PEPTIDES AFFECT STEM CELL AGING

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Aging is considered to be a multifactorial mechanism, which is accompanied by a progressive decrease in the pool of endogenous (internal) stem cells, as well as damage to their structure and functions with age increasing. Decreased stem cell regeneration contributes to the development of age-related diseases. Decreased regenerative capacity of endogenous stem cells is regulated due to reduced energy metabolism, disruption of DNA repair, slowing down of RNA and protein synthesis, and accumulation of cellular damage.

All cells in the body are formed from stem cells. That`s why stem cell dysfunction is important for understanding the aging process at the tissue and body levels. Senescent cells affect neighboring cells by releasing certain signaling molecules, which triggers a cascade of intracellular signaling events. It is believed that cellular aging is one of the mechanisms of the whole organism aging. It is important to note that the loss of proliferative activity due to stem cells aging is equivalent to the loss of their ability to regenerate damaged tissues. This highlights the need to study the mechanisms of stem cell aging.

Short peptides have been shown to regulate functional activity, proliferation, apoptosis, and stem cell differentiation. Based on the amino acid composition analysis of the Endoluten® polypeptide complex isolated from the pineal gland of young animals, the tetrapeptide Epitalon® (AEDG, Ala-Glu-Asp-Gly) was synthesized.

In turn, from the Ventfort® polypeptide complex, which was isolated from the vessels of young animals, the tripeptide Vesugen® (KED, Lys-Glu-Asp) was synthesized. Epitalon® and Vesugen® protected stem cells from replicative senescence by reducing gene expression and p16, p21 proteins synthesis, which responsible for the cell cycle [Sinjari B. et al., 2020]. Replicative senescence is the process of cell aging with an increase of cell culture passages number. Passage is the transfer of cells from one culture vessel to another for reproduction and accumulation of the cell mass required amount.

Based on the amino acid composition analysis of the Sigumir® polypeptide complex isolated from the cartilage and bone tissues of young animals, the tripeptide Cartalax® (AED, Ala-Glu-Asp) was synthesized. It was found that Cartalax® increased the functional activity of skin fibroblast stem cells during aging by increasing gene expression and dermal fibroblast differentiation proteins Engrailed 1, PDGFRα, Spry4, Twist2 synthesis [Гутоп Е.О. и др., 2022].

Two models of stem cell aging were studied: replicative aging (aging of cells by passages) and stationary aging caused by contact inhibition of cells within one passage. It was found that Vesugen® contributed to changes in the expression of IGF1, FOXO1, TERT, TNKS2 and NFκB

genes (responsible for increasing cell lifespan) in 2 models of cellular aging. Cartalax® contributed to the change in the expression of the IGF1 and NFκB genes in 2 models of cellular aging, as well as the TERT and TNKS2 genes during stationary aging. The KE dipeptide contributed to changes in the expression of the IGF1 and NFκB genes in two aging models, as well as the TERT and FOXO1 genes during stationary aging [Ashapkin V. et al., 2020].

Long-term cultivation of stem cells is necessary for clinical use in order to regenerate tissues and organs in cell replacement therapy. Thus, short peptides are potential substances that can be used as additional agents for maintaining the stem cells morphology and functions, as well as reducing the aging and apoptosis markers expression.

References

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