PE-22-28 Peptide: Depression and Neurogenesis Research

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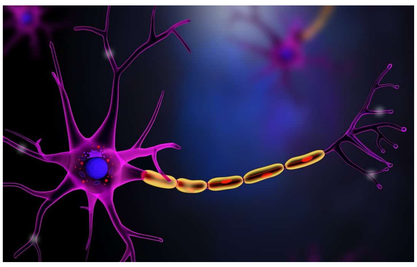

PE-22-28, a synthetic derivative of the naturally occurring peptide spadin, is garnering significant attention in research studies.

Spadin, derived from sortilin, appears to act as an antagonist to the TREK-1 (TWIK-related-potassium channel) receptor, making it a crucial player in the quest to understand the origins of depressive behavior, and as a potential regulator of neurogenesis.[1]

Studies in mice have illuminated the possible connection between TREK-1 and depression, with the deletion of this receptor rendering mice resistant to depressive states. Conversely, exposure to sortilin is speculated to promote resistance to depression while possibly fostering the growth of neurons and synaptic connections. Remarkably, shortened analogs of spadin, particularly exemplified by PE-22-28, appears to exhibit superior TREK-1 inhibition compared to the original spadin.[2] PE-22-28 has exhibited reported enhanced stability and is speculated to induce more neurogenic stability, positioning it as a promising candidate in neurological research.

Of paramount importance is the link between antidepressant substances and neurogenesis, where the growth of new neurons appears to signify a successful mitigation of depressive symptoms. PE-22-28 shines in this aspect, as it appears to induce neurogenesis within just few days.

Mechanism of Action

The mechanism of action of PE-22-28 peptide primarily revolves around its suggested role as an antagonist to the TREK-1 (TWIK-related-potassium channel) receptor.

By binding to and inhibiting TREK-1, PE-22-28 is speculated to modulate the potassium ion flow in neural cells, influencing neuronal excitability and neurotransmitter release. This inhibition is considered to ultimately lead to an enhanced neurogenic response, possibly promoting the growth of new neurons.[2]

PE-22-28's speculated potential to expedite neurogenesis sets it apart as a potential breakthrough in neurological disorder research. This is why scientists continue to undertake an extensive research to enhance the bioavailability and stability of spadin derivatives and analogs.

Among these investigations, one study[2] focused on PE-22-28, the seven-amino-acid derivative of spadin. Similar to its natural counterpart, researchers hypothesized that PE-22-28 might engage with the TREK-1 channel, obstructing its activity and potentially yielding further benefits such as emotional stability and mood enhancement.

Based on research, this peptide appears to exhibit promise in terms of potential enhanced stability compared to spadin, possibly faster onset of action in comparison to other putative trek-1 inhibitors, and potential for a longer half-life relative to naturally occurring spadin.

These multifaceted investigations hold the prospect of unraveling the full spectrum of PE-22-28's effects and potential neurological impact.

Research and Scientific Studies

PE-22-28 Peptide and Depression

Studies conducted in mouse models of depression have highlighted the remarkable efficacy of PE-22-28 in alleviating depressive symptoms. Impressively, PE-22-28 appears to possess potential to mitigate depression within a mere few days without adversely impacting other functions governed by the TREK-1 channel.

Notably, studies indicate that research models of depression demonstrate a reduced volume of the hippocampus, and conventional antidepressants are considered to enhance neurogenesis and possibly increase hippocampal volume, thereby combating the depressive episodes.[3] [4] PE-22-28's potential to counteract this volume loss through neurogenesis suggests that it may address the root cause of depression and may unveil underlying physiological pathways implicated in the disorder.

PE-22-28 Peptide and Neurogenesis

Traditional research in antidepressants to promote neurogenesis in the hippocampus appears to have found an intriguing parallel in the actions of PE-22-28, but with a remarkable acceleration.

In mice studies,[5] reports suggest that PE-22-28 may elicit heightened neurogenesis and synaptogenesis within few days, approximately doubling the population of BrdU-positive cells (utilized as a marker for DNA replication) and potentially boosting the rate of synapse formation. Reports state that during in vitro studies the peptide *"enhanced both mRNA expression and protein of two markers of synaptogenesis, the post-synaptic density protein of 95kDalton (PSD-95) and synapsin,"* and upon introduction, the peptide *"led to a rapid increase in both mRNA expression and protein level of brain-derived neurotrophic factor (BDNF) in the hippocampus, confirming the antidepressant action of the peptide."*

PE-22-28 is speculated to influence the brain cell division, and this speculation is supported by research studies outlining perceived impact on cAMP response element-binding protein (CREB), a transcription factor crucial for neuronal plasticity, memory formation, and spatial memory development. Notably, CREB not only underpins neuron growth but also appears to contribute to their protection.

PE-22-28 Peptide and Nootropic properties

The hippocampus, an area of the brain regularly considered in studies on depressive behavior, also is considered to hold a crucial role in learning and memory processes. Its remarkable plasticity renders it susceptible to various insults implicated in disorders from depression and anxiety to Alzheimer's disease. By potentially enhancing the regenerative capacity of the hippocampus, PE-22-28 may hold potential in this area of ailment research as well. Notably, considering the hippocampus's involvement in learning, memory, and spatial navigation, PE-22-28, or similar TREK-1 antagonists, may exhibit promising nootropic properties.

Interestingly, prior animal models suggested that the removal of the TREK-1 channel might lead to adverse consequences, including possible increased seizure susceptibility and possible diminished neuroprotective effects against excitotoxicity. It is striking, then, that neither spadin nor PE-22-28 appears to exacerbate seizure activity. In fact, spadin-treated mice exhibit heightened resistance to generalized seizures, with PE-22-28 appearing to exhibit even more profound protective effects.[3] These findings continue to challenge conventional notions and open new avenues for exploration in the field of TREK-1 modulation.

PE-22-28 Peptide and Post Stroke Depression

Post-stroke depression (PSD) is a prevalent complication that often proves resistant to conventional therapies following cerebral ischemia.

Emerging studies have shed light on the likely involvement of TREK-1 over-expression in the development of PSD. Experimental mouse models have indicated the potential to mitigate or reverse this upregulation using both SSRIs (selective serotonin reuptake inhibitors) and TREK-1 inhibitors, such as PE-22-28.[5] While both compounds appeared to induce beneficial reactions in mice, SSRIs were associated with a myriad of unintended side effects, unlike PE-22-28 peptide, which appeared to be devoid of such issues. Notably, the onset of action for the SSRI compound was notably protracted compared to the peptide, which exhibited apparently rapid effects.

PE-22-28 Peptide and Muscle Function

Emerging research hints at TREK-1's pivotal involvement in facilitating muscle responses to mechanical stimulation. Notably, inhibiting TREK-1 seems to enhance muscle contractility, while channel activation is considered to promote muscle relaxation.

Although this facet of the TREK-1 channel is in its early exploratory phase, it is steadily gaining significance. Exploring the contributions of molecules like PE-22-28 to muscle contraction and relaxation holds the promise of unraveling fresh avenues to comprehend the intricacies of muscle physiology.[6]

In Summary

The PE-22-28 peptide represents a significant advancement in the realm of spadin analogs with promising implications for research use. It appears to demonstrate remarkable efficacy in robustly stimulating neurogenesis and synaptogenesis within the hippocampus. Even after modifications aimed at enhancing half-life or altering routes of introduction, PE-22-28 is speculated to retain its ability to antagonize TREK-1. This multifaceted peptide not only appears to pioneer a new generation of depression research but also sheds light on the evolving field of nootropics.

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Dr. Marinov

Dr. Marinov (MD, Ph.D.) is a researcher and chief assistant professor in Preventative Medicine & Public Health. Prior to his professorship, Dr. Marinov practiced preventative, evidence-based medicine with an emphasis on Nutrition and Dietetics. He is widely published in international peer-reviewed scientific journals and specializes in peptide therapy research.

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