A Novel Therapy for Epilepsy-Rebuilding Inhibition in the Epileptic Brain

Published date: Oct. 17, 2019

Technology description

Currently, millions of Americans suffer from epilepsy and fully 1/3 of these patients do not respond to available treatments. Researchers at Brandeis University have discovered that the Sema4D-PlexinB1 interaction may be harnessed as a novel strategy for the treatment of seizure disorders.
A key aspect of neuronal circuit formation is achieving the proper balance of excitation and inhibition (E/I) within the circuit. A given neuron, through its synaptic connections, either excites or inhibits other neurons in the circuit, thus establishing this balance. Disruptions to the E/I balance can have pathological consequences for circuit function as demonstrated by the manifestation of devastating neurological disorders, including epilepsy and Autism Spectrum Disorders (ASD).
The current invention is a novel approach to treating disorders such as epilepsy that would restore the normal E/I balance in network activity bypermanently increasing the number of inhibitory synapses. Treatment of hippocampal cultured neurons with the protein Sema4D, acting through its receptor PlexinB1, causes a rapid increase (i.e. within 30 minutes) in the density of functional GABAergic synapses. It was also discovered that Sema4D could rapidly drive inhibition in the context of aberrant neuronal hyperexcitability induced in an organotypic hippocampal slice culture model of epilepsy. Researchers demonstrated that acute Sema4D treatment rapidly (within 2 hours) abates the hyperexcitability found in these slices.
Sema4D suppresses neuronal hyperexcitability. Modulating GABAergic synapses via the Sema4D-PlexinB1 interaction to restore the balance of excitation and inhibition in brain.The researchers are interested in finding industry partners to pursue issues around drug production and delivery. For example, Sema4D is a large polypeptide that is unlikely to cross the blood brain barrier, thus making it a poor drug candidate.Nonetheless, these experiments are important proof of principle examining the in vivo effects and anti-seizure potential of driving inhibitory synapse formation in rodent models, using Sema4D administration as a tool.
R&D Required:
The researchers are interested in finding industry partners to pursue issues around drug production and delivery. For example, Sema4D is a large polypeptide that is unlikely to cross the blood brain barrier, thus making it a poor drug candidate. Nonetheless, these experiments are important proof of principle examining thein vivoeffects and anti-seizure potential of driving inhibitory synapse formation in rodent models, using Sema4D administration as a tool.

Application area

This research also has therapeutic implications for other neurological disorders, such as ASD, where a shift in E/I balance is thought to represent the underlying pathology

Advantages

This approach could be beneficial to preventing the establishment of epilepsy, halting its progression, or suppressing hyperexcitability during a seizure event and is conceptually different from current anti-epileptic drugs most of which seek to ameliorate seizures by temporarily increasing the function of existing inhibitory synapses.Our idea is simple and has high impact potential: on command, we instruct neurons to assemble more inhibitory synapses in the brain, thus suppressing seizures and/or preventing epileptogenesis.

Institution

Brandeis University

联系我们

叶先生

电 话：021-65679356

手 机：13414935137

邮 箱：yeyingsheng@zf-ym.com