

Chapter 10
The Genetic Solution for Anti-Aging
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ABSTRACT

There are approximately 30,000 genes in the human body. A large number of genes are active at birth, but as we age numerous genes are silenced, resulting in typical signs of aging. It is proposed that a complex biochemical process defined by S.R. Burzynski as the “*Master Clock of Life*” controls the rate at which the genes are silenced in aging. If our genome were compared to a computer, the methylation of DNA would be “aging software.” Methylation is the reaction that adds inert chemical methyl groups to DNA. Once the promoter that controls activity of the gene is covered by this methyl “insulation,” the gene is switched off, and aging begins. Approximately 2% of genomic DNA contains genes and most of the remaining DNA is colloquially referred to as “junk” with unknown function. With every cell division, there is an addition of methyl groups to the promoters of the genes and removal of methyls from the “junk” section of DNA, comparable to the shift of grains of sand from upper to lower compartments of an hourglass. In aging cells with silent genes, the promoters are packed with methyls whereas the remaining DNA is depleted of methyl groups. The methylation clock can be adjusted to slow down aging by a new generation of nutritional and cosmetic agents that change the methylation pattern of DNA. It is proposed that these agents decrease the methyl shield around gene promoters and increase it in the “junk” portion of the DNA. Naturally-occurring and synthetically-produced peptides, amino acid derivatives, and phytochemicals were formulated into a supplement, brain supplement, cosmetic cream, and lotion. The users of the supplements reported increased energy, improved memory, decreased wrinkles, decreased blood cholesterol concentration, improved immunity and chronic joint inflammation, and improvement of prostate hypertrophy and benign breast nodules. The cosmetics provided significant reduction of wrinkles, confirmed by clinical trials.

Keywords: Anti-aging supplements, clinical trials, DNA-methylation, gene silencing, genetic aging, master clock

INTRODUCTION

There are approximately 30,000 genes in the human body. At birth, a large number of genes are active to promote growth and intellectual development. As we age, fewer and fewer of these genes are active, resulting in a slow-down in bodily functions, weakened immunity, reduced metabolism, loss of energy, baldness, and other typical signs of aging. A new generation of supplements and cosmetics is available that attempts to restore the activity of the genes to the level of young adult age.

GENE SILENCING – A NEW THEORY OF AGING

At a certain time during human life, shortly after conception, most of the genes are active^{1,2} (Fig. 1). Gradually, they are silenced during the development of embryo and fetus because their action is no longer needed. A substantial group of genes are silenced after the birth due to a transition from a different living condition in the uterus to the extra uterine environment after birth. At the age of 25, the body has the optimal combination of active genes, but soon thereafter various groups of genes are turned off as the result of aging.

Silencing of the genes is involved in hormonal changes during menopause, graying and loss of hair, reduced immunity, detoxification, and formation of cancer. Down regulation of tumor suppressor genes triggers increased activity of oncogenes, therefore increasing the risk of cancer. The continuous replacement of aging cells is becoming less efficient and the body is accumulating damage and malfunction of cells due to less effective programmed cell death.² The process of gene silencing involves chemical reaction known as methylation of the gene promoters.^{3,4} The end result is that “good” genes, which promote regeneration and general health, are “switched off” and “bad” genes that encourage deterioration and disease are “switched on”. My theory of gene silencing in aging was published over three years ago and confirmed by studies conducted by prominent groups of researchers in a number of different laboratories.^{5,6} These studies, which were performed in humans and in animals, confirmed that a substantial group of genes including tumor suppressors and genes for detoxification, cholesterol

metabolism, inhibitors of programmed cell death, and protein and RNA synthesis are silenced in aging.^{6,7} At the same time, a small group of genes including oncogenes, and those responsible for chronic inflammation and for silencing of the other genes become overactive, possibly, due to a disturbed balance between “good and bad genes”.

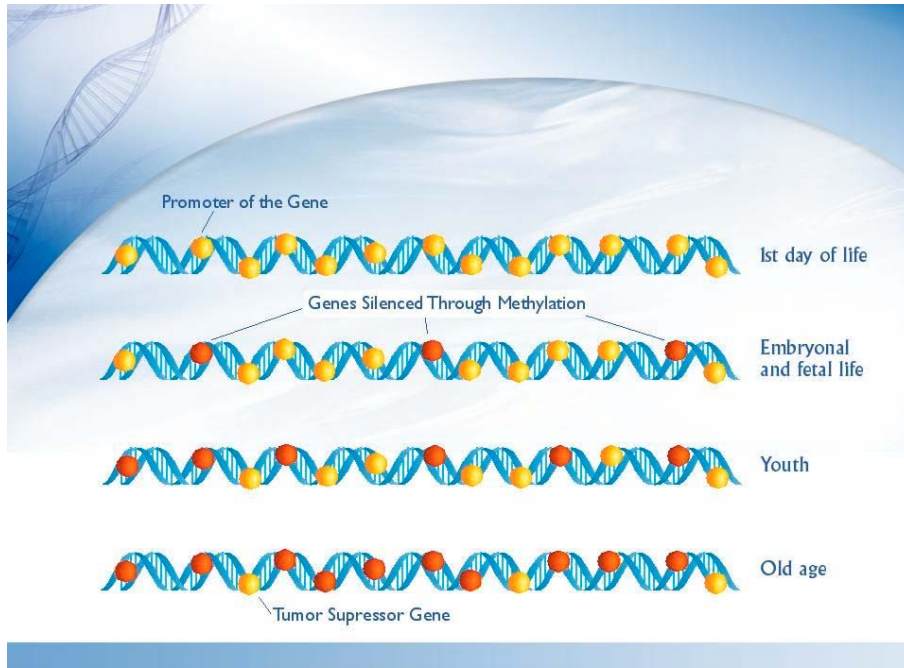


Figure 1. The genes are silenced during development and aging. Initially, most of the genes are demethylated and active, but during embryonal and fetal life they become silenced because their activity is no longer needed. After reaching the optimal combination of active genes at a young adult age, the genes are gradually silenced during the aging process.

MASTER CLOCK OF LIFE

It is proposed that a complex biochemical process defined by me as the Master Clock of Life and presented to the scientific community in 2005, controls the rate at which the genes are silenced in aging.⁸ The human body contains a myriad of different types of biological clocks which influence the master clock of life (Fig. 2). Among them we have daily clocks (circadian and division clocks), short time and long time clocks.⁸ As I mentioned before, the master clock of life controls how fast we age and the reversal of the clock may reverse the aging.⁹ A complete resetting of the master clock occurs after fertilization and formation of the new organism (Fig 3). Recent experiments by Harvard scientists indicate that the fusion of the embryonic stem cells with somatic cells reprograms the clock in adult aging cells.¹⁰

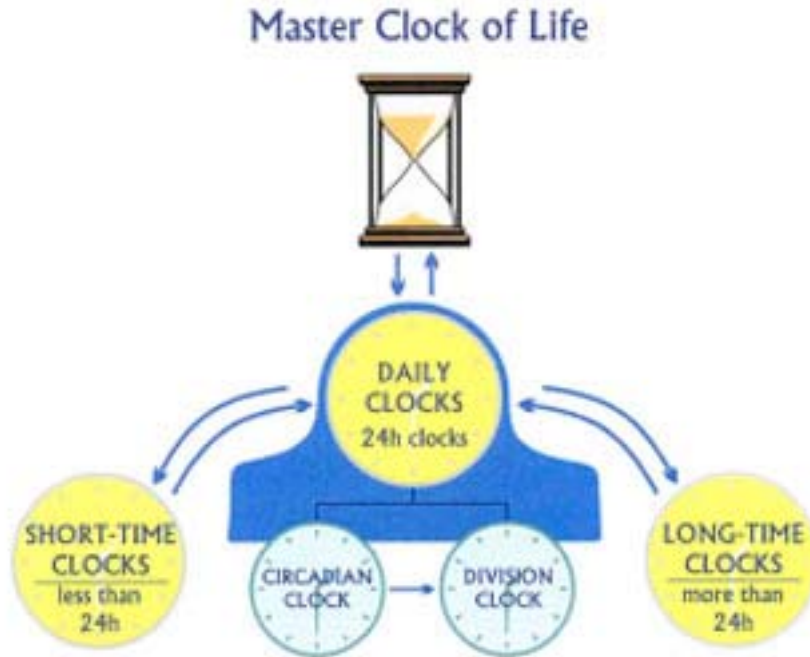


Figure 2. The human body contains numerous biological clocks including the Master Clock of Life, daily clocks (circadian and division clocks), short-time clocks, and long-time clocks. The clocks interact and organize the physiology based on cyclic environmental changes.



Figure 3. A complete resetting of the Master Clock occurs after fertilization and formation of new organism. This also is the result of fusion of the embryonic stem cells with aging somatic cells.

How to Turn Back the Master Clock of Life?

The master clock can be readjusted in a modest manner by a healthy lifestyle, exercise, proper diet, dietary restriction and a new generation of supplements and cosmetics (Fig. 4). Anti-aging interventions include lifestyle and environmental modification, therapeutic and nutritional replacement, and restoration of optimal gene expression. The age management therapy goal is to reverse age-related deterioration to the normal body function of young adults. On a molecular level, this translates to restoration of optimal gene expression, which involves the activation of silenced genes and the normalization of over-active genes.

Can the Master Clock of Life Be Turned Back?



Figure 4. The Master Clock can be readjusted in a modest manner by a healthy lifestyle, exercise, proper diet, and a new generation of supplements and cosmetics.

We isolated a number of small molecules that regulate gene expression existing in the blood, dairy products, and vegetables, and used them in cell cultures and animal and human clinical trials (Fig. 5). Among them are the naturally-occurring but produced synthetically amino acid derivatives:

- 3-phenylacetyl-amino-2,6-piperidinedione (A10)
- Phenylacetylglutamate sodium (PG)
- Phenylacetylisoglutamate sodium (isoPG)
- Phenylacetate sodium (PN)¹⁰

These compounds were formulated into a group of supplements and cosmetic products.

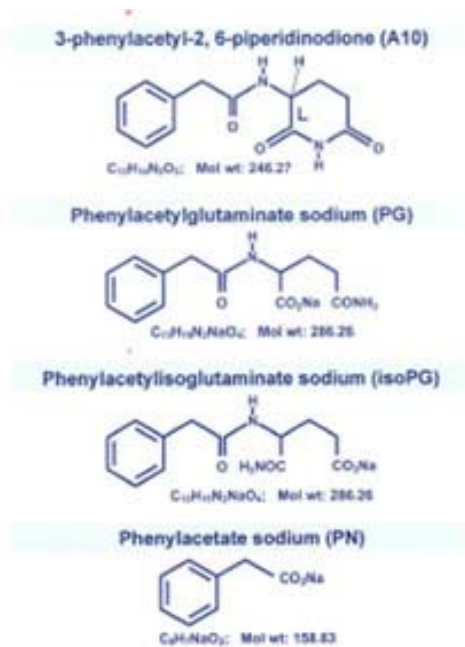


Figure 5. A group of small molecular compounds exist in the blood, dairy products, and vegetables, which may restore optimal gene expression.

Anti-Aging Effects of A New Generation of Cosmetics on the Skin

Facial cream containing 0.5% PG and 0.1% isoPG is a cosmetic formulation designed to help maintain healthier and younger looking skin, and reduce wrinkles. DNA microarray studies suggest that PG may restore a proper balance between the activities of two important genes involved in aging: oncogene *AKT2* and tumor suppressor gene *PTEN*¹¹ (Fig. 6).

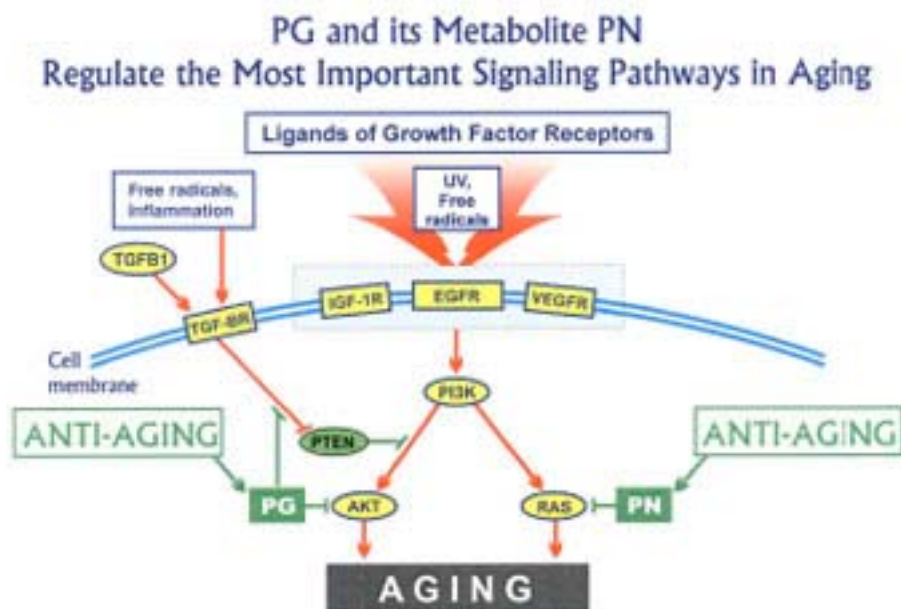


Figure 6. The most important signaling pathways in aging are regulated by PG and its metabolite PN. PG decreases the expression of oncogene AKT and it activates tumor suppressor genes PTEN and MAD, which play a crucial role in aging and cancer. PN interrupts signaling in RAS oncogene pathway.

A clinical study was designed to scientifically demonstrate the anti-wrinkle properties of the cream and to measure the level of acceptance and approval by new users. Twenty-two healthy volunteers were included in the study, which tested tolerance, anti-wrinkle efficacy, and acceptability of the cream. The study was performed at the Department of Pharmacology of the University Victor Segalen in Bordeaux, France and was supervised by the Ethics Committee of the university (but not monitored by the US FDA). No adverse reaction to the cream was detected. The tolerance of the facial cream was excellent.

To study anti-wrinkle efficacy, the cream was applied twice a day to the entire face for 4 weeks – except for one of the areas of “crow’s feet” wrinkles, which served as the “non-treated” area. Evaluation of efficacy was made through objective laser profilometry of silicone imprints at “crow’s feet” wrinkles from treated and untreated areas with data submitted for statistical analysis. The anti-wrinkle activity compared to the control was evaluated through measurements at the beginning and at the end of the trial of the following: volume of wrinkles, depth of wrinkles, and complexity of wrinkles. Statistical analysis of the data from the profilometric images showed that the treated and non-treated sites were comparable at the start of the study.

By the end of the studies all three variables, complexity, depth, and volume had each significantly decreased on the sites treated with the cream and there were either no change or continued expansion on the non-treated sites. Based on these results, anti-wrinkle efficacy was excellent. There were many favorable comments from the study volunteers about the cream. They appreciated the softness, suppleness, and additional skin comfort they noticed after the first cream application. All volunteers also liked the texture of the skin, ease of application, and penetration into the skin. Nineteen of the 21 volunteers in the study expressed a definite favorable desire to continue using the cream.

The study proves that it is possible to slow down the aging process through activation of silenced tumor suppressors and decrease of the activity of hyperactive oncogenes.

Anti-Aging Effects of New Generation of Supplements on the Entire Body

Cosmetic cream that contains PG and isoPG slows down the aging of the skin, however supplements with A10 and PG, administered orally, help the entire body. The following beneficial effects have been reported (note: these effects have not been verified by clinical studies nor confirmed by the US Food and Drug Administration):

- *General Effect on the Body:* Increased energy and decreased weakness and tiredness.
- *Skin:* Improved healing and reduction of wrinkles.
- *Cardiovascular:* Reduction of cholesterol and triglycerides concentration in the blood.
- *Hematological/Immunological:* Improvement of anemia, increased white blood cells, platelets, CD4+ counts, and decreased frequency of common viral infections.
- *Musculoskeletal:* Improvement in joint and muscle diseases, including rheumatoid arthritis.
- *Neurological:* Improvement of Parkinson’s disease and antidepressant effects.
- *Gastrointestinal:* Reduction of chronic diarrhea.
- *Genitourinary:* Improvement in symptoms of benign prostate hypertrophy. Decrease of benign breast nodules in women.
- *Prevention of Cancer:* Laboratory tests revealed that animals can be protected from development of breast, lung, and liver cancers, by adding small amounts of A10 to their food. This preventive effect against cancer was found in animals exposed to common carcinogens.

CONCLUDING REMARKS

Aging is associated with silencing of substantial number of genes through the reaction of methylation of gene promoters. A complex Master Clock of Life controls the rate at which genes are silenced. The clock can be turned back by the naturally-occurring molecules A10, PG and isoPG, which are ingredients of a new generation of supplements and cosmetics. Administration of these supplements and use of cosmetics, can produce a marked anti-aging effect.

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ABOUT THE AUTHOR

Stanislaw R. Burzynski was born in Lublin, Poland, January 23, 1943. He graduated with honors from the Medical Academy in Lublin, Poland and received his M.D. degree in 1967. Subsequently, in 1968 he earned his Ph.D. in biochemistry. He did his internship and residency from 1967 to 1970. From October 1970 to 1977 he was employed by Baylor College of Medicine in Houston, initially as a Research Associate and later as Assistant Professor. While at Baylor, Dr. Burzynski's research was sponsored and partially funded by the National Cancer Institute. Doctors associated with M.D. Anderson Cancer Research Center also cooperated in this research. On July 1, 1977, Dr. Burzynski resigned from Baylor College of Medicine and established Burzynski Research Laboratories. Over a number of years the company expanded to Burzynski Research Institute, Inc., Burzynski Clinic and Pharmaceutical Plant, Aminocare Products, LP, Ampolgen Pharmaceuticals, and Lubgen Pharma. Dr. Burzynski serves as the President, Chairman of the Board of the Institute and owner of the remaining companies. Dr. Burzynski is the discoverer of antineoplastons, which are components of biochemical defense against cancer. He is also the discoverer of new treatments for cancer, viral infections, including AIDS, autoimmune diseases, Parkinson's disease, neurofibromatosis, and restenosis, and is the author of a new theory of aging. Among his contributions are over 200 patents covering 42 countries and over 225 scientific publications. He is a member of numerous professional organizations, such as the American Association for Cancer Research, American Medical Association, The Royal Society of Medicine (UK), World Medical Association, Harris County Medical Society, New York Academy of Sciences, Society for Neuroscience, Texas Medical Association, The Society of Sigma Xi, and the Society for Neuro-Oncology. Dr. Burzynski is an internationally recognized physician and scientist who has pioneered the development and use of biologically active peptides in diagnosing, preventing, and treating cancer and other diseases since 1967.

