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AS WE SEE IT**Can We Control Aging, Disease And Death In Our Lifetime?**

The basic mission of The Life Extension Foundation is to develop new methods of preventing and reversing degenerative disease, aging and the processes by which we die.

In the year 2000, we spent a record number of dollars on a wide variety of pathbreaking research projects. The latest of these projects is the use of gene chips to develop a “gene expression profile” of the aging process in order to find out how aging can be retarded.

We know that caloric restriction is the only documented method of extending maximum life span in mammals. Caloric restriction also prevents and slows the progression of a wide variety of aging-related diseases. The high-tech gene chips we are using enable us to determine the effects on aging and longevity of thousands of genes at the same time in specific tissues. We are comparing these changes to those seen in caloric restricted animals with the objective of developing methods to extend the human life span.

In 2000, we funded some of the gene chip aging research conducted by Richard Weindruch, Ph.D. and Tomas Prolla, Ph.D. at the University of Wisconsin in Madison. Drs. Weindruch and Prolla discovered the gene chip method of studying aging in 1999 (see Life Extension magazine, November 1999) and have published their findings on muscle and brain in mice in journals such as Science.

In 2000, we also funded gene chip aging research in the liver and muscle of mice under the direction of Stephen Spindler, Ph.D. of the University of California in Riverside, and began funding gene chip research in monkeys at the Baltimore Gerontology Center of the National Institute on Aging (NIA) under the direction of Drs. Mark Lane and George Roth.

Searching for authentic anti-aging therapies

The gene chip research we are funding has enabled scientists to develop a fundamental new body of knowledge about the genetic events that underlie degenerative disease processes. Foundation supported scientists are discovering genes involved in the progressive, time-dependent loss of strength, vigor, coordination and cognitive ability as well as genes that protect us from diseases. This body of knowledge is important for the development of new medical therapies to prevent and treat age-related diseases.

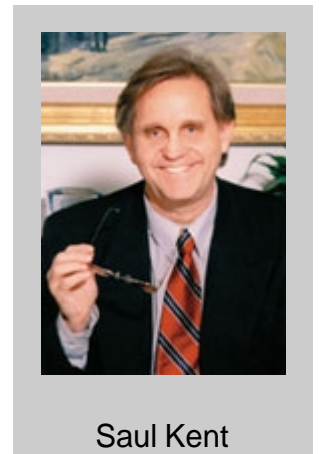
Drs. Lane and Roth have investigated several drugs as potential mimics of caloric restriction and we've discussed gene chip testing of these drugs with them. Any drug (or other treatment) that closely mimics caloric restriction would have the potential of slowing and/or reversing aging and extending the healthy human life span. As soon as such agents have been identified via gene chip analysis, we will fund life span studies to determine if they can, indeed, extend life span in mammals.

We'll provide you with further details of The Foundation's exciting gene chip project later, but first here's a rundown of some of the other research projects we are funding.

Advanced cryopreservation for transplant medicine

Right now, transplantation is a relatively small field because it depends upon drug-induced immunosuppression of the recipients of organs taken from live or recently deceased humans. These drugs, such as cyclosporine, are expensive, have toxic side effects and must be taken for the rest of the patient's life in order to prevent rejection of the transplanted organ. Moreover, there is a limited supply of such transplantable organs, which is inadequate to meet the needs of dying patients.

The single most important issue in transplant medicine today is the lack of enough organs to meet the demand worldwide. As a



Saul Kent



result, billions of dollars have been invested in new technologies to generate cells, tissues and organs for transplant. Among the new transplant technologies being developed are: tissue engineering (the merging of biologic and artificial systems); organ culture methods to grow transplantable tissues and organs in the laboratory; human therapeutic cloning (see Life Extension magazine, July 1999) from embryonic stem cells, which gets around the rejection problem; and xenotransplantation, in which it is proposed that tissues and organs from animal species such as pigs and monkeys be transplanted into humans.

Whatever the source of cells, tissues and organs for transplantation turn out to be, there is an across-the-board need for improved methods of cryopreservation for storage. Current methods of freezing are quite poor for cells and tissues and completely inadequate for organs. The Life Extension Foundation is funding the development of a technology called vitrification at a private laboratory in Southern California, which allows for long-term cryopreservation of tissues and organs without the formation of damaging ice crystals. The cryobiologists at this laboratory have developed the world's first synthetic ice-blockers and are close to the successful vitrification of rabbit kidneys. They have also targeted the heart and corneas (for eyes) in their vitrification research.

Today, transplantation is reserved for vital organs such as the heart, lungs, liver and kidneys, which need to be replaced or the patient will die. In the relatively near future, however, when scientists have developed technologies to grow immunologically identical tissues and organs, and/or to manipulate the immune system to prevent the rejection of tissues and organs, the field of transplant medicine will explode.

We believe it will soon become common to transplant tissues, organs and other body parts from diverse sources into sick and aging patients. Before long, medical scientists will be transplanting virtually every body part (except for certain brain areas) in order to cure and rejuvenate aging patients. The Foundation expects that its advanced vitrification technology will be used to set-up organ and body-part banks around the world to help keep people healthy and youthful into "old" age.

Battling toe-to-toe with death

Another project that LEF is funding is brain vitrification, which is a major step forward in our quest to develop Suspended Animation. When this procedure is developed further, patients who are dying of diseases or injuries that are not treatable will be placed into clinical biostasis and stored at very low temperatures until it becomes possible to revive and rejuvenate them (if that is necessary). In 2000, The Foundation worked with Stephen Valentine, a world-class architect, to design a high-tech facility (called The TimeShip) where the most advanced Suspended Animation reanimation research in the world will be conducted.

Another step in developing Suspended Animation is the ability to cool patients rapidly to protect against damage from ischemia (oxygen deprivation) and other types of cellular injury. Scientists at another private laboratory in Southern California funded by The Foundation have succeeded in developing a unique new method of rapid cooling using a type of perfluorocarbon as the cooling medium and the lungs as the mechanical means of cooling. This breakthrough technology has multiple potential medical applications including the treatment of patients with closed-head injury and stroke and extending the time for complex surgical procedures.

The most remarkable achievement in this laboratory has been the ability to reverse clinical death in experimental dogs. Dogs have been restored to life and good health after as much as 17 minutes without oxygen at normal body temperature. The key to LEF's unique resuscitation technology has been the combination of post-injury cooling and the use of drugs to prevent and reverse ischemia and other mechanisms of damage in the brain. The ability to prevent and reverse ischemia will play a major role in the the future of medicine. Ischemia plays a major role in generating damage from lethal diseases, injuries and aging.

Aging control for extended health and longevity

The development of authentic anti-aging and rejuvenation therapies in the 21st century should enable those of us who are still around to live in good health and youthful vigor for centuries. The Foundation has taken the lead in funding research to achieve this revolutionary goal.

The most promising approach to the control of aging is the gene chip research I discussed earlier. Scientists working with LEF are using gene chip technology to develop a database on the genetics of aging, as well as on the effects of drugs and nutrient supplements on aging in research animals. This database includes genetic profiles of normal aging in experimental animals, age-related diseases in special animal models, and retarded aging in calorie-restricted animals. By comparing gene expression in normally aging animals with gene expression in caloric restricted animals, these scientists have discovered that many of the genetic changes associated with aging are prevented or reversed in calorie-restricted animals.

How calorie restriction slows aging

Gene chip analyses in muscle, brain and liver of mice show that aging results in a differential gene expression pattern indicative of a marked inflammatory stress response, greater oxidative stress, reduced neurotrophic support in the brain and reduced expression of metabolic and biosynthetic genes. Most of these changes are completely or partially prevented or reversed by calorie restriction. Transcriptional patterns of CR-restricted animals suggest that caloric restriction retards the aging process by causing a metabolic shift towards increased protein turnover and decreased macromolecular damage.

Maximum life span studies

The use of gene chip technology to study aging and longevity is a major step forward in the development of interventive gerontology. It provides a dramatic shortcut to the identification of new therapies to prevent and treat the diseases of aging as well as aging itself. LEF-funded scientists are using this method to screen drugs, nutrient supplements and other modes of treatment for their ability to control aging and age-related diseases. They can do so in a small fraction of the time required to conduct life span studies in animals, which can take 3-to-5 years. It also enables scientists to study aging in specific tissues and organs, which is not possible in a life span study.

Because of the length and expense of conducting life span studies, few scientists have conducted them. However, even with the new gene chip technology, life span studies are necessary to prove that a particular therapy has the ability to slow or reverse aging. Only the significant extension of maximum life span in mammals can be considered evidence that a therapy may be able to control aging in humans.

The Life Extension Foundation showed great foresight in funding the first systematic series of life span studies ever conducted to determine if certain drugs, nutrients and combinations thereof, can extend maximum life span in mice. These studies were launched a few years ago at the University of Wisconsin under the direction of Dr. Richard Weindruch and at the University of California at Riverside under the direction of Dr. Stephen Spindler. (See Life Extension magazine, August 1997).

These studies have given us expertise in how to conduct life span studies and provided us with unique resources to study with gene chip technology. We will soon be conducting gene chip analyses of the effects of lifelong ingestion of various compounds on aging and age-associated diseases. By comparing the genetic profiles we find in these experimental animals with those in normally-fed and caloric restricted animals, we should gain new insights into aging and disease processes. We will be reporting the results of these analyses plus the final results of the life span studies later in 2001.

Other life span studies funded by LEF are being conducted at the University of Arkansas in Little Rock by Craig Cooney, Ph.D. These studies involve the effects on aging and longevity of SAME and other methylation-enhancing nutrients. Methylation is a fundamental chemical reaction that takes place in cells, which is crucial for cell growth, DNA repair, gene expression and the synthesis of proteins, neuro-transmitters and fat. One of the consequences of decreased DNA methylation is cancer. Aging is associated with decreased methylation.

How you can help to further this research

There are many dietary supplement companies in the United States today, but only The Life Extension Foundation funds the kind of research that is essential for scientists to find a cure for aging. We are committed to accelerating the pace of this research so that our members can personally benefit from it.

Every time you buy a product from us, you help to fund the work of pioneering scientists who are valiantly working against time to develop methods to prevent us from dying.

Membership in The Foundation is at an all-time high, and the prospect for rapid growth in 2001 looks very promising. We are growing in part because our members refer family members and friends to us. Please continue to recommend The Foundation to others, so that we can continue to fund life extension research.

Also, each of you should participate in our health freedom political campaigns by calling or writing your congressional representatives when we ask you to. Unless we break down today's bureaucratic barriers, the application of our research will be delayed, which is likely to lead to the premature death of some of our members.

The majority of Foundation members renew year after year. Please consider renewing when you receive your first renewal notice to save us postage. As many of you know, the dietary supplements we provide as a renewal bonus have a retail value that greatly exceeds the \$75 annual membership fee.

I want to thank Foundation members for enabling us to accomplish so much in the past 14 months. You can look forward to updates on our research projects in upcoming issues of Life Extension magazine.

For longer life,



Saul Kent

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