

The Genetic Solution for Anti-Aging Presentation

**The 1st Anti-Aging International Symposium,
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INTRODUCTION

Genomic DNA can be compared to a biochemical computer. This computer is the same for all cells of our body, but the software is different for various cell types and stages of development such as embryonic life, childhood, young adult period, and aging. Different types of cells in our body have also different "software" during the same developmental period. Methylation of DNA is the most important part of the "software" that silences and activates the genes. A complex master clock of life controls the rate at which genes are silenced (switched off) during the aging process. The clock can be reprogrammed through fundamental biological processes in the living cells. Limited turning back of the clock can be accomplished by a new generation of supplements and cosmetics, which are the subjects of this presentation.

GENE SILENCING IN AGING

Less than 2% of genomic DNA contains genes (**Fig. 1**). Most of the remaining 98% are referred colloquially as "junk" DNA, which consists mainly of retrotransposons and long terminal repeats. In the body of young, healthy individual, less than 1/10 of these 2% of DNA corresponding to genes is active. The remaining genes are silenced[1]. These genes played an important part earlier, during embryonal development and in the childhood[2]. They are silenced through methylation of promoters when their action is no longer needed (**Fig. 2**). The process of gene silencing continues after reaching the age of 25 years and results in graying and loss of hairs, reduced immunity, menopause, atherosclerosis, and cancer. It leads to reduced renewal of the body, aging and death. Silencing of some genes increases the activity of the opposing genes[1]. The studies on fibroblasts from young and old donors and patients suffering from premature aging in Werner syndrome confirmed altered activity of 6.3% of genes in normal and premature aging, and silencing of 70% of these genes (**Fig. 3,4**)[3]. A complex process regulates gene silencing and involves methylation of promoters regions, deacetylation of histones, chromatin remodeling and RNAi[4, 5]. DNA methylation seems to be the most important of these processes and consists of attachment of the methyl group to cytosine followed by guanosine. The methyl groups, which closely attach to the promoter region of the gene, form an inert insulation shield, which silences the gene[6].

MASTER CLOCK OF LIFE REGULATES SILENCING OF THE GENES

A complex biochemical process defined by me as master clock of life and presented to the scientific community last year controls the rate at which the genes are silenced in aging[7, 8]. In aging there is increased methylation of promoters regions of the DNA and decreased methylation of "junk" DNA. In cells with silenced genes, the promoters are packed with methyls, whereas, the remaining DNA is depleted of methyl groups (**Fig. 5**). 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 the lower compartment of

an hourglass (**Fig. 6**). The body is continuously renewing its organs through the activity of stem cells. After asymmetrical division, one stem cell differentiates into a specific lineage, and the other cell remains a stem cell (**Fig. 7**). These cells are able to live for the duration of human life due to the action of the enzyme telomerase. The gene of telomerase is also a subject to the mechanism of the master clock. At the beginning of life, the promoter region of this gene in stem cells is almost free of methyl groups, and the "junk" section is covered with methyls (**Fig. 8**). With each cell division, there is successive slight decrease of methylation of "junk" DNA and an increase of methylation of promoter of telomerase gene. Once the promoter is covered with methyls, the gene is silenced and the stem cell dies. The depletion of stem cells of the body leads to impaired renewal process and accelerated aging[7, 8].

NATURALLY OCCURRING MOLECULES TURN BACK THE MASTER CLOCK

A complete resetting of the master clock occurs after fertilization and formation of the new organism (**Fig. 9**). Recent experiments by Harvard scientists indicated that fusion of embryonic stem cells with somatic cells reprogram the clock in adult cells[9]. The master clock can be readjusted in a modest manner by healthy life style, exercise, proper diet, dietary restriction and a new generation of supplements and cosmetics (**Fig. 10**). Age management therapy attempts to restore the activity of the genes to the level at young adult age (**Fig. 11**). Small molecular peptides, amino acid derivatives and some organic acids can restore methylation of the DNA to the pattern typical for a young adult age, and reprogram the master clock of life (**Fig. 12, 13**). The following compounds which exist in human blood, dairy products and vegetables have been reproduced synthetically and are used as supplements: 3-phenylacetyl-amino-2,6-piperidinedione (A10), phenylacetylglutamine (PG), phenylacetylisoglutamine (isoPG) and phenylacetate sodium (PN) (**Fig. 14**). A10 is produced in the liver. PG, isoPG and PN are metabolites of A10 and exist in small concentration in blood, cow's milk, cheese, and numerous vegetables, including onion and red beets[10]. PG resets the master clock through restoration of methylation of "junk" DNA (**Fig. 15**). PN turns back the master clock by decreasing methylation of promoters regions. PG stabilizes the DNA and decreases the expression of oncogenes crucial in the aging process; such as *AKT* (**Fig. 16**). It also activates genes, which are silenced in aging, including tumor suppressors *PTEN* and *MAD*. PN works as a molecular switch, which interrupts signaling in *RAS* oncogene pathway and activates tumor suppressors, *p53* and *p21* through decreasing methylation of the promoters[11]. A10 and PG are ingredients of Supplement A and Supplement A Extra which are available in the U.S.A., European Union, and Korea. Administration of these two supplements resulted in increased energy, improvement of healing, decrease of wrinkles, decrease of cholesterol concentration in blood, improvement of cellular immunity and of chronic joint inflammation, decrease in frequency of viral infections, improvement of prostate hypertrophy, and decrease of benign breast nodules (**Fig. 17 – 19**). PG and isoPG are also used in cosmetic cream and lotion, which provided excellent reduction of wrinkles confirmed by clinical trials (**Fig. 20-21**)[1].

CONCLUSIONS

Aging is associated with silencing of a substantial number of genes through methylation of the DNA in promoters regions (**Fig. 22**). Hypermethylation of promoters is accompanied by decreased methylation of "junk" DNA. A complex master clock of life controls the rate at which genes are silenced. The clock can be turned back by naturally occurring molecules: A10 and PG, which are ingredients of supplements A and A Extra, and cosmetic cream and lotion. Administration of these supplements and use of cosmetics produces marked antiaging effects.

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