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# BOOK OF ABSTRACTS



Effective current approaches  
in anti-aging medicine  
and gerontology

## **AGEING PROCESS AND POSSIBILITIES FOR ITS INHIBITION THROUGH THE LENS OF THE GENERAL ADAPTATION SYNDROME THEORY BY H. SELYE**

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Hans Selye (1907–1982) described a general adaptation syndrome (GAS), which is characterized by the development of body reactions to various stressors (1936, 1950, 1956). GAS consists of several stages: alarm stage (24–48 hours), resistance stage (from 5 days or more) and the exhaustion stage, which occurs in case of insufficient body resistance. The alarm stage is characterized by the increased function of the adrenal cortex, increased cortisol level, involution of the thymic lymphatic system and the appearance of ulcers in the gastrointestinal tract. Depression of epiphysis function and, as a consequence, decreased level of melatonin is also noted. Approximately 48 hours later the stage of resistance begins, and all the above manifestations gradually disappear. This is due to the restoration of the immune system functions and its central organ - the thymus, as well as the epiphysis. However, in some cases the stage of resistance is delayed, and pathological process takes on a chronic form, which may lead to the exhaustion stage [7].

It was suggested that the delay in the development of the resistance stage is related to the insufficiency of the functions of the thymus and pineal gland at the genetic level [1, 2]. In accordance with this V. Morozov and V. Khavinson conducted studies on isolation of physiologically active substances from the thymus and epiphysis of calves, which can stimulate the restoration of these organs' functions [2, 6]. The isolated substances were of peptide nature and had a low molecular weight of up to 5000 Da. The introduction of these complex peptide preparations to animals in various experiments restored and boosted the stage of resistance. Then, the most biologically active peptides were isolated from the peptide extracts of the thymus and the pineal gland, their chemical structure was established, and the synthesis from amino acids was carried out. Glu-Trp dipeptide (Thymogen) was isolated and synthesized from peptide preparation of the thymus (Thymalin), and Ala-Glu-Asp-Gly tetrapeptide (Epitalon) was isolated and synthesized from peptide preparation of the epiphysis (Epithalamin) [3, 6]. The 30-years study of the original peptide preparations and their synthetic analogues showed their ability to increase the average life expectancy of various animal species, reduce the incidence of tumor development, enhance the function of the immune and antioxidant systems, increase melatonin concentration, increase the telomere length and the number of cell divisions, regulate gene expression and protein synthesis, as well as normalize many other vital body functions [2, 4]. In studying the mechanism of action of peptides, the possibility of molecular interaction

between peptides and DNA, which is based on their complementary correspondence, has been established. Each peptide is capable of binding to a specific chemical structure of a specific gene [4, 8]. These results were obtained *in vitro*, *in vivo*, as well as in human studies [2, 4].

Due to the fact that the stages of the general adaptation syndrome are accompanied by a decrease in the functional activity of various organs, a large-scale study was conducted to isolate biologically active peptides from the main tissues of the body (brain, blood vessels, heart, liver, bronchi, kidneys, pancreas and prostate, testes and others). Restoration of the functional state of various cell populations is extremely important in the long-term course of the resistance stage due to the insufficient functionality of the organs. Application of peptides isolated from various organs - both individually and in various combinations – boosted organism resistance and contributed to vanishing of pathological processes [2].

It should be noted that the ageing process is characterized by a decrease in gene expression and corresponding proteins synthesis, and it can be considered as a prolonged stage of resistance. Ageing is characterized by a decrease in the function of the immune system, pineal gland (a decrease in the concentration of melatonin in the blood), brain, endocrine and antioxidant systems, reproductive function, etc. Administration of peptides, in the second half of life, as a rule, has led to significant increase in life expectancy [2, 5].

The use of thymus (Thymalin) and pineal gland (Epithalamin) preparations in the elderly and senile patients allowed to partially restore the functions of the immune and endocrine systems, epiphysis (increase melatonin concentration), brain and reproductive system, which led to a significant reduction in mortality rates compared to patients in the control groups during the period of 6-15 years. Complete absence of allergic and other side effects should be noted, both during the administration period and in the long term. This human subject research has been performed for the first time which makes it unique [2].

Thus, this long-term (1973-2018) study showed that biologically active substances of peptide nature are able to restore and maintain the functions of the main organs and body systems, both during the resistance stage of the general adaptation syndrome and the aging process. Evaluation of the results of the peptides application in 17 species of living organisms allowed us to identify a single mechanism for regulation of gene expression and protein synthesis in living nature [5, 8]. This indicates the universal process of the emergence and maintenance of life in the course of evolution.

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## **UNIVERSAL MECHANISM OF PEPTIDE REGULATION OF GENE EXPRESSION, PROTEIN SYNTHESIS AND LIFE EXTENSION IN NATURE**

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Alteration in gene expression results in various pathologies and ageing. All functions of cells, organs and organisms are determined by gene expression and protein synthesis. Searching methods and means for regulation of gene expression is a key trend in basic science. The body itself contains principal regulatory substances high activity of which can contribute to the achievement of the upper species limit. A special place belongs to a group of peptides developed and studied by V. Khavinson and colleagues. The research was carried out on various species (plants, bacteria, insects, amphibians, birds, rodents, monkeys and humans). It demonstrated a significant increase in animals' average life expectancy as compared to control due to peptides' anti-carcinogenic activity, evidenced by a decreased incidence of malignant tumors. Application of pineal peptide promoted