Conference

The syntetic eptapeptide Semax, a fragment of the ACTH hormone, sustains differentiated neuroblastoma, by improving the cellular bioenergetic: investigations toward New Therapeutic Solutions.

Maria Carmela Di Rosa,[a,c] Marianna Flora Tomasello,[a,*] Mariangela Amorini,[b] Miriam Saab,[b], Giuseppe Lazzarino,[b] Irina Naletova,[a] Francesco Attanasio.[a]

Semax is the active component of a drugs developed in Russia in the1982 and originally used as a treatment for brain hypoxia and ischemia, brain traumas, and to facilitate adaptive processes to extreme situations. Semax is now used as a nootropic for mental enhancement in healthy people and for treating many cognitive disorders. Semax is a syntetic eptapeptide consisting of the Met-Glu-His-Phe fragment of ACTH and the C-terminal tripeptide Pro-GlyPro. N-terminal fragments of the adrenocorticotropic hormone (ACTH) are well known for their potent neuro-regenerative and cognitive activities.[1] The C-terminal PGP fragment provide resistance to enzymatic cleavage. Semax is devoid of hormonal activity but is still able to stimulate learning and memory formation in rodents and humans.[2] However, the molecular mechanisms underlying the action of Semax, are still unknown. At the cellular level, Semax was shown to prevent the death of cultured neurons, and to increase the expression of neurotrophine and their receptors,[3] thus implying that Semax might modulate brain functions by influencing neurotrophins functions. Here we investigated the mechanism by which Semax acts and describe the effects at the cellular level on RA-differentiated SHSY5SY cells. Interestingly, when differentiated in the presence of Semax, cells present improved mitochondrial functions and mass, increased ATP levels and improved resistance to stressors. Furthermore, we found that Semax increase the BDNF expression and release, trough the activation of the p-CREB signalling pathway. We suggest that Semax promotes cognitive brain functions by modulating the expression of the BDNF/trkB system which in turn stimulate the mitochondrial function. Thus, Semax provide neurons with the ability to better exploit feuls, either under basal or stressful conditions, which results in the improvement of neurons viability as demonstrated by the means of several experimental approaches. The finding that Semax, by modulating neurotrophins levels, improve the mitochondrial functions, has important implications for neurodegenerative and psychiatric diseases. Therefore, the therapeutic potential of Semax is far from being exhausted and new indications for its application could be discovered by an in-depth study of its mechanism of action.

References

1 D. de Wied, Behavioral pharmacology of neuropeptides related to melanocortins and the neurohypophyseal hormones, European Journal of Pharmacology 375 (1) (1999) 1 – 11. doi:10.1016/S0014-2999(99)00339-8.

2 I. Ashmarin, V. Nezavibat'ko, N. Myasoedov, A. Kamenskii, I. Grivennikov, M. Ponomareva-Stepnaya, L. Andreeva, A. Y. Kaplan, V. Koshelev, A nootropic analog of adrenocorticotrophic hormone 4-10–semax (experience of 15 years of development and investigation), Zh. Vyssh. Nerv. Deyat 47 (1997) 420–430.

3 T. Kolomin, M. Shadrina, P. Slominsky, S. Limborska, N. Myasoedov, et al., A new generation of drugs: synthetic peptides based on natural regulatory peptides, Neuroscience & Medicine 4 (04) (2013) 223.

[a] *CNR - Istituto di Cristallografia, Catania, Italy.*

[b] Department of Biomedical and Biotechnological Sciences, School of Medicine, Section of Medical Biochemistry, University of Catania, Catania, Italy

[c] *Department of Biomedical and Biotechnological Sciences, University of Catania, Catania, Italy*

Creative Commons Attribuzione - Non commerciale - Condividi allo stesso modo 4.0 Internazionale

† oral communication at 1 st Conference on Crystallography, Structural Chemistry and Biosystems, (Catania) 04-06/10/2021