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Editorial

Editorial of Special Issue "Advances in Neuropeptide Biology"

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This editorial aims to summarize the contents of the six scientific papers included in the Special Issue "Advances in Neuropeptide Biology".

Neuropeptides are small chains of amino acids that work as chemical messengers. They are mainly released by neurons in the central and peripheral nervous system, acting as neurotransmitters and neurohormones. To date, more than 100 different neuropeptides have been identified. The neuropeptides exert their effects at a cellular level by binding to specific G-protein coupled receptors (GPCRs). Changes in their expression in the brain and in peripheral organs can contribute to the onset of several diseases, including cancer.

It is well known that various neuropeptides are implied in the regulation of gastrointestinal functions; however, they can also act as promoting factors in cancer development and progression. In this Special Issue, the review of Srivastava et al. focused on their potential utility as drug targets from different inhibitor molecules to prevent cancer [1].

Among the wide variety of effects exerted by neuropeptides, Marcos and Coveñas [2] focused their attention on the role of orexins on feeding behavior. Orexin-A and orexin-B exert their effects by interacting with their respective receptors, OX1R and OX2R. These neuropeptides are involved in the control of food intake and associated behaviors, and their levels are elevated during food deprivation. Moreover, metabolic status regulates the action of orexins on the intake of food, and the expression of orexin varies during the development of obesity. This information suggests that an innovative pharmacological approach to counteract obesity could be based on the development of new and more specific orexin receptor antagonists.

Pituitary adenylate cyclase-activating polypeptide (PACAP) is a neuropeptide whose effects have been largely investigated. It acts by binding to a specific PAC1 receptor, in addition to two other receptors (VPAC1R and VPAC2R), which have a similar binding affinity to the vasoactive intestinal peptide (VIP). PACAP is largely expressed in the nervous system and is also implicated in various neurodegenerative diseases. In fact, downregulation of PACAP was observed in patients with post-traumatic stress disorder, multiple sclerosis and Alzheimer's disease. PACAP is also involved in brain aging. In addition, accelerated systemic senile amyloidosis was observed in heterozygous PACAP-deficient mice [3]. In particular, histopathological analysis showed amyloid deposits in various organs, particularly in the kidney, spleen, skin and intestines. Moreover, heterozygous PACAP gene-deficient mice showed high levels of cholesterol and lipoprotein in plasma, as well as differences in several blood parameters.

Moreover, PACAP has been shown to be involved in the regeneration of peripheral nerves. In fact, it has been demonstrated that Schwann cells respond to exogenous stimulation with the peptide by inducing the expression of tissue plasminogen activator (tPA) and urokinase plasminogen activator (uPA) via PAC1 receptor activation. tPA and uPa represent two important plasminogen activators, whose proteolytic activities is essential during nerve regeneration. The paper of Broome et al. [4] showed that doxycycline and minocycline promote Schwann cell activities associated with improved axonal regeneration through the induction of PAC1-mediated proteolytic activity of tPA and uPA.

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PACAP exerts a protective role not only in the nervous system, but also in many other peripheral organs, including the eye, where it has also been shown to exert positive effects in the cornea [5]. Here, the peptide demonstrated its ability protect the corneal epithelium against UV-B radiation, by affecting ROS generation and JNK pathway activation induced by UV-B rays. These PACAP-mediated mechanisms led to the reduction in apoptotic cell death induced by UV-B irradiation [6].

Overall, these six contributions published in this Special Issue further confirm and strengthen the essential role of neuropeptides either in physiological or pathological conditions.

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