

Gray is the New Gold

***Longevity Science and the
Flourishing Aging Society***



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About the Kronos Longevity Research Institute

Kronos Longevity Research Institute (KLRI), a not-for-profit 501(c)(3) organization, is a leader in developing new modes of prevention and treatment to enhance human longevity. KLRI is the only independent research institute devoted exclusively to translating basic discoveries in the process of aging into useful tools, improved medical care and healthier lives. KLRI's research is conducted by its own highly regarded scientists and through collaboration with some of the nation's leading medical research centers. Because KLRI conducts pioneering research in an area of science that is poorly understood, KLRI offers the potential to make seminal contributions that benefit not only the growing population of older Americans, but people everywhere and generations to follow.

KLRI's Mission

KLRI is dedicated to understanding the human aging process and preventing age-related disease. KLRI conducts and fosters research that moves basic discoveries into clinical practice and communicates our research results to scientific and healthcare professionals and to the public so that people may enjoy longer and healthier lives.

KLRI's Vision

KLRI will be the leading independent research institute for translating basic discoveries on aging and longevity into improved preventions and treatments. We will be recognized as the thought-leader in the field of clinical gerontology and an authoritative source of sound scientific information.

Research to promote a longer, healthier life for you, your children and your grandchildren.

Executive Summary

Americans are living longer, healthier, more active lives. They are staying in the workforce longer and investing more in the economy. *Gray is the new gold.*

Growing older, however, often means a decline in health and greater susceptibility to chronic conditions like arthritis and dementia, as well as increased risk for cardiovascular disease and cancer, placing burdens on both family and society.

Scientists are making discoveries every day about how aging works and how to keep it from slowing us down so that we stay healthier and feel younger longer. Dietary changes, genetic engineering and hormone activity can all play a role in the aging of the body's systems. Scientists are discovering that the aging of those systems can be delayed and thereby delay the onset of deadly diseases.

Slowing the aging process is not a new idea, and there is no quick fix or magic mirror, but with greater public focus on the advantages of a senior workforce and greater investment in the biology of aging, we can turn *gray into gold* by helping older Americans remain healthy, productive members of society.

One of the challenges facing us as a society is that we tend to look at diseases on an individual basis rather than take the body as a whole, and this creates tunnel vision.

“We don’t pay much attention to you until you’re sick,” says Dr. S. Mitchell Harman, director and president of the Kronos Longevity Research Institute (KLRI) in Arizona, a not-for-profit research organization that conducts clinical research on the prevention of age-related diseases and the extension of healthy human life. “Most of the cancer drugs make you sick and interventions are expensive and hard on the patients,” he adds. “If we could stop that cancer in the first place, wouldn’t we be much better off?”¹



Gray is the New Gold

I. Introduction

It's a great time to be gray. Older Americans are living longer and healthier lives than ever, thanks to advances in nutrition, education, environmental mitigation, and of course, modern medicine. They are able to engage in sexual and social activities once thought to be the exclusive province of young adults. They are more active in their grandchildren's lives than ever before. And they are increasingly contributing to the nation's wealth by staying in the workforce longer, investing more money in the economy, and saving health-care costs by maintaining their health for greater periods of time. *Gray just may be the new gold.*



However, growing older often comes with a downside. For many of us, there is a period as we age past 65 when our health declines and we are unable to lead the full, active lives we once did. Sometimes age comes with chronic conditions from arthritis to dementia. In the best cases, they affect us for a few months. Sometimes, they drag on for years, creating a physical and financial burden on loved ones who care for us and on society as a whole.

Historically, lifelong exposure to environmental toxins, addiction to unhealthy behaviors like smoking, eating poorly, and the normal wear and tear on our bodies have taken their toll on life expectancy and quality of life in our later years.² But scientists are making discoveries every day about how aging works and how to keep it from slowing us down.

“If we could make you physiologically 20 years younger than your stated age, you could avoid the problems associated with old age,”³ says Dr. S. Mitchell Harman, director and president of the Kronos Longevity Research Institute (KLRI).

The effort is not focused on just helping people live longer. “We’re not trying to increase lifespan so we add 20 years of life at the end when you’re frail,” says Dr. Anna McCormick, chief of the Genetics and Cell Biology Branch and the Genetics Program Director at the

National Institute on Aging (NIA).⁴ “We want to increase the middle part – the healthspan,” she says.

... scientists have discovered ways to slow the aging process in animals with great promise ...

In that effort, scientists have discovered ways to slow the aging process in animals with great promise for delaying the onset of deadly and debilitating diseases like cancer, cardiovascular disease, diabetes and Alzheimer’s in people.

The aging process can be slowed in a variety of ways, including making dietary changes, genetic engineering and hormone activity. These developments show great promise for an advancing society and call for greater financial investment to translate basic science into practice.

We are not doomed to walk down the path laid out by the less-than-perfect genes and practices of our ancestors. We have the power to take charge of our biological destiny. “The belief that aging is an immutable process, programmed by evolution, is now known to be wrong.”⁵

While there is no magic pill to reverse the ravages of time, scientists say there is significant potential in combining a number of interventions to help keep us in our prime.

In 2002, Cambridge associate and biogerontologist Aubrey de Grey developed the radical idea that reversing cellular aging could extend life. De Grey predicted that the next great social debate would occur when aging research matures to the point that public funds can be used to speed effective aging treatments.⁶

That future is now.

The population of the United States over 65 years of age is set to double in the next 75 years, with major implications for the medical system. If we do nothing, the graying of America might bankrupt the Medicare program and personal wealth with the chronic-care costs of the frail and disabled. But if we take action quickly to focus on what causes aging and how to reverse it, those costs could de-



cline over time.⁷ We can turn *gray into gold* if we reinvest in society in ways targeted towards keeping older Americans as healthy productive members.

This future requires a reevaluation of the amount of money spent, as well as the priorities of spending. It requires a good look at health research and the entire picture of aging prevention rather than just the concentration of energy on one aging disease at a time after it begins to take its toll on human lives.

“Not enough attention has been given to the fertile soil as to how diseases arise,” says Dr. Robert Butler, president and CEO of the International Longevity Center – USA (ILC-USA) in New York, a not-for-profit, nonpartisan organization specializing in longevity research, policy and education.⁸

“We need to look at the biology of aging as well as disease,” Butler says.⁹

Scientists know that as people age, they become more susceptible to debilitating and deadly diseases. Let’s take one gigantic example – cancer.

... 1.4 million Americans will develop cancer in 2007 alone.

The National Cancer Institute (NCI) predicts that 1.4 million Americans will develop cancer in 2007 alone. About 10 million have been diagnosed with the disease in their lifetime.¹⁰

The American Cancer Society says the major risk factor for cancer is age because about 77 percent of all cancers are diagnosed in people aged 55 and up.¹¹ About 80 percent of breast cancer cases occur in women over 50,¹² and more than 70 percent of all cases of prostate cancer are diagnosed in men over age 65.¹³

In 2006, the National Institutes of Health (NIH) estimated the cost of treating all cancers at \$206 billion.¹⁴

These are staggering numbers, and no one would suggest the money spent to treat cancer patients is for naught, but the trouble with looking at diseases exclusively on a one-by-one basis is that it creates tunnel vision.

“We don’t pay much attention to you until you’re sick,” Harman says. “Most of the cancer drugs make you sick and interventions are expensive and hard on the patients,” he adds. “If we could stop that cancer in the first place, wouldn’t we be much better off?”¹⁵

Research tells us that increasing longevity would make us better off socially and financially because we would be able to tap the expertise and wealth that many healthier older Americans possess.

II. Current Aging Research

Eat Less to Live Longer?



Yeast, worms, flies and rodents all show a marked physical response when food supplies drop off. Their cells slow development, halt reproduction, reduce their metabolic rate, and sometimes enter a hibernation-like state. As early as the 1930s, scientists like Cornell University veterinary nutritionist Clive McCay discovered that putting male rats on a calorie-restricted diet extended their lifespan by up to 75 percent.¹⁶

More recent studies published in the *New England Journal of Medicine* and elsewhere show rodents on calorie-restricted diets not only live longer, but experience cancer, cataracts, diabetes and hypertension much later in life than their counterparts who are eating at will.

“However long you live, you will probably have some period of illness and disability on average, between three and five years,” Harman says. The difference is that with lifespan extension, this period will occur much later. “That’s exactly what we see in these animals in which we restrict calories by 25 to 30 percent. They develop the same diseases, but later [than their counterparts on regular diets].”¹⁷

Restricting calories practically prevents the development of autoimmune diseases in certain strains of mice. For example, when mice susceptible to a lupus-like disease are fed at will, they con-



tract the disease and usually die around 12 months of age. The mice on calorie-restricted diets appear less likely to contract the disease and live about 20 months.¹⁸

Perhaps most dramatic are the caloric restriction studies now underway in rhesus monkeys. At the Wisconsin National Primate Research Center, older rhesus monkeys on normal diets are frail and wrinkled, barely energetic enough to grab a piece of fruit while their thin and energetic peers on calorie-restricted diets parade around their cages.¹⁹

Dr. Don Ingram, who recently left the NIH in Maryland after 26 years to return to his native Louisiana, has been a leader in the study of calorie restriction.

In a recent interview with Pennington Biomedical Research Center (PBRC) in Baton Rouge, where he is a faculty member, Ingram said: “If you’re going to stop growing and reproducing, you better have a way to survive, and these organisms have a number of genes that, when stimulated by low energy (food) intake, lead to a cascade of responses that eventually result in slowing many aging processes, and thus produce subsequently greater health and longer life.”²⁰

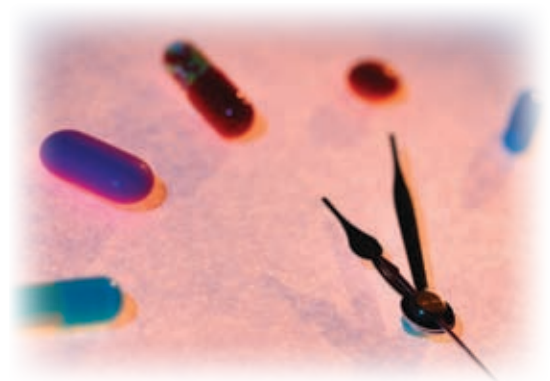
PBRC is working with grants from the NIA to study these effects in humans.²¹

... develop a compound that would mimic in humans the effects of eating a third less calories ...

Ingram is working to develop a compound that would mimic in humans the effects of eating a third less calories because, as any dieter knows, sticking to a long-term diet, particularly such a severe one, is unrealistic for most people.²²

Reducing Cell Damage Slows Aging

Aside from a severe calorie-restricted diet or a simulated one, scientists are exploring other interventions to slow the aging process in humans, honing in on how to reduce cell damage due to compounds called “oxygen free radicals.” These compounds are mainly generated as a byproduct of normal cell processes that produce energy. They act like powerful explosives, damaging nearby molecules. As cells age,



they become increasingly unable to use oxygen and fuel efficiently to generate energy. This effect is known as “oxidative stress.” There is much evidence that oxidative stress plays an important role in causing age-related diseases like cancer and Alzheimer’s.

KLRI, in collaboration with Dr. L. Jackson Roberts at the Vanderbilt University College of Medicine, began a study in August 2006 to explore differences in how younger and older men and women react to acute oxidative stress produced by temporarily blocking arterial blood flow to the forearm. Through this study, they hope to develop a way to test potential interventions, like antioxidants, nutrients, and exercise, for their impact on oxidative stress.²³

The Right Nutrition and Exercise Can Help



We have known for years that exercise can keep people stronger longer, but a recent study by the Group Health Center for Health Studies in Seattle suggests regular exercise may also stave off mental decline.²⁴

The study shows that people in poor physical shape are more likely to develop dementia. “The two processes are intimately connected,” Dr. Eric Larson, a co-author of the study, recently told the *New York Times*. “People more likely to develop dementia show early signs of physical function decline, and people, especially in old age, will develop decline in physical function as a result of dementia that may be too mild to be detected.”

On the dietary side, KLRI is studying the effects of high doses of omega-3 polyunsaturated fatty acids, the good fats found in fish and other foods. Preliminary findings in a small study to be published in a prominent medical journal show that healthy men and women over 60 years of age taking these supplements showed significant improvement in mental tests and improvements in their body’s use of insulin after just eight weeks. Follow-up studies are planned that would combine the supplements with exercise and other interventions.²⁵



Resveratrol, a compound found naturally in red wine and thought to have anti-aging properties, will be studied by KLRI in collaboration with a prominent neuroscience research group in Phoenix. They will explore how the compound may affect insulin sensitivity in diabetics over 55 years of age,²⁶ and its effects on brain aging, mental function, body composition and muscle function.

Unlocking the Mysteries of Hormones

The NIA is conducting trials on whether estrogen therapy protects older women from mental decline, with completion expected by December 2008.²⁷

KLRI is sponsoring a long-term research project with nine academic research centers on the potential power of estrogen therapy to ward off heart disease in women who have recently entered menopause called Kronos Early Estrogen Prevention Study (KEEPS).

... administration of a skin (transdermal) patch versus an oral dose, makes a difference in the outcomes.

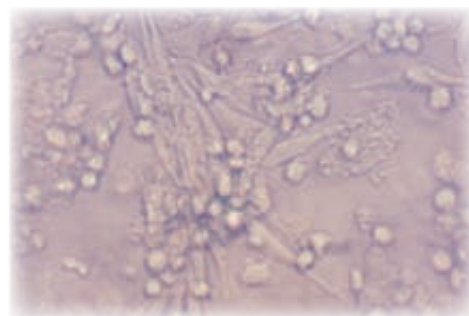
KEEPS is looking at whether estrogen therapy, given at low doses to recently menopausal women, protects them against hardening of the arteries. It is also studying whether different therapy delivery systems, i.e. the administration of a skin (transdermal) patch versus an oral dose, makes a difference in the outcomes.

On another hormone front, in partnership with a research team at Boston University, KLRI is studying testosterone in older men. As men age, their testosterone levels naturally decline. The Testosterone Effects on Atherosclerosis in Aging Men (TEAAM) is designed to assess testosterone effects on hardening of the arteries, as well as how beneficial testosterone therapy can be in maintaining bone density, muscle mass, energy and sex drive.

A study recently published in the *Archives of Internal Medicine* suggests that men with high testosterone levels may also live longer than those with low levels.²⁸ "A lot of men have gotten the idea that testosterone is the fountain of youth," says Harman. "This is clearly not the case, but it seems to be some help for older men with low levels," he says.²⁹

Some Cells Take on Many Roles

KLRI is developing a study to explore the impact of the injection of umbilical cord blood stem cells on the immune system of diabetics. Type 1 diabetes occurs due to destruction of the insulin secreting cells of the pancreas by the person's own immune cells (autoimmunity). A fraction of cells found in the umbilical cord blood of newborn infants have the ability to develop into almost any type of cell, and show promise in regulating immune function and perhaps becoming insulin-secreting cells as well.³⁰



This type of approach, replacing cells that have lost normal function with new young cells, has promise for rejuvenating aging bodies by replacing worn-out cells.

III. Societal Benefits of Aging Research

A Looming Fiscal Crisis

The stakes are high.



Currently, 99 percent of Medicare spending is on beneficiaries with at least one chronic condition, while 96 percent of spending is on beneficiaries who have multiple chronic conditions. In fact, people with chronic conditions account for 83 percent of all healthcare spending.³¹

Seventy million people will be eligible for Medicare by 2029. Their sheer numbers have the potential to crush the program under its own fiscal weight unless significant changes are made. Aside from the addition of a prescription drug benefit in 2003, the 1960s-era government program has been largely unchanged for decades. It is still primarily focused on paying to treat diseases – not prevent them.

The impending wave of older Americans flocking to Medicare with their accompanying healthcare costs should not be surprising news.

“They’re not coming on a rocket ship – they’re here now,” says Dan Perry, executive director of the Alliance for Aging in Washington, D.C., a not-for-profit advocacy group dedicated to promoting healthy and independent older Americans.³²

Aside from healthcare costs, the growth of the older American population may have significant fiscal implications for the U.S. pension system and Social Security.³³

But we can avert a potential crisis through aging research and its applications, Perry says.

And why else would we want to keep older adults living longer?

Healthy Older Americans are Productive Members of Society

It takes 20 years of investment in education, healthcare and nutrition to create one productive year in the economy, Perry says, so for every one-year delay in retirement, you get one more productive year.

Greater income equals greater health, but recent research suggests the formula may run the other way, as well, i.e. that greater health equates wealth.³⁴ Healthy populations are more productive because they are both physically and mentally stronger. Healthy people who live longer also invest more in education, earn more, and stay in the workforce longer.³⁵

... 78 million American adults in the Baby Boomer generation ... are redefining retirement.



The 78 million American adults in the Baby Boomer generation – those born between 1946 and 1964 – are redefining retirement. Instead of just sitting around the house watching TV or playing Bingo, older Americans are working, volunteering, and traveling.

“They’re shifting gears to do something else ... and finding a balance between work, leisure and travel,” Connie Davis, an associate financial advisor with

Moller and Associates, a Granville, New Jersey practice of Ameriprise Financial Services, told the *Newark Advocate*.³⁶

Healthcare, assisted living, long-term care, life insurance, travel services, and financial services geared towards older Americans, which Dr. Butler dubs the “Silver Industries,”³⁷ have grown up to serve this ever-expanding sector of the population. The Silver Industries have the potential to grow even more as people live longer and healthier and have more money to spend.

... gray may be the new gold; mentally, physically and economically.

Hence, *gray may be the new gold; mentally, physically and economically.*

A 2005 analysis by *Business Week* found that increased productivity of older Americans and an increase in their workforce participation could add nine percent to the gross domestic product by 2045.³⁸ That could be more than \$3 trillion a year on top of what the country would otherwise produce, making research that leads to healthier, longer lives a sound investment.

Leonard Davis School of Gerontology Dean Elizabeth Zelinski told *Business Week*: “Assuming that the improved health trends continue, boomers should be able to work productively into their late 70s.”³⁹

Senate Aging Committee Chairman Herb Kohl (D-WI) sees the potential in harnessing the power and experience of older Americans. He introduced two bills this spring designed to encourage older workers to stay in the workforce and encourage employers to keep them there.

One bill would provide a tax credit to employers who offer more flexible or part-time work and give older workers a tax credit to help them care for aging family members.

Another would improve government training programs and extend employer-based healthcare insurance.



... 80 percent of Baby Boomers expect to work past traditional retirement age.

“Fortuitously, studies show that as older Americans live longer and healthier lives, many are planning to work longer. According to a recent survey, 80 percent of Baby Boomers expect to work past traditional retirement age. Some may recognize the physical and mental benefits of work, while some may need the additional income to remain financially secure as they struggle to stretch their retirement savings,” Kohl said in a recent op-ed in the *Roll Call* newspaper.⁴⁰

IV. The Challenges of Funding Aging Research

Last fall, 99 scientific leaders from 16 countries in the field of aging met with lawmakers in Washington, D.C., and called on governments and health organizations worldwide to make research into healthy aging a major priority.⁴¹

“Extending the duration of physical and mental capacity would permit people to remain in the labor force longer, amass more income and savings, and thereby lessen the effect of shifting demographics on age-based entitlement programs, with a net benefit to national economies,” the aging experts say in an open letter.

But it would take a sea change in both thinking and funding, experts say.

It will be difficult, but not impossible. “We’ve made changes before,” says the ILC-USA’s Butler.⁴²

Seventy years in August 2007, the NCI was born. NCI was created by Congress on August 5, 1937, “for the purposes of conducting researches, investigations, experiments, and studies relating to the cause, diagnosis and treatment of cancer; assisting and fostering similar research activities by other agencies, public and private; and promoting the coordination of all such researches and activities and the useful application of their results, with a view to the development and prompt widespread use of the most effective methods of prevention, diagnosis, and treatment of cancer.”⁴³

It was the first effort of its kind, coming out of a groundswell of demand for the government to focus efforts specifically on combating the killer disease. It led to the creation of many other “institutes” at the NIH.



The NIA was founded at NIH in 1974 to lead research on the biomedical, social and behavioral aspects of the aging process, prevention of disease and disability, and promotion of quality of life for older Americans.⁴⁴ It marked the beginning of a shift in focus to look at aging as a whole – not as a disease to be managed, but a state of being to be enhanced.

“About 25 years ago, there wasn’t a whole lot to aging research,” says NIA’s McCormick, “but the government investment [since then] has begun to pay off.”⁴⁵



In 1993, NIA formed a network of investigators to identify the genetic and molecular basis of longevity in several animal species and to extend those findings to humans. It’s called the Longevity Assurance Gene (LAG) project. The LAG project has identified several genes responsible for aging and has broken them down into categories to be studied.⁴⁶

All this on a budget of just over \$1 billion in 2006.⁴⁷

Part of the reason the investment is relatively small is that the work is sometimes esoteric, doesn’t have a lot of patient advocacy groups behind it, and is just not very sexy. “It’s hard to sell basic research,” McCormick says. “It’s easier to sell research to prevent autism or prevent or treat Alzheimer’s disease because there’s something to get a grip on.”⁴⁸

But the potential applications of aging research have profound implications for everyone. So where should we start?

For a new \$3 billion investment – just one percent of the current Medicare budget – key aging experts propose that aging research can move us closer to the goal of healthier, longer lives for older Americans.⁴⁹ Plus, according to a recent article in the journal, *The Scientist*, we could potentially save millions in future health expenses. Butler and others suggest in the article that one third of the \$3 billion go to basic biology, one third to study aging-related diseases in coordination with NIH, one sixth to clinical trials including people 65 and older, and the final sixth go to a national preventive medicine research initiative.

“If we succeed in slowing aging by seven years, the age-specific risk of death, frailty, and disability will be reduced by approximately half at every age. People who reach the age of

50 in the future would have the health profile and disease risk of today's 43 year-old; those aged 60 would resemble current 53-year-olds, and so on."⁵⁰

“If we succeed in slowing aging by seven years, the age-specific risk of death, frailty, and disability will be reduced by approximately half at every age.”

“Equally important, once achieved, this seven-year delay would yield equal health and longevity benefits for all subsequent generations, much the same way children born in most nations today benefit from the discovery and development of immunizations,” the article says.⁵¹

Perry, who co-authored the article with Butler and others, suggests thinking about the funds from a business perspective. Most companies invest four to five percent of their funds into research and development, and high tech companies invest an average of seven to eight percent. Biotech and life sciences invest up to ten percent. Just one percent of the Medicare budget is “vastly more than we are spending now,” he says.⁵²

V. Conclusion



Gray can be the new gold if we prioritize our goals as a society. Helping older Americans live longer, healthier lives creates benefits that stretch far beyond the current generation, and science is just beginning to discover the secrets of longevity. Gray may be the new gold if we consider the longterm benefits of this research.

“[We] must change the way our nation thinks about life after 65,” says Sen. Kohl. “A one-size-fits-all retirement approach will no longer match the very different plans that seniors and Baby Boomers have for their later years. We must make it easier for seniors to stay in the work force if they wish to continue contributing their skills and expertise. And as the statistics show, rethinking retirement is vital, not only to the quality of life for an aging population, but also to our nation's economic future.”⁵³

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- ⁵³ Kohl, H. Rethinking Retirement is Necessary. Roll Call. 2007 Feb 12.



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