REGULATION OF AMYLOID BETA MOLECULAR COMPOSITION FOR THE TREATMENT OF ALZHEIMER'S DISEASE (Ramot)

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THE NEED

Currently available treatment options for AD are symptomatic and do not modify the progression of the disease. This disease-modifying technology achieves previously unattainable blockage of cognitive deterioration in AD. The technology reverses the Aβ40/42 decline leading to Aβ aggregation, synaptic and cognitive deficits by a combined treatment of electrical stimulation of the perforant pathway and a pharmacological therapy selectively inhibiting neurotransmitter release. Many of the products in development for AD aim to reduce the aggregation of Aβ and promote its clearance using pharmacotherapy. Most of these products show no clinical significance in phase 3 trials, as AD patients are often resistant to pharmacotherapy. The combination of pharmacotherapy with brain stimulation represents a promising alternative to overcome resistance to treatment. Compared to other products in development, the technology aims to enhance the Aβ40/42 ratio and not to block Aβ formation, as optimal level of Aβ is essential for proper information transfer. Compared to other brain stimulatory techniques, this technology enables the determination of the most effective stimulation per patient according to the post- stimulation change in Aβ40 and EEG. As such, the technology presents a personalized previously unattainable disease-modifying treatment to block and reverse the cognitive deterioration in AD.

Electrical stimulation of the perforant pathway of the brain combined with reduction in basal neurotransmitter release was proven to enhance the Aβ40/42 ratio in rats. Thus, the present technology may significantly alter the otherwise inexorable deterioration in sporadic AD.

TECHNOLOGY

A combination of pharmacological therapy with electrical stimulation has been developed to reduce cognitive decline in Alzheimer's disease (AD). This technology is potentially disease-modifying since it could block and even reverse cognitive deterioration in AD patients by reducing Aβ aggregation correlated with cognitive decline. The technology offers personalized therapy, as the effective electrical stimulation and pharmacological treatment can be determined per patient. As such, the technology provides a personalized treatment for effectively blocking and reversing cognitive decline in AD.

ADVANTAGES

• Overcomes pharmacotherapy resistance of AD patients since it combines electrical stimulation
• Has an output indicating the effectiveness of the treatment – the Aβ40/42 ratio
• Offers personalization as the effective stimulator can be determined according to the Aβ40/42 ratio
• Aims to enhance the Aβ40/42 ratio and not to block Aβ formation, as optimal level of Aβ is essential for proper information transfer
• Can utilize non-invasive electrical stimulation techniques (tDCS, rtACS, rTMS)

APPLICATIONS

• A therapeutic tool to enhance the Aβ40/42 ratio and reduce the subsequent Aβ aggregation in AD
• A therapeutic tool to reverse Aβ aggregation caused by a decline in the Aβ40/42 ratio in AD
• A research tool to examine the role of Aβ40/42 ratio in the pathogenesis of AD
• A research tool to examine the role of Aβ40/42 ratio in brain plasticity and learning
• A screening tool for anti-AD drugs based on electrical stimulation combined with treatment of the proposed drug by examining the Aβ40/42 ratio
• A possible tool for enhancing synaptic plasticity

REFERENCE

Dolev, Iftach, et al. "Spike bursts increase amyloid-[beta] 40/42 ratio by inducing a presenilin-1 conformational change." Nature neuroscience 16.5 (2013): 587-595.

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