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LGI1 gene therapy for epilepsy

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Summary

Gene therapy presents a promising alternative for treating drug-resistant focal epilepsy. LGI1, an extracellular protein is often downregulated in focal epilepsy. Over expression of LGI1 using an AAV vector can reduce neuronal and network excitability seen in epilepsy.

Background

Epilepsy is a widespread serious neurological disorder that impacts 1% of the global population. It is estimated that 30% of these individuals are refractory to pharmacological treatment, and surgical removal of the focal brain area remains the primary option for achieving seizure control, albeit feasible for only 5-10% of patients.

Gene therapy, therefore, presents a promising alternative of pharmaco-resistant focal epilepsy, and researchers have demonstrated the effectiveness of viral overexpression of the potassium channel Kv1.1 to reduce neuronal excitability. This approach offers a potential solution that could avoid the adverse consequences associated with surgical resection.

Technology

Leucine-rich glioma-inactivated 1 (LGI1) is an extracellular secreted protein that acts in the extracellular space to modify the excitability of neurons and has been shown to be involved in the trafficking and function of Kv1.1, enhancing the activity of the channel.

It has been observed that LGI1 is reduced in patients with temporal lobe epilepsy, leading to heightened neuronal and network excitability. This suggests that overexpressing LGI1 could address a key pathological feature of certain forms of epilepsy.

The academic team has developed a gene therapy construct that increases the expression of the LGI1 gene to treat epilepsy. They have created an AAV vector (AAV2/9) that delivers the LGI1 gene under the control of a CAG promoter. In a rat model of mesial temporal lobe epilepsy, this construct increased LGI1 levels and significantly reduced seizure frequency.

Overexpressing LGI1 may have a broader effect on surrounding excitatory neurons, potentially addressing some limitations associated with Kv1.1 overexpression. This approach could potentially target a larger area and affect neurons more uniformly.

Market

In the first instance, the target market would be refractory epilepsy. Epilepsy affects 1% of the world's population and 30% remain refractory. In the US alone approximately 660,000 patients have been diagnosed with refractory epilepsy and these patients account for 80% of the cost of epilepsy. The US would be the largest market for epilepsy as 50% of all available treatments are sold in the US.

IP

Pending PCT application (PCT/EP2023/053351)

Further Information

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