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Pieces of the Puzzle

An Interview with Leonid A. Gavrilov, Ph.D.

Leonid A. Gavrilov, Ph.D., is a Research Associate at the Center on Aging, National Opinion Research Center, University of Chicago. He received his Master's degree in chemistry, with a specialization in mathematical modeling and chemical kinetics, and his Ph.D. in genetics from Moscow State University. Dr. Gavrilov's areas of specialization include the biodemography of human longevity and analysis of human mortality and aging, the mathematical modeling of aging and mortality, and the genetics of aging and longevity. He is on the editorial boards of Journal of Anti-Aging Medicine, ScientificWorld *Journal, and* Experimental Gerontology. *Dr. Gavrilov and his wife, Natalia Gavrilova, co-authored the book* The Biology of Life Span: A Quantitative Approach.

Dr. Gavrilov, please provide our readers some insight into your background and how you became interested in studying aging and longevity.

I have a Master's degree in chemistry (chemical kinetics and enzymology) and a Ph.D. in biology (genetics), both from Moscow State University, Russia. I then spent a decade of intensive research and self-education, during which I wrote a book entitled *The Biology of Life Span*,[1] which was published in the United States in 1991. While working on this book, I tried to understand what happens in aging, and why we age and die. I performed an extensive and critical review of abundant scientific literature on aging and longevity, trying to reconcile different findings and theories. I also collected and analyzed thousands of life tables (lifespan survival data) for various human populations and other biological species. It was a tremendous amount of work, which was done in collaboration with Dr. Natalia Gavrilova, my wife. We were fortunate to make a number of new findings, which have since been cited in the scientific literature.

Writing a book was a good method of self-education in aging studies. How do I know that this self-education was correct? Well, indicators include the fact that our book was selected and cited by the *Encyclopedia Britannica* as a recommended reference on longevity. The book also received positive reviews in a dozen scientific journals, including *Nature*, the *British Medical Journal*, and *BioEssays*, and more than 100 citations in the scientific literature. We believe that our research and self-education efforts were not in vain.

Another very good test of our scientific credentials occurred five years ago, when Natalia and I immigrated to the United States from Russia and applied for research funding in this new and highly competitive environment. We were lucky to be awarded research grants from the National Institute on Aging, of the NIH, to study familial transmission of human longevity, and the effects of parental age at conception on a person's lifespan. With this funding, we were able to continue our research and to publish our findings. I find it somewhat ironic that my scientific background is now featured in "Who's Who in America" (Marquis Who's Who, 2002 edition), despite the fact that I am still a citizen of Russia.

Now please allow me to answer the second part of your question: how I became interested in studying aging and longevity. The decision to study aging was made early in my life, when my school years were coming to an end and the question of what I should do next was becoming an urgent one. I was very idealistic at that time and I had read a lot of science fiction.

I thought that perhaps the only way to succeed in a really worthwhile project, such as understanding how the human brain thinks or probing deep space exploration was to have enough time to accomplish the necessary research. This led me to confront the aging problem as a way to overcome natural time constraints. I also thought that in order to be able to understand the chemistry of aging and to make an anti-aging drug, I would first need to study chemistry in a university. I certainly do not regret that decision.

I received a free and rather good initial education at the Department of Chemical Kinetics, founded by the Nobel laureate Nicolai Semyonov—discoverer of free radical chain reactions. Thus, I became familiar with the free-radical theory of aging and the mechanisms of damage protection by antioxidants at the very beginning of my scientific career.

I was also very much impressed by the power of quantitative approaches to science. I find it amazing that it is possible to discriminate between intricate, competing mechanisms (hypotheses) of chemical reactions, simply by quantitatively analyzing the exact time trajectories (kinetics) of concentrations of reaction components and the products of the reaction. My immediate thought was that perhaps a similar quantitative approach could be applied to the biological aging problem, in an effort to uncover the mechanisms of aging through quantitative analysis of age-related mortality kinetics.

It was this concept of quantitative analysis that shaped all of my future research efforts. This appreciation of the great power of quantitative analysis was reinforced by my subsequent education and research work toward obtaining a Ph.D. in genetics. It is truly amazing that the very idea of genes, their existence in pairs (alleles), their random and independent segregation in offspring, and the concept of dominance all came to Gregor Mendel as a result of his thoughtful quantitative analysis of simple observations of trait frequencies in parents and offspring. Later, this purely quantitative approach to the analysis of trait frequencies also allowed the Nobel laureate Thomas Hunt Morgan to discover that genes are organized in groups in a linear fashion (in chromosomes), to create the first gene maps, and to describe the crossing-over phenomenon. Finally, another Nobel laureate, Barbara McClintock, discovered the phenomenon of genetic instability and "jumping genes" (transposons) through the quantitative analysis of observations on color variation among kernels of maize.

I find a special charm in these elegant studies, in which great scientific discoveries were made through the clever use of quantitative analysis of very simple observations, rather then fancy and expensive cutting-edge techniques. These historical examples convinced me in the very beginning of my scientific career that the most powerful scientific instrument is still the human brain. I based all of my future research work on this precept, placing the main emphasis on human scientific intelligence. This quantitative approach can be summarized by the following motto: "Think, measure and count; count, measure and think." This is why the title of our book is not *The Biology of Life Span*, but rather *The Biology of Life Span: A Quantitative Approach*. The quantitative approach became a cornerstone of all our scientific studies.

Please describe your current position and your scientific responsibilities.

I am fortunate to be a recipient (Principal Investigator) of the Independent Scientist Award from the National Institute on Aging, which provides five years of funding for research on aging and longevity. My scientific responsibility, as I understand it, is to do good science and to publish new relevant findings in peer-reviewed journals. For example, recently we have developed and published a new unifying theory of aging and longevity based on a reliability approach. This new theory provides a general explanation of aging for organisms as well as for technical devices. It was published in the *Journal of Theoretical Biology*.[2] I also developed a course, "Biodemography of Human Mortality and Longevity," which I teach at the University of Chicago. Teaching activities are very useful for scientific research, because they stimulate teachers to clarify scientific issues for their students to the extent that they begin to understand those issues themselves. For example, our recent scientific article, "Evolutionary The-

ories of Aging and Longevity,"[3] was written and published largely thanks to teaching activities.

Dr. Gavrilov, in your view, what is aging, how does it occur, and how does it express itself in human clinical disease?

Aging is a term used to define a set of processes that contribute to health deterioration and, with the passage of time, ultimately, to death. In other words any process that contributes to age-related decline in performance, productivity, and health is a component of the aging process that deserves our attention and intervention. One can think of aging as a group of processes responsible for such manifestations as increasing risk of frailty, disability, morbidity (for age-related degenerative diseases, in particular), and, ultimately, increasing mortality rates. This interpretation of aging is consistent with the general definition of aging systems in mathematical reliability theory and reliability engineering: an aging system is a system that demonstrates an age-dependent increase in failure rates. Failure occurs when the systems deviate from anticipated and desired behavior.

Leonid A. Gavrilov, Ph.D.

The main problem with studying aging is that it is a many-headed monster and manifests many types of failures and often multiple failures. Therefore, attempts to describe this complex, multidimensional phenomenon through the change of just one index—described as biological age, physiological age, or real age—may be misleading and even a deceptive oversimplification. More adequate scientific language to describe the aging phenomenon can be found in general system theory, and in reliability theory, in particular. Interestingly, reliability theory predicts that a system may deteriorate with age even if it is built from non-aging elements with constant failure rates. The key issue here is the system's redundancy for irreplaceable elements, which is responsible for the aging phenomenon. In other words, each particular step in system destruction/deterioration may appear to be random (occasional failure by chance, and not actual aging), but if system failure requires a sequence of several such steps, then the system as a whole may demonstrate aging behavior.

Why is this important? Because the significance of beneficial anti-aging interventions is often undermined by claims that these interventions are not proven to delay the process of aging itself, but instead that they simply delay or "cover-up" particular manifestations of aging. In contrast to these pessimistic views, reliability theory states that there may be no specific underlying, elementary aging process itself, instead aging may be largely a property of a redundant system as a whole, because it has a network of destruction pathways, each being associated with particular manifestations of aging (types of failure). Therefore, we should not be discouraged by only partial success of any particular anti-aging intervention. Instead, we can appreciate the availability of so many opportunities to oppose aging in numerous different ways.

Thus, efforts to understand the routes and early stages of age-related degenerative diseases should not be discarded as irrelevant to our understanding of "true biological aging." On the contrary, attempts to build a wall between biogerontology and clinical medicine are counterproductive. After all, the main reason people are concerned about aging is because it is related to health deterioration and increased morbidity. The most important pathways linked to age-related changes are those that make older people sick.

How has the scientific community's view of aging in general evolved in recent years? Is there a consensus on what aging is and how it occurs? What are the most important controversies in the field at present?

Views on aging have changed dramatically. They have also become more diverse and polarized in recent years. Just a decade ago, the consensus was to consider aging as an irreversible, universal, and intrinsic process. Aging was often thought of as an immutable, fundamental process, about which little could be done. For example, there was a belief that mutations could only shorten lifespan, not increase it. Even if some mutants lived longer lives, the belief was that this life extension came with the cost of having a crippled life.

Aging was considered to be a generalized deterioration. Therefore, the search for specific interventions that would have broadly applicable, positive effects on lifespan was considered a completely futile task, destined for failure for fundamental reasons. There was also a belief that each biological species has a specific maximal lifespan, which is immutable within a given species.

I remember well the 1980s, when we first challenged the concept of species-specific maximal lifespan, argued that there was no fixed limit to longevity, and even suggested a reliability theory of aging that predicted late-life mortality deceleration and leveling off. The debates were heated. Our own arguments were only taken seriously after publication of our book in 1991. We are pleased now to observe that the idea of a fixed maximal lifespan limit has been rejected by many other researches, and there has been a real fuss over the concept of late-life mortality deceleration. The idea of immutability of aging is also being challenged now in professional scientific journals.

Aging studies are now undergoing a paradigm shift, and frankly, I would call it a scientific revolution. Controversies are inevitable in such transition periods and they do indeed exist. The most important current controversy is related to an evolutionary explanation of aging. Evolutionary biologists were always very generous with gerontologists in providing advice and guidance on how to do aging research. Surprisingly, this generous intellectual assistance proved to be extremely injurious for aging studies. The reason is that evolutionary theory was interpreted in such a way that the search for single gene mutations, or life-extending interventions, with very large positive effects on lifespan was considered a completely futile task, destined for failure for fundamental evolutionary reasons. Researchers were convinced by the forceful, evolutionary arguments of George Williams, which held that " . . . natural selection will always be in greatest opposition to the decline of the most senescence-prone system." Therefore, he continued, "senescence should always be a generalized deterioration, and never due largely to changes in a single system. . . . This conclusion banishes the 'fountain of youth' to the limbo of scientific impossibilities where other human aspirations, like the perpetual motion machine and Laplace's 'superman' have already been replaced by other theoretical considerations. Such conclusions are always disappointing, but they have the desirable consequence of channeling research in directions that are likely to be fruitful.[4]"

As a result of this triumphant evolutionary indoctrination, many exciting research opportunities for lifespan extension were squandered for half a century until the recent and astonishing discovery of single gene mutants with profoundly extended longevity. This shifted the tide in aging research, despite all discouraging predictions and warnings based on evolutionary arguments.

Recent discoveries of lifespan-extending mutations are spectacular. A single-gene mutation, *daf-2*, more than doubles the lifespan of nematodes, keeping them active, fully fertile (contrary to predictions of some evolutionary theories), and with normal metabolic rates. Another single gene mutation, called methuselah, extends the average lifespan of fruit flies by about 35%; it also enhances their resistance to various forms of stress, including starvation, high temperature, and toxic chemicals. Finally, a single-gene mutation was found in mice that extends their lifespans by about 30% and also increases their resistance to toxic chemicals.

Researchers involved in these studies came to the following conclusion: "The field of ageing research has been completely transformed in the past decade. . . . When single genes are changed, animals that should be old stay young. In humans, these mutants would be analogous to a ninety-year-old who looks and feels forty-five. On this basis we begin to think of ageing as a disease that can be cured, or at

least postponed. . . . The field of ageing is beginning to explode, because so many are so excited about the prospect of searching for—and finding—the causes of ageing, and maybe even the fountain of youth itself.[5]" Now, when single gene, life-extending mutations are found, evolutionary biologists are presented with the task of reconciling these new discoveries with their theories. Gerontologists will also have to learn a lesson from the damage caused by decades of misguided research, when evolutionary biologists equated the search for major life-extending mutations and other life extension interventions to the construction of a perpetual motion machine. We do live in an interesting time, when new ideas about aging are forming!

Can aging be altered, and if so, how might we intervene?

My answer to this question may be rather unusual and may therefore require a detailed justification. Human aging has already been altered dramatically in developed countries over the last fifty years, although these significant changes are not yet completely understood or appreciated by either the scientific community or the public. Now, why should we question and perhaps reconsider the conventional idea of the immutability of human aging? The idea of aging immutability was supported in the past by demographic observations suggesting that the increases in human life expectancy have been due mainly to the prevention of deaths at young ages, while the death rates at older ages (say, above age 80) have remained surprisingly stable. This concept is known in demography as "rectangularization of the survival curve." Historically, the survival curve (number of survivors as a function of age) has evolved toward a rectangular shape. According to this concept, we are evolving as a society in the direction of fewer deaths at younger ages and "compression of mortality" at older ages, as more people survive to the maximal possible human lifespan. This fixed biological limit to human longevity was believed to be determined by the immutable aging process.

In 1985, we challenged this conventional concept in our study, "A new trend in human mortality decline: Derectangularization of the survival curve," which was published in the journal of the American Aging Association.[6] Specifically, we discovered a new trend in mortality decline in developed countries like Sweden after the 1950s. We found a preferential and accelerating decrease in death rates among very old people. This paradoxical observation was later published in a more elaborated form in our book in 1991. After years of denial and doubt, when the unprecedented historical decline in the oldest-old mortality rates could no longer be ignored or disputed, claims were made that the decline was not related to changes in human aging, but instead represented the undesired consequences of medical success in sustaining life, as more and more people were being kept alive by artificial means in greatly debilitated and degraded conditions.

The key issue is that not only have the death rates started to decline preferentially among the oldest age groups, but the health status of this same age group has improved significantly over time. Thus, the time schedule for aging manifestations has been dramatically altered over the last fifty years in developed countries, and this fortunate trend seems to accelerate over time. If human aging is already altered, then next question is, why does it happen? I wish I knew the answer to that question. I can point to some plausible working hypotheses that merit exploration.

Aging retardation may be partially related to better nutrition among later historical birth cohorts. Early-life nutrition history is, in fact, a very serious matter, because a trivial deficiency in micronutrients such as vitamins has the same devastating impact on DNA integrity as ionizing radiation (according to the findings of Professor Bruce Ames at the University of California, Berkeley[7]). There was a remarkable improvement in vitamin consumption over the last century, and this might have contributed to the observed postponement of aging manifestations. For example, the United States began adding vitamin D to milk and some other dairy products in the 1930s because of the high prevalence of rickets and osteomalacia in northern climates at that time. We know now that vitamin D supplementation, along with calcium in milk, also reduces the risk of bone

fractures in elderly women through the amelioration of osteoporosis.

Another possible contributing factor to the remarkable postponing of aging may be a historical decline in disease load in early life. Accumulating evidence suggests that many diseases and disabilities of older age have their roots in previous exposures to infectious agents in early life. For example, chronic inflammation, which is common in many infectious diseases, is also related to later onset of arthritis, atherosclerosis, diabetes, Alzheimer's disease, and cancer. Perhaps with improved sanitation, antibiotics, improved immune response through better nutrition, and vaccination, the late-life debilitating effects of early-life infections have been somewhat ameliorated.

Many people expected that a cure for aging would come in the form of a magic pill, an anti-aging drug. Instead, we largely overlooked the real and continuing progress in aging retardation, because it was so unanticipated and gradual. For how long will this historical trend of aging amelioration continue? How far will it go? Can this beneficial process be accelerated? These are all good questions to study, in addition to the traditional search for anti-aging drugs. My personal view is that future generations may be puzzled as to why we have overlooked some simple and readily available interventions, while spending so much effort on expensive and complex projects that result in dead ends. The most likely scenario for the future is a set of partial successes instead of one breakthrough. We need to understand the current trend of aging retardation and to try to accelerate this trend. Perhaps we need to pay more attention to latent infections in early life, to prevention of pro-inflammatory conditions, or to radically changing the whole culture of human nutrition. For example, encouraging accomplishments in smoking prevention in the U.S. offer hope that perhaps similar efforts could be applied to control the obesity epidemic in this country. A diet that is high in vitamins, important minerals and other micronutrients, and high in fiber content, while low in calories and animal fat, may have a profound effect on further postponement of age-related degenerative diseases in later life.

In summary, we can now speak about significant plasticity of aging, in contrast to the previous concept of aging immutability. By acknowledging the plasticity of aging, I do not wish to undermine the importance of future pharmacological interventions into the aging process, and other potentially promising approaches, including cell therapy. On the contrary, these new experimental approaches might have a bright future, especially as we begin to recognize that even simple approaches may bring about meaningful results.

What is the current state of aging research? How can we improve on ongoing research efforts to understand and intervene in human aging?

The current state of aging research can be described as a paradoxical one. On the one hand, almost every month we hear in the mass media about exciting new discoveries in aging studies. This creates an impression that aging studies are flourishing. What we do not hear in the news is how many interesting research opportunities are lost because of insufficient funding, and how desperate scientists are in their attempts to get research funding for aging studies. Currently, only 10–20% of research projects on aging are funded, so many promising ideas remain unexplored.

Much more generous funding of aging research is a key issue now, if we really wish to improve on ongoing research efforts to understand and intervene in human aging. Consider, for example, our research team. Currently we have to spend more than half of our professional time on paperwork, just to get research funding. The amount of professional time and effort being wasted on paperwork is alarming. Our group now has three promising research projects on aging and longevity that fall into the "high risk/high gain" category, and therefore have no chance of receiving funding from conventional sources. We would be delighted if private philanthropists like Bill Gates or George Soros would consider these projects, if they were ever to choose to support aging studies. Also, with the support of private foundations such as the MacArthur Foundation, so many interesting projects on aging could be accomplished!

What are the most promising avenues of research and why?

The answer to this question depends on the scientific goals you have in mind. If we are really interested in extension of healthy lifespan in humans, not just in fruit flies, then perhaps we need to pay more attention to human studies and to intervening in the human lifespan. In addition, we have to overcome two methodological obstacles. First, opportunities for experimentation in humans are limited. Second, studies on human lifespan take a long time. Both problems could be resolved through epidemiological and biodemographic studies of human longevity, in which we would analyze the experiments that Mother Nature has already performed. Quantitative analysis of retrospective data on human longevity, including genealogical data, seems to be an extremely promising approach. These kinds of studies may provide us with new and important information in a very short period of time.

We have developed a detailed agenda of particularly promising avenues of research and published it in this journal.[8] This project could provide us with decisive knowledge on the mechanisms of human longevity in just five years. What is the major obstacle to starting this project? It is the lack of research funding.

How do we know that these avenues of research are really promising? For one thing, we have already made some amazing preliminary findings. For example, we found a very unusual pattern of human lifespan inheritance. Traditionally, it was assumed that familial transmission of human lifespan from parents to children should follow a linear relationship, which is common to all other quantitative traits. In other words, for each additional year of parental lifespan, the children were expected to have some fixed gain in their average lifespan, too. Contrary to these conventional expectations, we discovered a very different, threshold pattern of lifespan inheritance. In fact, there is no lifespan heritability if parental lifespan is below a threshold age of 75–85 years, and heritability of human lifespan is very strong if parents live longer lives.[9]

We have also found that an early circumstance of human life, such as the month of birth, may have a profound effect thirty years later on the chances of human survival. This finding indicates that there may be critical periods early in human development that are particularly sensitive to seasonal variations in living conditions, such as seasonal vitamin deficiencies or seasonal exposure to pathogens.[10] We recently reconfirmed our initial findings on larger datasets. Another promising avenue of research is related to our finding that paternal age at a person's conception may be an important predictor of lifespan. This finding suggests that the mutation load in paternal sperm cells may play a significant role in determining the length of human life.

What are the most significant obstacles to anti-aging medicine? How can they best be overcome?

The most important obstacle to anti-aging medicine is public confusion as to the exact meaning and scientific credibility of anti-aging medicine. This confusion is reflected in the title of a recent scientific article, "Is There an Antiaging Medicine?" published in the *Journal of Gerontology*.[11] The term "anti-aging medicine" is currently used by three disparate groups of people in three completely different ways, which is the cause of the confusion. For one large group of scientists that publishes its research findings in the *Journal of Anti-Aging Medicine* and other related peer-reviewed scientific journals, anti-aging medicine represents the ultimate goal of their research work. Their research focuses on developing the medicines of the future that will control the aging process, and delay, prevent and even reverse the deleterious effects of aging. More than 100 important research articles have been published in the *Journal of Anti-Aging Medicine*, and these articles are now actively cited and used by the international scientific community.

If you search the scientific literature for the term "anti-aging," you will find that this term is now used routinely (like the terms "antioxidant" or "antibiotic," for example), including in the texts of scientific articles, their abstracts, key words selected by the authors, and even the titles of the scientific publications. I recently performed such an analysis of the scientific literature and published my findings in an arti-

cle that contains a list of legitimate anti-aging studies published in reputable journals by established researchers.[12]

The second group of people using the term "anti-aging medicine" is a group of medical practitioners. They are confronted with the real and often urgent health needs of their aged patients. For these physicians, anti-aging medicine is an everyday practice, attempted through trial and error, and aimed at alleviating, postponing, and hopefully even preventing or reversing some detrimental manifestations of aging. This is a rather diverse group. Some of their activities are very useful, such as strategies for early detection and treatment of conditions that tend to accelerate the progress of age-related degenerative diseases. For example, early detection and treatment of diabetes, hypertension, hypercholesterolemia, latent chronic infections, chronic inflammation, obesity, and vitamin and micronutrient deficiencies may postpone the onset of many detrimental manifestations of aging. However, because of the commercialization of the anti-aging industry, advertisement hype and spam are not uncommon. In some cases, there has even been the distinct smell of quackery and fraud. Unfortunately, these marginal "anti-aging" groups often rely on excessive advertising, thereby discrediting the very notion of anti-aging medicine.

Finally, there is a third group of people who believes that anti-aging interventions are neither possible nor desirable. They consider anti-aging medicine as an attempt to "tamper with aging," which is both immoral and futile in their opinion. For them, "if it's 'anti-aging' it's quackery by definition."[13] They select the most ridiculous and marginal cases of "anti-aging" quackery and expose them to the public, as if these cases are representative of anti-aging studies and anti-aging medicine.

How can these obstacles to anti-aging medicine best be overcome? For one thing, we need to educate the public and even some researchers on the existence of legitimate anti-aging science, with its legitimate goal of developing the foundations for the future of anti-aging medicine. This educational effort is already in progress. For example, recently the journal *Science* published our consensus letter, "Antiaging Technology and Pseudoscience,"[14] signed by Dr. Michael Fossel, Editor of the *Journal of Anti-Aging Medicine,* and by other Editorial Board members of the journal, including myself. This publication received significant attention and initiated an interesting discussion published in *Science* online.[15] In this letter we clearly spelled out the difference between the scientific, peer-reviewed *Journal of Anti-Aging Medicine* and popular magazines, which often serve as advertising forums for the anti-aging industry. Much more needs to be done to engender support and recognition for anti-aging medicine as a legitimate goal of scientific research. To address this issue, a year ago we established a scientific and educational website entitled, "Unraveling the Secrets of Human Longevity" (www.src.uchicago.edu/~gavr1/). This information resource contains more than 100 scientific documents supporting the ideas of anti-aging studies, and it has received about 30,000 visitors so far. I would urge other researchers to join our efforts and to contribute to the further development of anti-aging medicine by spreading a word of support.

What advice would you give those starting their careers in this field?

First, I would welcome new researchers and congratulate them for the choice they have made. Aging and longevity studies are important and will provide a sense of purpose to your life and inspiration for further research. I would offer three main types of advice. First, keep sight of the big picture and a broad encyclopedic vision of the problem. In aging studies there is always the risk of being overwhelmed and distracted by details. There is also a temptation to be driven by new fancy techniques, causing the initial goals of research to be forgotten. For example, there is great interest now in studies of differential gene expression during aging. However, aging may also be related to a simple decrease in cell numbers over time (loss of redundancy).

Second, be persistent in your research efforts and be prepared for occasional failures. Scientific research is always at risk of failure, because it is an exploration of unknown areas, often by trial and error. Therefore, consider a failure not as an indication of your research performance, but rather as a signal for choosing alternative research tactics. Also, be prepared for the pos-

sibility of failing in trying to obtain funding for your research proposals. Once again, be responsive to criticism and change tactics, but be persistent in strategic matters.

Finally, use a data-driven approach, instead of following a doctrine. Theories of aging are important for organizing accumulated facts into a comprehensive body of knowledge and for planning further research. Yet, too often, researchers are becoming hostages of their own theories, when they try to adapt the facts to their concepts. I would advise against treating aging theories too literally as theories; rather, view them as a set of ideas that themselves require further elaboration and validation. Keep an open mind and a critical vision. For any statement, claim, or reported finding, try to seek an alternative opinion and listen to alternative arguments carefully. Make final conclusions yourself, and make them based on the facts rather than on the apparent credibility of the sources. Famed authors and their publications in prestigious scientific journals may still be wrong. Be aware of conflicts of interest and, in difficult situations, rely on your common sense.

Do you have any other observations, insights, or suggestions regarding the field of aging and anti-aging medicine?

Yes, I believe that it is extremely important for researchers to understand that the prospects for a revolution in future life extension depend on their own behavior through the mechanism of a self-fulfilling prophecy. For example, if we convince the public and ourselves that nothing can be done or should be done about aging, then the outcome is clear. The main challenge lies in mobilizing public support for relevant research projects. From this perspective, recent attempts to discredit anti-aging research efforts and to present them as a kind of scientific "porn" should be taken very seriously; in my opinion, these attempts should not be endorsed. Moreover, it would be very useful to establish a prestigious Anti-Aging Science Award in order to stimulate legitimate anti-aging scientific studies and public support for them.

Anti-aging research projects will require large-scale, long-term intervention trials with human subjects, which is a very expensive endeavor and will require careful governmental supervision to minimize health risks. A successful anti-aging project may even require the joint effort of many nations in a collaborative spirit. It is important, therefore, to put the issue of aging prevention at the center of public debates now, so that by the next presidential election it becomes a key political issue. We should not lose any opportunity to express publicly our opinions on anti-aging studies and to support our arguments clearly and vigorously.

Thank you, Dr. Gavrilov.

—Interview by Vicki Glaser

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