on a large supply of Life Extension products. The reason is simple: until the end of this month, prices on all supplements are discounted below the low prices members enjoy throughout the year.

For longer life,

William Faloon

References

1. Available at: http://www.nci.nih.gov/cancer_information/prevention. Accessed November 15, 2004.
2. Available at: <http://www.nia.nih.gov/AboutNIA/StrategicPlan/ResearchGoalA/Subgoal1.htm>. Accessed November 15, 2004.
3. Available at: <http://www.ki.se/cmb/bmt/aging.pdf>. Accessed November 15, 2004.
4. Corliss, R, Lemonick M. How to live to be 100. TIME. August 30, 2004:38-46.
5. Ljungquist B, Berg S, Lanke J, McClearn GE, Pedersen NL. The effect of genetic factors for longevity: a comparison of

identical and fraternal twins in the Swedish Twin Registry. *J Gerontol A Biol Sci Med Sci*. 1998 Dec;53(6):M441-6.

6. Iliadou A, Lichtenstein P, de Faire U, Pedersen NL. Variation in genetic and environmental influences in serum lipid and apolipoprotein levels across the life span in Swedish male and female twins. *Am J Med Genet*. 2001 Aug 22;102(1):48-58.
7. McLaughlin PJ and Weihrauch JL. Vitamin E content of foods. *J Am Diet Assoc*. 1979;75(6):647-65.
8. Schwenke DC. Does lack of tocopherols and tocotrienols put women at increased risk of breast cancer? *J Nutr Biochem*. 2002 Feb;13(1):2-20.
9. Heinonen M, Piironen V. The tocopherol, tocotrienol, and vitamin E content of the average Finnish diet. *Int J Vitam Nutr Res*. 1991;61(1):27-32.
10. Murphy SP, Subar AF, Block G. Vitamin E intakes and sources in the United States. *Am J Clin Nutr*. 1990 Sep;52(2):361-7.
11. Panfili G, Fratianni A, Irano M. Normal phase high-performance liquid chromatography method for the determination of tocopherols and tocotrienols in cereals. *J Agric Food Chem*. 2003 Aug 2;51(14):3940-4.
12. Available at: http://www.sciamdigital.com/browse.cfm?sequencenameCHAR=item&methodnameCHAR=resource_getitembrowse&interfacenameCHAR=browse.cfm&ISSUEID_CHAR=24E2FCFA-2B35-221B-6B5BE66B604912C9. Accessed November 15, 2004.
13. Available at: <http://www.un.org/NewLinks/older/99/older.htm>. Accessed November 15, 2004.
14. Sohal RS, Toy PL, Allen RG. Relationship between life expectancy, endogenous antioxidants and products of oxygen free radical reactions in the housefly, *Musca domestica*. *Mech Ageing Dev*. 1986 Oct;36(1):71-7.
15. Cao SX, Dhahbi JM, Mote PL, Spindler SR. Genomic profiling of short- and long-term caloric restriction effects in the liver of aging mice. *Proc Natl Acad Sci USA*. 2001 Oct 11;98(19):10630-5.
16. Sohal RS, Agarwal S, Candas M, Forster MJ, Lal H. Effect of age and caloric restriction on DNA oxidative damage in different tissues of C57BL/6 mice. *Mech Ageing Dev*. 1994 Nov 20;76(2-3):215-24.
17. Walford RL and Spindler SR. The response to calorie restriction in mammals shows features also common to hibernation: a cross-adaptation hypothesis. *J Gerontol A Biol Sci Med Sci*. 1997 Aug;52(4):B179-83.
18. Weindruch R. Caloric restriction and aging. *Sci Am*. 1996 Feb;274(1):46-52.
19. Spindler SR. Calorie restriction enhances the expression of key metabolic enzymes associated with protein renewal during aging. *Ann N Y Acad Sci*. 2001 May;928:296-304.
20. Kayo T, Allison DB, Weindruch R, Prolla TA. Influences of aging and caloric restriction on the transcriptional profile of skeletal muscle from rhesus monkeys. *Proc Natl Acad Sci U S A*. 2001 Apr 24;98(9):5093-8.
21. Weindruch R. The retardation of aging by caloric restriction: studies in rodents and primates. *Toxicol Pathol*. 1996 Dec;24(6):742-5.
22. Aspnes LE, Lee CM, Weindruch R, Chung SS, Roecker EB, Aiken JM. Caloric restriction reduces fiber loss and mitochondrial abnormalities in aged rat muscle. *Faseb J*. 1997 Jul;11(7):573-81.
23. Fishbein L, ed. *Biological Effects of Dietary Restriction*. New York: Springer-Verlag;1991.
24. Sohal RS, Weindruch R. Oxidative stress, caloric restriction, and aging. *Science*. 1996 Aug 5;273(5271):59-63.
25. Weindruch R, Sohal RS. Seminars in medicine of the Beth Israel Deaconess Medical Center. Caloric intake and aging. *N Engl J Med*. 1997 Nov 2;337(14):986-94.
26. Weindruch R, Walford RL. Dietary restriction in mice beginning at one year of age: Effects on life span and spontaneous cancer incidence. *Science*. 1982 Apr;215(4538):1415-8.

27. Weindruch R, Walford RL, Fligiel S, Guthrie D. The retardation of aging in mice by dietary restriction: longevity, cancer, immunity and lifetime energy intake. *J Nutr.* 1986 May;116(4):641-54.
28. Roth GS, Lane MA, Ingram DK, et al. Biomarkers of caloric restriction may predict longevity in humans. *Science.* 2002 Jul 2;297(5582):811.
29. Bluher M, Khan BP, Kahn CR. Extended longevity in mice lacking the insulin receptor in adipose tissue. *Science.* 2003 Feb 24;299(5606):572-4.
30. Kenyon C. I want to live forever. *New Scientist.* 2003 Nov 18;180(2417):46.
31. Lane MA, Ingram DK, Ball SS, Roth GS. Dehydroepiandrosterone sulfate: a biomarker of primate aging slowed by calorie restriction. *Clin Endocrinol Metab.* 1997 Aug;82(7):2093-6.
32. Kemnitz JW, Roecker EB, Weindruch R, Elson DF, Baum ST, Bergman RN: Dietary restriction increases insulin sensitivity and lowers blood glucose in rhesus monkeys. *Am J Physiol.* 1994 May;266(4 Pt 1):E540-7.
33. Ramsey JJ, Colman RJ, Binkley NC, et al. Dietary restriction and aging in rhesus monkeys: the University of Wisconsin study. *Exp Gerontol.* 2000 Dec;35(9-10):1131-49.
34. Roth GS, Ingram DK, Black A, Lane MA. Effects of reduced energy intake on the biology of aging: the primate model. *Eur J Clin Nutr.* 2000 Jul;54 Suppl 3:S15-20.
35. Ingram DK, Anson RM, de Cabo R, et al. Development of calorie restriction mimetics as a prolongevity strategy *Ann N Y Acad Sci.* 2004 Jul;1019:412-23.
36. Deutsch JC, Santhosh-Kumar CR, Kolhouse JF. Efficacy of Metformin in non-insulin-dependent diabetes mellitus. *N Engl J Med.* 1996 Feb 25;334(4):269-70.
37. Charles MA, Eschwege E. Prevention of type 2 diabetes: role of metformin. *Drugs.* 1999;58 Suppl.1:71-3.
38. Fontbonne A., Charles MA, Juhan-Vague I, et al. The effect of metformin on the metabolic abnormalities associated with upper body fat distribution. Results of the BIGPRO 1 trial. *Diabetes Care.* 1996 Oct;19(9):920-6.
39. Glueck CJ, Wang P, Fontaine R, Tracy T, Sieve-Smith L. Metformin induced resumption of normal menses in 39 of 43 (91%) previously amenorrheic women polycystic ovary syndrome. *Metabolism.* 1999 May;48(4):511-9.
40. Velazquez EM, Mendoza S, Hamer T, Sosa F, Glueck CJ. Metformin therapy in polycystic ovary syndrome reduces hyperinsulinemia, insulin resistance, hyperandrogenemia, and systolic blood pressure, while facilitating menstrual regulation and pregnancy. *Metabolism.* 1994 Jun;43(5):647-54.
41. Tadolini B, Juliano C, Piu L, Franconi F, Cabrini L. Resveratrol inhibition of lipid peroxidation. *Free Radic Res.* 2000 Aug;33(1):105-14.
42. Simonini G, Pignone A, Generini S, et al. Emerging potentials for an antioxidant therapy as a new approach to the treatment of systemic sclerosis. *Toxicology.* 2000 Dec 30;155(1-3):1-15.
43. Zou JG, Wang ZR, Huang YZ, Cao KJ, Wu JM. Effect of red wine and wine polyphenol resveratrol on endothelial function in hypercholesterolemic rabbits. *Int J Mol Med.* 2003 Apr;11(3):317-20.
44. Haider UG, Sorescu D, Griendling KK, Vollmar AM, Dirsch VM. Resveratrol increases serine 15-phosphorylated but transcriptionally impaired p53 and induces a reversible DNA replication block in serum-activated vascular smooth muscle cells. *Mol Pharmacol.* 2003 May;63(4):925-32.
45. Zbikowska HM, Olas B. Antioxidants with carcinostatic activity (resveratrol, vitamin E and selenium) in modulation of blood platelet adhesion. *J Physiol Pharmacol.* 2000 Oct;51(3):513-20.
46. Pace-Asciak CR, Hahn S, Diamandis EP, Soleas G, Goldberg DM. The red wine phenolics trans-resveratrol and quercetin block human platelet aggregation and eicosanoid synthesis: implications for protection against coronary heart disease. *Clin Chim Acta.* 1995 Apr 31;235(2):207-19.

47. Burkitt MJ, Duncan J. Effects of trans-resveratrol on copper-dependent hydroxyl-radical formation and DNA damage: evidence for hydroxyl-radical scavenging and a novel, glutathione-sparing mechanism of action. *Arch Biochem Biophys.* 2000 Oct 15;381(2):253-63.
48. Jang JH, Surh YJ. Protective effect of resveratrol on beta-amyloid-induced oxidative PC12 cell death. *Free Radic Biol Med.* 2003 May 15;34(8):1100-10.
49. Chanvitayapongs S, Draczynska-Lusiak B, Sun AY. Amelioration of oxidative stress by antioxidants and resveratrol in PC12 cells. *Neuroreport.* 1997 May 14;8(6):1499-502.
50. Yang YB, Piao YJ. Effects of resveratrol on secondary damages after acute spinal cord injury in rats. *Acta Pharmacol Sin.* 2003 Aug;24(7):703-10.
51. Sinha K, Chaudhary G, Gupta YK. Protective effect of resveratrol against oxidative stress in middle cerebral artery occlusion model of stroke in rats. *Life Sci.* 2002 Jul 28;71(6):655-65.
52. Cal C, Garban H, Jazirehi A, Yeh C, Mizutani Y, Bonavida B. Resveratrol and cancer: chemoprevention, apoptosis, and chemosensitizing activities. *Curr Med Chem Anti-Canc Agents.* 2003 Apr;3(2):77-93.
53. Pervaiz S. Resveratrol—from the bottle to the bedside? *Leuk Lymphoma.* 2001 Mar;40(5-6):491-8.
54. Ding XZ, Adrian TE. Resveratrol inhibits proliferation and induces apoptosis in human pancreatic cancer cells. *Pancreas.* 2002 Dec;25(4):e71-6.
55. Gusman J, Malonne H, Atassi G. A reappraisal of the potential chemopreventive and chemotherapeutic properties of resveratrol. *Carcinogenesis.* 2001 Sep;22(8):1111-7.
56. Lu R, Serrero G. Resveratrol, a natural product derived from grape, exhibits anti-estrogenic activity and inhibits the growth of human breast cancer cells. *J Cell Physiol.* 1999 Jul;179(3):297-304.
57. Serrero G, Lu R. Effect of resveratrol on the expression of autocrine growth modulators in human breast cancer cells. *Antioxid Redox Signal.* 2001 Dec;3(6):969-79.
58. Mitchell SH, Zhu W, Young CY. Resveratrol inhibits the expression and function of the androgen receptor in LNCaP prostate cancer cells. *Cancer Res.* 1999 Dec 1;59(23):5892-5.
59. Narayanan BA, Narayanan NK, Stoner GD, Bullock BP. Interactive gene expression pattern in prostate cancer cells exposed to phenolic antioxidants. *Life Sci.* 2002 Apr 1;70(15):1821-39.
60. Wietzke JA, Welsh J. Phytoestrogen regulation of a vitamin D3 receptor promoter and 1.25-dihydroxyvitamin D3 actions in human breast cancer cells. *J Steroid Biochem Mol Biol.* 2003 Mar;84(2-3):149-57.
61. Ulsperger E, Hamilton G, Raderer M, et al. Resveratrol pretreatment desensitizes AHTO-7 human osteoblasts to growth stimulation in response to carcinoma cell supernatants. *Int J Oncol.* 1999 Dec;15(5):955-9.
62. Nakagawa H, Kiyozuka Y, Uemura Y, et al. Resveratrol inhibits human breast cancer cell growth and may mitigate the effect of linoleic acid, a potent breast cancer cell stimulator. *J Cancer Res Clin Oncol.* 2001 May;127(4):258-64.
63. Zhuang H, Kim YS, Koehler RC, Dore S. Potential mechanism by which resveratrol, a red wine constituent, protects neurons. *Ann N Y Acad Sci.* 2003 Jun;993:276-86.
64. Floreani M, Napoli E, Quintieri L, Palatini P. Oral administration of trans-resveratrol to guinea pigs increases cardiac DT-diaphorase and catalase activities, and protects isolated atria from menadione toxicity. *Life Sci.* 2003 Jun 2;72(24):2741-50.
65. Ferguson LR. Role of plant polyphenols in genomic stability. *Mutat Res.* 2001 May 18;475(1-2):89-111.
66. Casper RF, Quesne M, Rogers IM, et al. Resveratrol has antagonist activity on the aryl hydrocarbon receptor: implications for prevention of dioxin toxicity. *Mol Pharmacol.* 1999 Nov;56(4):784-90.
67. Hsieh TC, Burfeind P, Laud K, et al. Cell cycle effects and control of gene expression by resveratrol in human breast

carcinoma cell lines with different metastatic potentials. *Int J Oncol*. 1999 Sep;15(2):245-52.

68. Torres-Lopez JE, Ortiz MI, Castaneda-Hernandez G, Alonso-Lopez R, Asomoza-Espinosa R, Granados-Soto V. Comparison of the antinociceptive effect of celecoxib, diclofenac and resveratrol in the formalin test. *Life Sci*. 2002 Mar 22;70(14):1669-76.

69. Mahady GB, Pendland SL, Chadwick LR. Resveratrol and red wine extracts inhibit the growth of CagA+ strains of *Helicobacter pylori* in vitro. *Am J Gastroenterol*. 2003 Jul;98(6):1440-1.

70. Yen GC, Duh PD, Lin CW. Effects of resveratrol and 4-hexylresorcinol on hydrogen peroxide-induced oxidative DNA damage in human lymphocytes. *Free Radic Res*. 2003 Jun;37(5):509-14.

71. Revel A, Raanani H, Younglai E, et al. Resveratrol, a natural aryl hydrocarbon receptor antagonist, protects lung from DNA damage and apoptosis caused by benzo[a]pyrene. *J Appl Toxicol*. 2003 Jul-Aug;23(4):255-61.

72. Adhami VM, Afaq F, Ahmad N. Suppression of ultraviolet B exposure-mediated activation of NF-kappaB in normal human keratinocytes by resveratrol. *Neoplasia*. 2003 Feb;5(1):74-82.

73. Tsang WY, Lemire BD. Mitochondrial genome content is regulated during nematode development. *Biochem Biophys Res Commun*. 2002 Mar 15;291(1):8-16.

74. Hill AA, Hunter CP, Tsung BT, Tucker-Kellogg G, Brown EL. Genomic analysis of Gene Expression in *C. elegans*. *Science*. 2000 Nov 27;290(5492):809-12.

75. Houthoofd K, Braeckman BP, Johnson TE, Vanfleteren JR. Extending life span in *C. elegans*. *Science*. 2004 Sep 27;305(5688):1238-9.

76. Bartke A, Coschigano K, Kopchick J, et al. Genes that prolong life: relationships of growth hormone and growth to aging and life span. *J Gerontol A Biol Sci Med Sci*. 2001 Sep;56(8):B340-9.

77. Brown-Borg HM, Borg KE, Meliska CJ, Bartke A. Dwarf mice and the ageing process. *Nature*. 1996 Dec 7;384(6604):33.

78. Flurkey K, Papaconstantinou J, Miller RA, Harrison DE. Life span extension and delayed immune and collagen aging in mutant mice with defects in growth hormone production. *Proc Natl Acad Sci USA*. 2001 Jul 5;98(12):6736-41.

79. Miller RA. Kleemeier Award Lecture: Are there genes for aging? *J Gerontol A Biol Sci Med Sci*. 1999 Aug;54(7):B297-307.

80. Lee CK, Allison DB, Brand J, Weindruch R, Prolla TA. Transcriptional profiles associated with aging and middle age-onset caloric restriction in mouse hearts. *Proc Natl Acad Sci USA*. 2002 Dec 12; 99(23):14988-93.

81. Lee CK, Klopp RG, Weindruch R, Prolla TA. Gene expression profile of aging and its retardation by caloric restriction. *Science*. 1999 Sep 27;285(5432):1390-3.

82. Lee CK, Weindruch R, Prolla TA. Gene-expression profile of the aging brain in mice. *Nat Genet*. 2000 Aug;25(3):294-7.

83. Lane MA, Baer DJ, Rumpler WV, et al. Calorie restriction lowers body temperature in rhesus monkeys, consistent with a postulated anti-aging mechanism in rodents. *Proc Natl Acad Sci USA*. 1996 May 30;93(9):4159-64.

84. Available at: http://www.lef.org/featuredarticles/spindler_press_release01.html. Accessed November 15, 2004.

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