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THE MECHANISMS OF AGING

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Epiphysis (pineal gland) is neuroendocrine organ common for mammals, has intimate links with hypothalamis and peripheral endocrine glands. Pineal gland via nervous system accepts light signals from retinal cell and plays an important role in regulation of biological rhythms in organism. Hormones and peptides produced by pineal gland posses a wide spectrum of physiological functions. Data available suggest that age-related changes in pineal functional activity are sufficient for process of organism aging. Pinealectomy or inhibition of pineal function reduces life span of animals, whereas pineal hormone melatonin and created by authors peptide pineal preparation epithalamin increases life span. Clinical observations evidence a perspectiveness of practical use of epithalamin for prevention of premature aging.

Key words: *aging, pineal gland, peptides, gerontology, prevention of age-related pathology*

Gerontology facing the demographic crisis

The XX-th century coming to its end nowadays appeared to become outstanding not only because of the revolutionary discoveries in the different fields of science, technology, fundamental changes in the life of the society, but also because of the unprecedented growth of the expected human life span connected with these discoveries and changes. In accordance with the World Health Organization data (Global..., 1990) only during the period from 1960 to 1990 the average life span increased for 13.5 years. In those born in the period of 1985-1990 the expected life span will make up 74.0 years in the economically developed regions, and 61.5 years in the countries being less developed economically. The longest expected life span is already achieved in Japan (78.3 years), Iceland (77.5), Sweden (77.1), Switzerland (77.1), and Netherlands (76.9). In 1900 the expected life span in the USA made up 46.4 years for men and 49.4 years for women, in 1950 these indices were 65.6 and 71.0 years correspondingly, and it is expected that by the year 2000 this rate will reach the level of 72.1 years for the male population and 79.5 years for the female one. In accordance with the calculations the men born in 2050 will live for 73.6 years, and the women - for 81 years.

These processes together with the reduction in the birth rate lead to the considerable aging of the population on the whole, i.e. to the increase in the rate of the elderly people in the whole population of those living on the Earth. In 1988 488 millions people were elder than 60 years, and by 2000 this index will make up 612 millions people; more over, 61% of these elderly people will live in the economically developed countries (Global...,1990). All of these facts will make the mankind on the whole, the state organizations, the organizations of the health service and wellfare to face a number of serious practical problems. One of the most important of these problems and also the one being very difficult for practical realization is the problem of prolongation of the period of active life being free of diseases characteristic to the elderly age. The solution of this problem is impossible without the theoretical comprehension of the aging nature and elaboration of the scientific recommendations and the use of the means increasing the life span - geroprotectors.

During the period of our century more than 100 different theories and hypotheses explaining the nature and mechanisms of aging have been created. All of them can be classified in accordance with two main categories: 1) the theories implying deterministic, "programmed" changes in the genes' structure or expression; and 2) the theories considering the aging as a result of stohastic, "accidental" damages in the structure and function of macromolecules, cells, organs and their systems (Dilman, 1971). It is well understandable that this difference is rather conventional because the stohastic damages in the individual cells may lead to the quite predicted phenomena in the large populations of cells and organs composed from these cells, and in the organism as awhole.

In principle, the history of gerontology is the history of search for " the clock of aging". Some of the investigators give the role of the time counter to the macromolecules (DNA, proteins, nucleoproteids) in which the damages induced by the external and internal agents (mutations,"cross-links", etc.) leading to the disturbances and then to the cessation in the functioning of cells, organs and systems, accumulate with the aging. The theory of marginotomia - the reduction in the DNA length for a certain region (telomere) with each cell division - has attracted a great attention to itself (Olovnikov, 1973; Harley et al., 1992). This discovery allows the scientists to understand the ability of the cells of our tissues to divide themselves a very certain number of times being cultivated outside the organism which was found by L.Hayflick ("Hayflick limit") (Hayflik and Morehead, 1961).

The age-related decrease in the secretion of sex hormones by the gonads and dehydroepiandrosteron by the adrenal glands forms, in accordance with some of the hypotheses, the basis for the mechanism of the organism aging, while the substitutional administration of these substances may remove some of the illnesses being characteristic to the senile age. The works of W.Denckla who had reported that the thyroid gland in elderly people produced a special "thormone of death" triggering the process of decrepitude and fade of the organism became a sort of a sensation at one time. The reduction of the protective role of the immune system with the age is one of the main manifestations of aging. The attempts to

Table 1. Candidates to play the role of "the clock of aging"

The supposed "clock of aging"	Theory, hypothesis
DNA	The theories of the "error catastrophe", accumulation of spontaneous mutations, marginotomia (telomere loss)
Macromolecules	Theory of "cross-links"
Mitochondria	Free radical theory
Cell	"Hayflick limit"
Gonads	Involution of the reproductive function
Adrenal glands	The reduction in the dehydroepi androsterone production
Thyroid gland	Denckla' "hormone of death"
Immune system	Immunoaging
Hypothalamus	Neuroendocrine theories
Pineal gland	Melatonin level and rhythm as the measure of the internal time in the solar clock of aging

use the substances stimulating the function of the main effectors of the immune system - thymic, and the bone marrow cells - resulted in some cases in the increase in the animals' life span. The congestion of cells of the special part of the brain - hypothalamus - play's the leading role in controling of the main functions of the organism - reproductive and adaptative ones, regulation of fat-carbohydrate and water-salt metabolisms. No wonder that a lot of a number investigators give the leading role in the mechanism of aging to the age-connected changes in the function of hypothalamus (Dilman, 1971).

On the basis of one or another views and theories, there are different candidates for the role of biomarkers of age, i.e. the parameters the value of which allows us to evaluate not the chronological aging of the organism measured in hours, days, months and years, but the biological age of the individual organism that may lag behind or anticipate the chronological age. The most obvious biomarkers of the whole organism aging are the time of switching on and cessation of the reproductive function, activity of the immune system and the systems of adaptation to the stress factors, the body weight (the amount of fat in it), the ability of the organism to utilize glucose, and some others.

It is well understandable that the selection of one or another "clock" of aging is determined by the methodical opportunities and experimentally proved facts that the researcher has at his disposal as well as by the level of the development of science on the whole. It is also obvious that the more fundamental the process lying on the basis of the "aging clock" is, the larger a circle of phenomena it explains, the more reliable the theory and its predictive strength are. And that's exactly what makes the theory to be the instrument of influence on the process of aging and gives the hope to increase the life span of the human being. It is necessary to stress that the candidate for playing the role of the biological "clock" has to answer the same requirements as the measure of any type of time, i.e. this has to be a certain oscillatory process chosen as the standard of the frequency that has to be responded to the calculation of the number of these oscillations. In the hierarchycal system, to the group of which the organism itself belongs, it is possible to choose its own standard of the frequency of time on every level of its organization (molecular, cellular, ogran, and systemic).

One of the fundamental theories being most fruitfully developed in recent years, which explains not only the process of aging but also the wide circle of pathologic processes connected with it including cancer, cardio-vascular diseases, age-connected immunodepression and brain dysfunctions, cataract, is the free radical theory of aging (Cutler, 1991; Harman, 1992, Martin et al., 1996). Such molecules as superoxide (O_2^{-2}), H_2O_2, hydroxyl radical (HO), and possibly synglet oxygen (O) being produced mostly in mitochondria, damage the cellular macromolecules (DNA, proteins, and lipides).

It is supposed that exactly the accumulation of such damages in the cells of organism lies on the basis of aging and of the diseases connected with it. It is already calculated that

Table 2. Factors protecting macromolecules from the damages caused by the free radicals (39)

Agent	Target	Function
O	Superoxide dismutase	Converts O to H_2O
H_2O_2	Glutathione peroxidases	Converts H_2O_2 to H_2O and O_2
H_2O_2	Catalase	Converts H_2O_2 to H_2O and O_2
Free radicals	Beta-carotene (provitamin A)	Fat soluble free radical savenger
"	Vitamin E (alpha-tocopherol)	"
"	Vitamin C (ascorbic acid)	Water soluble free radical savenger
"	Uric acid	"
"	Melatonin	Fat and water soluble free radical savenger
Transitional metals	Metal chelators	Prevent transition metals iron and copper from catalizing free radical reactions

in spite of the fact that only 2-5% of the oxygen inhaled with the air is converted into the toxic radicals of oxygen, the organism produces about 1 ton of oxygen radicals during the period of 70 years of the human's life. The overwhelming majority of them are being neutralized before they have the time to damage one or another component of the cell. Thus, not more than 4 of every 1 million of superoxide radicals formed in the organism escape the attention of fermental protection. Table 2 shows the main endogenous factors of the organism that protect the macromolecules from the damages caused by the free radicals. It is shown that the species life span correlates directly with the activity of superoxide dismutase, the level of beta-carotene, alpha-tocopherol and uric acid in the blood serum (Cutler, 1991).

The results of the experiment in which the transgenic strain of drosophila with the additional copies of genes determinating the excess activity of superoxide dismutase and catalase lived 20-37% longer in comparison to the controls (Orr and Sohal, 1994) had become the brilliant argument in favor of the free-radical theory of aging. The increase in the life span was observed in case of use of vitamin E, chelating agents and some of the synthesized antioxidants not only in the experiments with flies but also in the laboratory mice and rats (Cutler, 1991).

It is reasonable to suppose that the candidates to play the role of the natural measure of the internal time - "the aging clock" - have to be searched among the structures providing the production of endogenous antioxidants. It seems to us that pineal gland (epiphysis) can be the most probable candidate to play this role. Let us try to motivate this point of view.

The role of the pineal gland in the organism

The most essential phenomenon for the nature on the Earth is the alternation of day and night, light and darkness. Our planet rotating round its own axis and at the same time round the Sun measures off the days, seasons, and, alas!, the years of our life. Chronobiology, the science studying the changes in the organism connected with the nature rhythms, having appeared in the ancient times, is being rapidly developed nowadays.

More and more data concerning the role of pineal gland as the main pacemaker of the organism functions are being accumulated. What happens when we open our eyes being awaken? The sensitive cells of the retina perceiving the light, the information about it's intensity and quality, transfer it through the optic nerve, across the brain oscillator (suprachiasmatic nucleus) of the hypothalamus and the upper cervical ganglion to the pineal gland, this "the third eye" of the organism, the specific cells of which - pinealocytes - contain the complex and keenly reacting to the light system consisting of the enzymes - N-acetyltransferase and hydroxyindolyl-O-methyltransferase and substrates of transformation of amino acid tryptophan to the indolamines - serotonin, N-acetylserotonin and melatonin,

the key hormone of pineal gland (Anisimov and Reiter, 1990; Slepushkin et al., 1990; Arendt, 1995). It is necessary to note that not only the indole derivatives of tryptophan but also peptides having a high biological activity are produced the pineal gland (Morozov and Khavinson, 1983, 1996; Arendt, 1995).

Light inhibits the production and secretion of melatonin, and that is why it's maximum level in the pineal gland and in blood of humans and many species of animals is registered in the night hours, and the minimum one - in the morning time and during the day; more over, the night level may be 3-10 times higher in comparison to the day one. This peculiarity in the pineal glands rhythm has a fundamental significance for the functioning of the organism, first of all, its regulatory systems - neuroendocrine and immune (Slepushkin et al., 1990; Arendt, 1995). The pineal gland function decreases with aging which manifests, first of all, by the breach in the rhythm of melatonin secretion and decrease in the level of its secretion (Reiter et al., 1980; Touitou et al., 1981).

If the pineal gland is likened to the biological clock of the organism, melatonin can safely be likened to the pendulum that provides the function of this clock, and the decrease in the amplitude of which leads to their stopping. We think that the comparison of pineal gland to the solar clock in which melatonin plays the role of shadow of the gnomon - the rod casting a shadow of the Sun will be a more precise one (Anisimov, 1996). During the day the Sun is high up in the sky, and the shadow is short (the level of melatonin is minimum), in the middle of the night - the peak in the melatonin synthesis in the pineal gland and its secretion to the blood. The important thing is that melatonin has a circadian rhythm, i.e. the unit of its measurement is the chronological metronome - the daily rotation of the Earth round its axis.

If the pineal gland is the solar clock of the organism, it is obvious that any changes in the duration of the light time have to influence considerably it's functions and finally - the rate of it's aging. Like the women, the female rats or hamsters are the animals with the spontaneous ovulation, but unlike the near-moon menstrual cycle in women, these rodents have a very short 4-5- days ovulatory cycle named estrous cycle, all the changes in which are very easy to register. The artificial 2-4 hours increase in the duration of the light time leads to the relatively rapid increase in the duration of the estrous cycle, and, in a certain percent of cases, to its breach. If in the room in which the laboratory animals are being kept the light is switched on during the whole night, i.e. if we create the regimen of constant lighting, the so-named syndrome of persisting estrus characterised by the anovulation which naturally finishes the reproductive function being the biological equivalent of the menopausal period in women, will develop in the overwhelming majority of the animals. The development of follicular cysts, hyperplasia of the theca tissue is observed in the ovaria of such animals. The cyclic production of gonadotropic hormones and prolactin in the pituitary and estrogens in the ovaria is replaced by their acyclic secretion which is accompanied by the development of hyperplastic processes in the uterus and mammary gland. Several months later the fibro-cystic disease, hyperplasia and polyps of the endometrium are already registered in the majority of rats being kept at the constant light regimen, and later on - the other neoplasms including the malignant ones are also diagnosed in them which finally leads to the decrease in the life span of the animals (Anisimov and Reiter, 1990; Arendt, 1995).

The cessation of the cyclic activity of the ovaria in women being 45-50 years of age (menopause) naturally finishes the reproductive function. However, in case of some diseases the menopause comes before the proper time. For example, in case of the sclerocystic ovarian syndrome the absence of ovulation, infertility, disturbances in the endocrine and hormonal balance characteristic for the elderly age, the high risk of the development of the cancer of the uterus and breast are seen in the young women, which allowed us to consider this disease to be the syndrome of the intensified aging (Dilman, 1971). It is also known that the anovulatory cycle is a significant oncological risk factor in women. The excess in the lighting can also be one of the reasons of its increase. Thus, it is known that in a number of economically developed countries located mostly in the northern regions, the disturbances in the menstrual cycle and different forms of fibro-cystic disease are registered in women

more often in comparison to the other regions. They also suffer from the breast cancer and endomentrial cancer more often in comparison to the women from the other regions. The leading role in the development of this pathology is given to such factors as diet peculiarities and the life style, but it is not possible to exclude the possibility of the fact that the "white nights" and the excess of the artificial electric lighting (light-at-night) have a promoting influence in this case. The correlation between the frequency of anovulation and the risk of the development of breast cancer and the work in the night time or with the computer display video terminal that are the source of not only the excessive lighting but also the electromagnetic fields of different frequency that have the inhibitory influence on the melatonin level also needs to undergo the special epidemiologic studies. The studies carried out in our laboratory showed that the frequency of the persistent estrus in mice being irradiated by the video display terminal of personal computer 1 hour daily during the period of one year was several times higher in comparison to the control group of animals. No increase in the level of melatonin at night was registered in the volunteers when bright light was switched on at the night time. At the same time, for the thousands of workers and employees the night character of their work is the routine reality.

So, if the light-at-night inhibiting the production and secretion of melatonin is, undoubtedly, the factor contributing to the premature switching off of the reproductive function and the development of the age-connected pathology including cancer, it is necessary to ask the question - is the darkness more favorable for health factor? The nature has organised itself a relatively cruel experiment of this kind. The number of people being born blind, and those who have partially or completely lost their sight in the early age is large enough. It was found out that in spite of the great stress in which the blind people live, the life span of those of them who have completely lost their sight is significantly larger in comparison to those who have lost their sight only partially (Arendt, 1995). Blinded rats live also longer (Lehrer, 1981). The risk of breast neoplasms in blind women is reduced. The experiment allows us to answer the given question more definitely. In the female rats being bulbectomized in the early age the ability of carcinogenes to cause mammary carcinoma was reduced (Anisimov and Reiter, 1990).

The data on the influence of the reduced lighting and even complete darkness on the development of neoplasms are of great interest. A series of studies showed that the keeping the rats in such conditions considerably inhibits the development of mammary carcinomas in them. It was also found out that the effectiveness of treatment of these tumours with the use of the known antitumour drugs increased if the treatment was carried out in the darkness (Anisimov and Reiter, 1990).

Pineal gland and life span

So, the change in the duration of the light time into one or another side considerably modifies the body functions, in particular, the reproductive and immune, the development of the age-connected pathology, and, finally, may influence the life span. What will happen if the solar clock themselves are broken - the pineal gland is removed or the substances produced by it are used for the prevention of the age-related disturbances in its function (Table 3)?

In 1959 it was found out for the first time that the pinealectomy in the young age leaded to the considerable decrease in the life span of rats in comparison to the controls (Malm et al., 1959). Let us notice that in the pinealectomized animals the immunity is depressed and the development of many of the neoplasms is accelerated (Anisimov and Reiter, 1990). In 1960 the Romanian gerontologist C.I.Parhon reported on the prolongation of the life span of the old rats with the help of the crude pineal extract (Parhon, 1960). In 1973 we have reported (Anisimov et al., 1973) that the peptide pineal extract (that was later named epithalamin, Morozov and Khavinson, 1983) restored the regular estrous cycles in the old persistent estrous female rats and also the sensitivity of their hypothalamic sex centres to the feedback inhibition by estrogens - the mechanism to which the leading role in the age-related switching off of the reproductive function is given.

At the same time we had started the studies of the effect of this preparation on the life span of the female rats. In was found that

Table 3. The stages of the study of the role of pineal gland as the aging clock

The phenomenon revealed	Authors
Morphological signs of the age-related pineal involution	Khelimski, 1958
The pinealectomy reduces the life span of rats	Malm et al., 1959
Crude pineal extract increases the life span of old rats	Parhon, 1960
Polypeptide pineal extract restores the reproductive function in old rats	Anisimov et al., 1973
Polypeptide pineal factor prolongs the duration of the reproductive function and provides the 25% increase in the mean life span (MLS) in the female rats	Dilman et al., 1979
Age-related decrease in the melatonin secretion by the pineal gland	Reiter et al., 1981 Touitou et al., 1981
Epithalamin provides the 31% increase in the MLS of the female C3H/Sn mice	Anisimov et al., 1982
Melatonin injections to the old mice C57BL provide the 20% increase in their MLS	Pierpaoli, Maestroni, 1987
Epithalamin injections started at the age of 3,5 and 12 months increases the MLS in the female SHR mice	Anisimov et al., 1989
The use of Epithalamin in the geriatrics practice	Khavinson, Morozov, 1990
Epithalamin treatment increases the night melatonin secretion in young and old rats and being started at the age of 15 months increase the MLS in the female rats	Anisimov et al., 1992
Melatonin is the effective endogenous savenger of free radicals in vitro	Poegeller et al., 1993
Transplantation of the young pineal gland to the old pinealectomized mice in situ increases the MLS	Lesnikov, Pierpaoli, 1994
Melatonin and epithalamin inhibits the free-radical processes in vivo	Anisimov et al.,1995
Epithalamin increases mean life span and slow down aging rate in D.melanogaster	Anisimov et al.,1997

epithalamin increased the duration of the reproductive period (estrous function) and also provided the 25% increase in the mean life span of the animals. More over, it restored the fertility in a part of the old female rats. It was also shown that epithalamin slowed down the age-related disease of the immune functions in animals and increased the hormone production by the thymus (Dilman et al., 1979, Anisimov et al., 1992).

The studies of the epithalamin influence on the life span were continued. Approximately one third times increase in the life span was noticed on the two strains of mice (Anisimov et al., 1982, 1989). In all of these experiments the substance injection was started at the age of 3-3,5 months which corresponds to the age of 25-30 years in the human's life. However, is there anybody who think about aging, and more over, about the use of the substances that can slow down its coming, being so young? So, the experiments were carried out on mice and rats, and in these experiments the substance began to be injected at the age precedeing the switching off of the reproductive function. It was found out that epithalamin increased the life span of the animals in this case too (Anisimov et al., 1982; 1989). At the same time, the mean life span of the tumour-free animals considerably increased in these experiments, i.e. the own geroprotective effect of the preparation manifested itself in this case. It is necessary to stress that the use of epithalamin in all the above-mentioned experiments was accompanied not only by the increase in the life span but also by the decrease in the frequency of the tumours development (Anisimov et al., 1982; 1989; 1992; 1994). Recently we have shown that epithalamin increases mean life span and slow's down the aging rate (by 2 times) in *Drosophila melanogaster* (Anisimov et al., 1997; Khavinson et al., 1996).

In 1987 the Switzerland researchers W.Pierpaoli and G. Maestroni (1987) reported that the old mice who had been given melatonin with the drinking water during the night time lived 20% longer in comparison to the control ones, and looked like much more cheerful. As the basis for their research they took the well-known data on the age-related decrease in the night-time melatonin production in animals and humans, and working on the study of its influence on the immune

system, they expected that its restoration in the old mice would have a positive effect on their status and life span. The result of their experiments proved these suppositions. Melatonin also increased the mean life span in rats (Oakin-Benhadan, 1995). However, some of these resulrs were seriously criticized (Reppert and Weaver, 1995; Turke, 1996). However, W.Pierpaoli did not stop on that stage, and, having performed the transplantation of the pineal gland of the young donors into the thymus gland of the old mice, he could observe not only the restoration of its structure and function but also the increase in the animals' life span. At the same time, all the manifestations of the age-related pathology, including the frequency of the neoplasms development were decreased in these animals (Pierpaloi et al., 1991, Pierpaoli and Regelosn, 1994).

So, the transplantation of the "young" pineal gland to the thymus or to the place of the removed gland of old mice, injection of Epithalamin or melatonin, led to one and the same result - the increase in the animals' life span. The fact that remained to be determined was the links between the effects of melatonin and pineal peptides. It has been found out that the injections of epithalamin to the young and old mice increases the production of melatonin and its secretion into the blood in them (Anisimov et al., 1992). It is possible that the intrapineal system of the regulation of melatonin biosynthesis by peptides secreted by pinealocytes is revealed, being similar to the analogous systems in the other endocrinous glands.

How does melatonin slows down the process of aging? According to R.J.Reiter (Rweiter et al., 1994; Poegeller et al., 1993, this natural metabolite of the amino acid tryptophan is 5-14 times more active as the free radicals' scavenger than glutathione peroxidase is in the *in vitro* experiments. We have recently found out that melatonin has antioxidant activity *in vivo* too (Anisimov et al., 1995). Moreover, it appeared that epithalamin having no these characteristics *in vitro*, has manifested itself to be even more effective in comparison to melatonin activity in the inhibition of free radical processes being injected to rats in the dose that increases their life span (Anisimov et al., 1995). The key role of free radicals in the mechanisms of aging and development of the age-connected pathology was already discussed above. It was recently shown that melatonin was able to inhibit the formation of agressive metabolites of carcinogenes, i.e. the substances causing the cancer development, in the organism (Poegeller et al., 1993). Both melatonin and Epithalamin stimulate the immunocompetent cells and slow down the aging of the immune system, they also normalize a number of age-related disturbances in the fat-carbohydrate metabolism, prolong the ovarian cyclic activity in the female mice and rats, restore the reproductive function in the old animals increasing the learning capacity of the animals. And of course, the important, if not the most important characteristic of these substances is their ability to prevent the development of both spontaneous and induced by various chemical carcinogenes and ionizing radiation neoplasms (Anisimov, 1987; Anisimov and Reiter, 1990; Anisimov et al., 1994).

It is necessary to stress that the studies of the role of pineal preparations as the regulators of the "solar clock of aging" function have already come out of the laboratories' borders. In 1990 V.Kh.Khavinson and V.G.Morozov reported results of the study of the effectiveness of epithalamin as the geroprotector in persons being elder than 60 years. More than 200 persons being at the age of 60-88 were examined by the investigators. The use of the preparation during the period of 3-10 years was accompanied by both subjective improvement in the patients' general condition and objective normalization of the biochemical, hormonal and some of the immunologic parameters. The raising hopful results were also obtained in the use of the substance in the complex treatment of some of the oncological diseases and vegetodyshormonal myocardial dystrophy.

For several years the scientists of St. Petersburg Institute of Bioregulation and Gerontology together with the physicians of the Municipal Geriatric Centre have been already following up the large group of people of the middle ages who receivi epithalamin, for the purpose of the evaluation of the possibility of aging delay and prevention of its premature manifestations including the age-related pathology. These studies will require much more efforts, funds, and, of course, time, but even nowadays it is already possible to express the hope that their results will be invaluable not

only for gerontology but also for the practical geriatrics.

So, the idea that the pineal gland is the solar clock of aging has a serious enough experimental background. It is important to stress that without rejecting the majority of the theories seeing the reason for aging in the events happening in the organism on one or another level of organization (molecular, cellular, systemic), the idea of the solar clock of aging unites the modern scientific data on the aging' mechanisms with the more and more realizing by the mankind idea about the indissoluble unity of life and cosmos. Let us remind the words of A.M.Tchijevsky, the founder of heliobiology, "the life on the Earth is indebted mostly to the Sun ray". The Sun is not only the source of the life on the Earth but also the natural factor controlling the function of the internal clock of its inhabitants, and, hence, the life span of them.

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