



THE (A)SYMMETRY OF THE MALE GRAYING BEARD HAIRS AS AN INDICATION OF THE PROGRAMMED AGING PROCESS

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SUMMARY – Aging interventions will be ineffective if we do not understand the basic principles of aging. Currently, there is no consensus on the issue whether aging is programmed or not. The hypothesis presented in this article indicates that aging (at least graying of male hairs) is programmed. This hypothesis is supported by the symmetry of the graying of male beard hairs. According to stochastic theories of aging, aging is a passive non-programmed process where random dispersion of graying hairs should result. On the contrary, programmed theories of aging would predict that there should be symmetry on the left and right parts of the face showing the same proportion, pattern and time of appearance of graying hairs.

Key words: *Graying beard hair; Graying hair; Aging; Programmed theory of aging; Stochastic theory of aging*

Introduction

What triggers the aging process? Why do living beings age? Could this process be slowed down or even reversed? Is aging programmed, is it under genetic control or not? Although significant advances in biochemical and medical science have been made in the last 50 years, answers to these questions remain a matter of debate among different aging theorists¹⁻³.

Several theories aimed to specify and define the aging process, each from a different perspective, but none was able to explain the whole complexity of senescence. Traditional theories of aging oppose that aging is genetically programmed, or that it is the result of adaptation. In general, theories that explain aging have been classified into the programmed (or deterministic) and stochastic (random; damage/error) ones. The two main (and subdivided) categories of aging as explained by modern biological theories are: (a) programmed: (1) programmed longevity, (2) endocrine theory, (3) immunological theory, (4) theory of phenoptosis, (5) nutrient sensing theory, (6) theory of biological clocks (epigenetic theory) and (7) demographic theory of aging⁴; and (b) damage or error theories: (1) wear and

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tear theory, (2) rate of living theory, (3) cross-linking theory, (4) free radical theory and (5) somatic DNA damage theory⁵.

Stochastic models explain aging process as a result of progressive accumulation of random molecular damage and see aging as an entirely passive process^{4,6}. According to the most popular stochastic wear and tear theory of aging, first propounded by August Weismann in 1882, the effects of aging are caused by progressive damage to cells and body systems over time. The consequences of aging are thus attributed to gradual damage to cells and body systems over time, indicating that deterioration is random and is not under active control by the genes or any other biological 'program'. Programmed theories, however, suggest that aging is genetically encoded and regulated by genes or other biological clocks operating throughout the lifespan⁵. Aging thus follows a biological timetable which is programmed or regulated by changes in gene expression and/or deterioration of several diseases^{1,5,7-9}.

Evidence indicating that aging is under a genetic program

Some gerontology researchers and evolutionary biologists try to explain aging as being programmed, although this view is advocated only by the minority of aging researchers^{1,9-21}.

There are several examples suggesting that aging might be programmed, for example, model organisms, being able to increase longevity under different stressful life circumstances due to the phenomena of hormesis²²⁻²⁵. Other studies later confirmed the association between telomere shortening and longevity²⁶⁻³². Shortening of telomeres contributes to aging by the following two mechanisms³³: if telomeres are too short in stem cell tissue, the cells cannot be regenerated, and cells with short telomeres are the cause of increased inflammation³⁴. However, some animal species suffer deterioration with age although their telomeres do not become shorter with advanced age and human neurons suffer aging although being post-mitotic. Aging could be explained as a process of adaptation to endogenous and/or exogenous factors, as a population turnover, evolution, prevention of demographic influences, and to stabilize the population^{20,35-38}.

Recent studies focus attention on telomere shortening as a strong prognosticator of age-adjusted death rate^{26,27,30,32,39,40}. Recently, highlights have been orient-

ed also towards thymus involution. During the evolution of the body, the thymus gland becomes smaller and loses functionality. This effect causes several errors in non-detection of microbes and/or tissues attacked and/or autoimmune response, etc.³³. However, not every organ is unified with the modes of aging. During the neuronal growth, the brain is not limited by the influence of telomere or by the thymus, but by the epigenetic programming^{41,42}. Several authors suggested the existence of epigenetic aging clock^{43,44}. Even Leonard Hayflick's discovery of limited replicative capability indicates that cells are programmed to die (or enter senescence)^{45,46}. If aging is programmed, what is the master clock regulating it? Up to now, no such clock has been discovered, but many possibilities have been proposed, e.g., thymic involution, the suprachiasmatic nucleus, telomere shortening, the hypothalamus, and replicative senescence⁴⁷.

Graying of the hair

The hair follicle pigmentary unit is also strongly responsive to changes associated with age. The precise mechanisms which account for the decrease of melanogenically active melanocytes from anagen adult hair follicles with aging, are still unsubstantiated. Gray hair follicles have noticeably lowered the number of differentiated and functioning melanocytes found in the hair bulb. On the other hand, hair follicles known as 'senile white' follicles may have no melanocytes in the hair bulb region of the hair follicle⁴⁸. It has been established that the loss of hair shaft melanin is related to reduction of the bulb melanin content, as well as of the bulb melanocyte population. Hair graying is presumably an aftermath of the entire and specific emptying of the bulb and in the outer root sheath melanocytes of human hair⁴⁹. When the reservoir of stem cells is depleted, the production of pigment ceases and the hairs turn gray. Does the hair follicle have a 'melanogenetic clock', which decelerates or ceases melanocyte activity, resulting in graying of the hair?

Hypothesis

If graying of the beard is not programmed, then a random distribution of gray (hairs) parts should be observed (Fig. 1b). On the other hand, if graying is programmed, the symmetrical areas on the left and on the right side of the face should appear, as presented in Figure 1a.

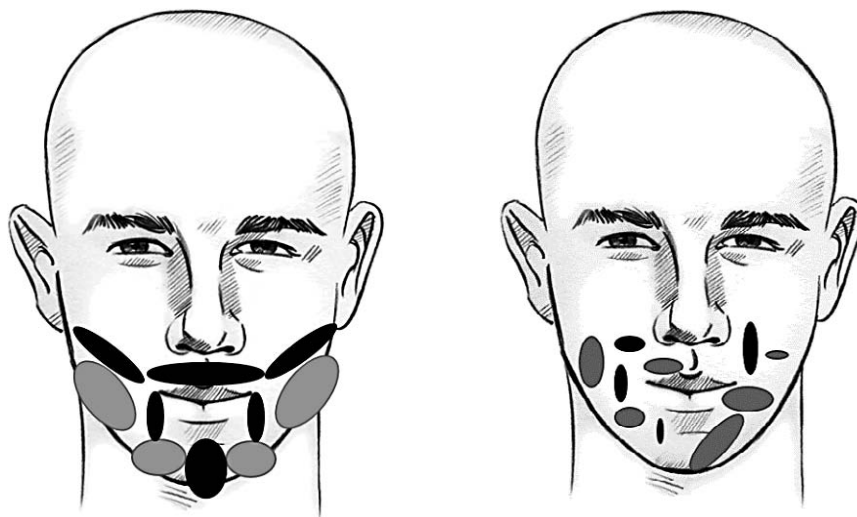


Fig. 1. Symmetrical pattern of graying zones of the face (a) and random pattern of graying zones of the face (b).

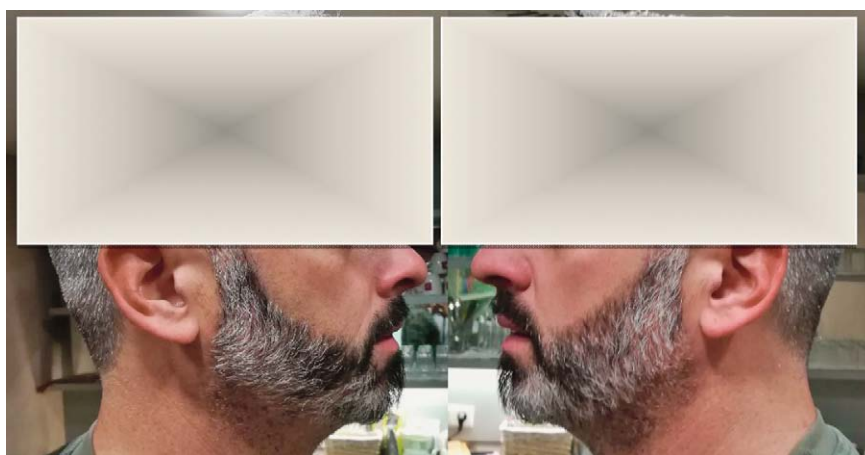


Fig. 2. Picture of a male, 38 years, with graying beard. Picture shows a symmetrical pattern of graying area, taken from the right and left parts of the face.

Methods

Two different commercially available programs (Facial Symmetry and PicHacks-The Symmetrical Face Generator) were applied for preparation of face mirror pictures. Fifteen pictures of male adults with different degree of gray beard areas were chosen and facial symmetry/mirror pics were prepared. Pictures in Figures 2 and 3 were taken with a color 16-megapixel camera, showing frontal and two lateral face pictures of a 38-year-old male adult, who gave a written con-

sent for participation. Pictures in Figures 4-14 were downloaded from publicly accessible web pages and belong to known celebrity persons.

Results

The pictures in Figure 2 indicate a symmetrical distribution pattern of graying hairs, as it can be observed when a mirror picture of the left and the right side of the face is composed with a computer program.



Fig. 3. Original face picture (A) and simulation of the symmetry of the left (B) and right (C) side of the face with a computer program using two computer programs, Facial Symmetry and PicHacks-The Symmetrical Face Generator.

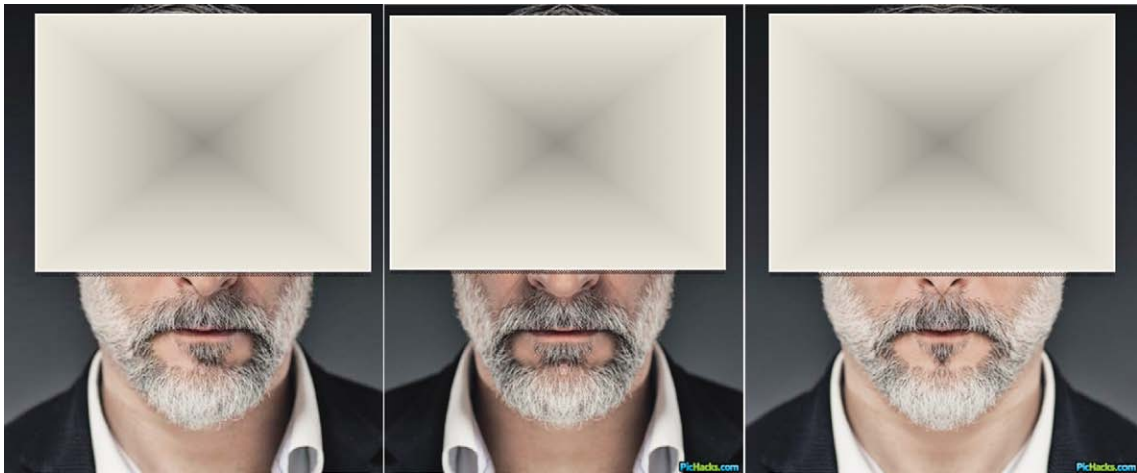


Fig. 4. Original face picture (A) and simulation of the symmetry of the left (B) and right side (C) of the face with the PicHacks-The Symmetrical Face Generator computer program.

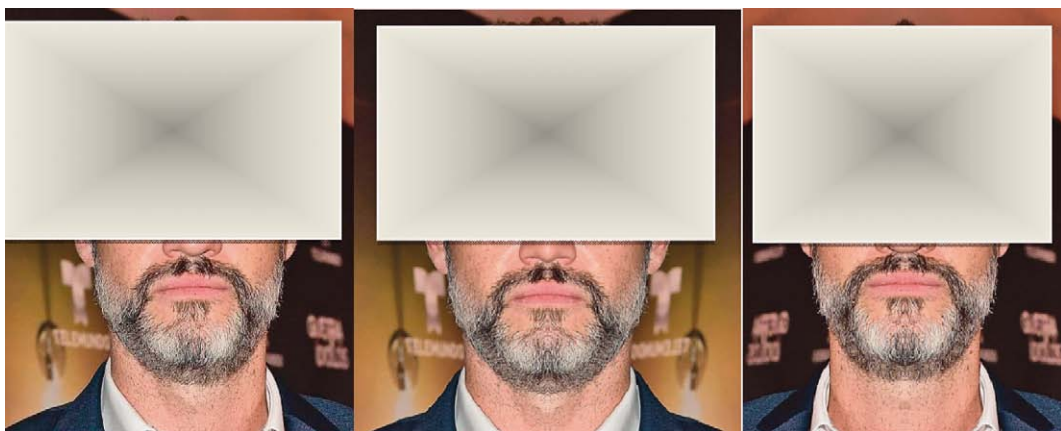


Fig. 5. Original face picture (A) and simulation of the symmetry of the left (B) and right side (C) of the face with the PicHacks-The Symmetrical Face Generator computer program.



Fig. 6. Original face picture (A) and simulation of the symmetry of the left (B) and right side (C) of the face with the PicHacks–The Symmetrical Face Generator computer program.

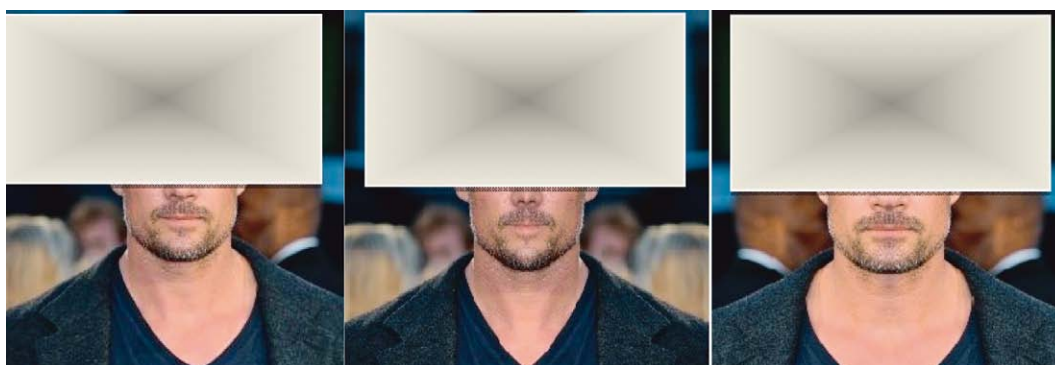


Fig. 7. Original face picture (A) and simulation of the symmetry of the left (B) and right side (C) of the face with the PicHacks–The Symmetrical Face Generator computer program.

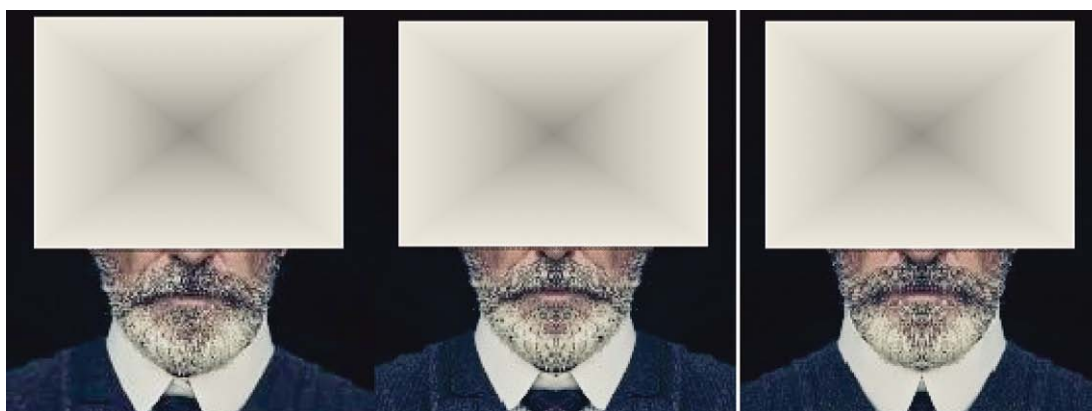


Fig. 8. Original face picture (A) and simulation of the symmetry of the left (B) and right side (C) of the face with the PicHacks–The Symmetrical Face Generator computer program.

Figures 3-13 indicate a symmetrical distribution pattern of graying hairs, as it can be observed when a mirror picture of the left (B) and the right part (C) of the face is composed with a computer program.

Discussion

The aging process is similar in all humans and other living organisms. If mutations in the nuclear and mitochondrial DNA, cellular proteins and lipids ac-



Fig. 9. Original face picture (A) and simulation of the symmetry of the left (B) and right side (C) of the face with the PicHacks-The Symmetrical Face Generator computer program.



Fig. 10. Original face picture (A) and simulation of the symmetry of the left (B) and right side (C) of the face with the PicHacks-The Symmetrical Face Generator computer program.

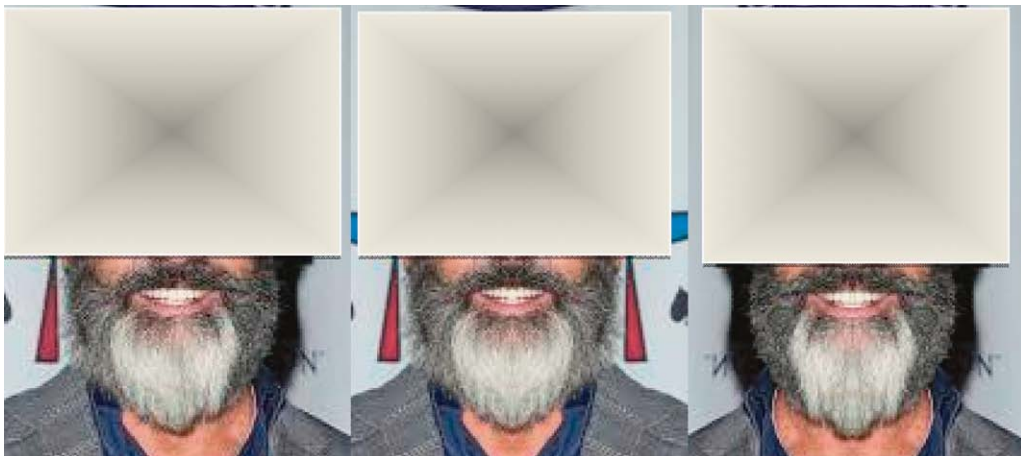


Fig. 11. Original face picture (A) and simulation of the symmetry of the left (B) and right side (C) of the face with the PicHacks-The Symmetrical Face Generator computer program.



Fig. 12. Original face picture (A) and simulation of the symmetry of the left (B) and right side (C) of the face with the PicHacks–The Symmetrical Face Generator computer program.

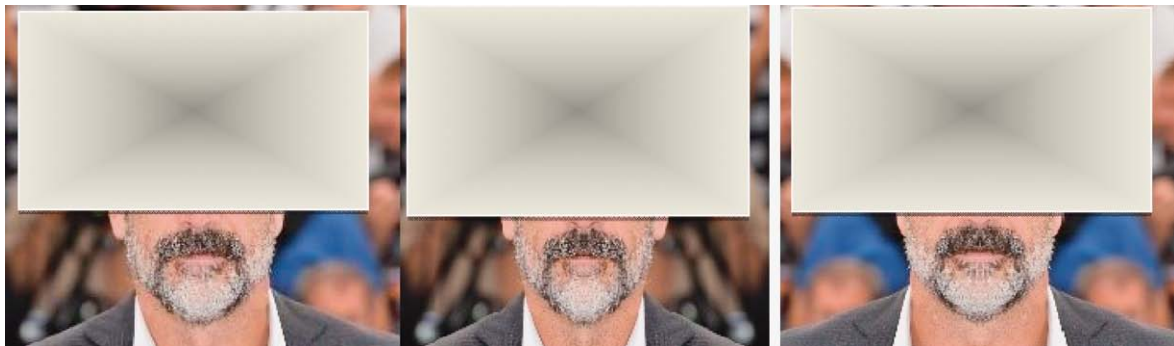


Fig. 13. Original face picture (A) and simulation of the symmetry of the left (B) and right side (C) of the face with the PicHacks–The Symmetrical Face Generator computer program.



Fig. 14. Identical twins becoming gray at approximately the same age, rate and pattern.

accumulate randomly as we age, we should then age in many different rates and ways as we do. Methylation, histone alterations, inflammation and other causes of DNA alteration would result in random modification of epigenome and in nonsymmetrical variation of the random graying patterns.

Additionally, there are syndromes which can accelerate aging. Early graying can be observed in prema-

ture aging syndromes, e.g., Hutchinson progeria and Werner syndrome, where aging process is intensified. Premature graying can also be experienced by people suffering from pernicious anemia, autoimmune thyroid disease or Down syndrome⁵⁰⁻⁵².

Conceding that the genes control exhaustion of the pigmentary potential of every hair follicle, this phenomenon will thus occur synchronously in individual

hair follicles and the pattern of graying hair should be symmetrical on both sides of the face. The results presented with aging of the hair follicles of the male beard indicate a symmetrical pattern of the graying parts on the left and right sides, as can be observed in Figures 2-13. These findings suggest that graying areas are not formed as random distribution.

Genetic factors seem to be decisive in hair greying, as identical twins apparently become grey at approximately the same age, rate and pattern (Fig. 14). The controlling program/clock/, however, has not yet been identified. Even though several aging genes have been discovered, the interferon regulatory factor (IRF4) and B-cell lymphoma 2 have been identified to have a significant impact on hair graying. It has recently been discovered that IRF4 gene may play a significant role in hair graying. The IRF4 gene, when expressed, is important in melanin production, which governs hair pigmentation^{53,54}. Wood *et al.*⁵⁵ have ascertained that hair follicles develop small quantities of hydrogen peroxide. This reactive species builds on the hair shafts, potentially leading to a progressive loss of hair color. Free radical theory of aging additionally supports the theory of programmed aging. Reactive oxygen species contribute to the accumulation of oxidative damage to the hair follicle stem cell niche, which leads to selective apoptosis and diminution of melanocyte stem cells, reducing repopulation of the newly formed anagen follicles^{56,57}.

By manipulation of a single gene or by affecting signaling pathways with a single molecule, longevity could be significantly extended. Different mutations in various organisms, from microorganisms to mice, can extend life expectancy. For example, a mutation in the age-1 gene of the nematode *Caenorhabditis elegans* significantly prolongs both the maximum and the average lifespan^{58,59}. Functioning of the SERPINE1 gene that encodes PAI-1 to be mutated and non-functional has also been recently reported in humans, i.e. in Berne Amish families with prolonged life span⁶⁰. In all species including mammals, mutations that deactivate specific signaling pathways (e.g., insulin/IGF-1, mTOR, AMPK signaling) impede the aging process and promote longevity⁶¹⁻⁶⁷. These mutations display evolutionarily preserved pathways for aging, some of which supposedly enhance longevity as a reaction to sensory cues, caloric restriction, or stress⁶⁸.

By comparison, the symptoms of human senescence are unvarying, and include skin wrinkles and male baldness, insulin-resistance and osteoporosis, high blood pressure and atherosclerosis, obesity and diabetes, cancer and Alzheimer's disease⁶⁸. What is more, in certain species (e.g., Pacific salmon), all members die at the same specific time and from the same cause, which indicates that many aspects of the aging process are programmed.

Limitations of the study

The main limitation of the present study was a small sample consisting of only 12 bearded persons. Another limitation was that only indirect correlation between graying of the beard parts and programmed aging was presented, which does not necessarily reflect the causal link between them. Further biochemical and genetic research is needed to confirm the causality.

Conclusions

Many of the presented aging theories correlate in a complex manner. In order to promote successful aging and to enhance the lifespan of the humankind, it is necessary to delve into and to test the recognized and emerging aging theories. It seems that aging is controlled also by our genes, as indicated in the references presented and, as in our case, by the graying patterns of the hairs. On the other hand, it should be emphasized that aging can be modulated to a certain degree by diet and healthy lifestyle.

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Sažetak

(A)SIMETRIJA MUŠKIH SIJEDIH BRADA KAO INDIKACIJA PROGRAMIRANOG PROCESA STARENJA

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Intervencije starenja bit će neučinkovite ako ne razumijemo osnovne principe starenja. Trenutno ne postoji konsenzus o tome je li starenje programirano ili ne. Hipoteza postavljena u ovom članku ukazuje na to da je starenje (barem posijeđivanje muških dlaka) programirano. Tu hipotezu potkrepljuje simetrija posijeđivanja dlaka muške brade. Stohastička teorija starenja tvrdi da je starenje pasivni neprogramirani proces u kojem bi se trebala dogoditi slučajna disperzija sijedih vlasi. Suprotno tome, programirane teorije starenja predviđaju da na lijevom i desnom dijelu lica treba postojati simetrija koja pokazuje jednak omjer, uzorak i vrijeme pojave sijedih dlačica.

Ključne riječi: *Sijeda dlaka na bradi; Sijede vlasi; Starenje; Programirana teorija starenja; Stohastička teorija starenja*