WashU

Office of Technology Management

TARGETING NEURONAL HYPEREXCITABILITY TO TREAT CENTRAL AND PERIPHERAL NERVOUS SYSTEM NF1 TUMORS

Anastasaki, Corina, Gutmann, David

Zou, Dianxiong

T-020010

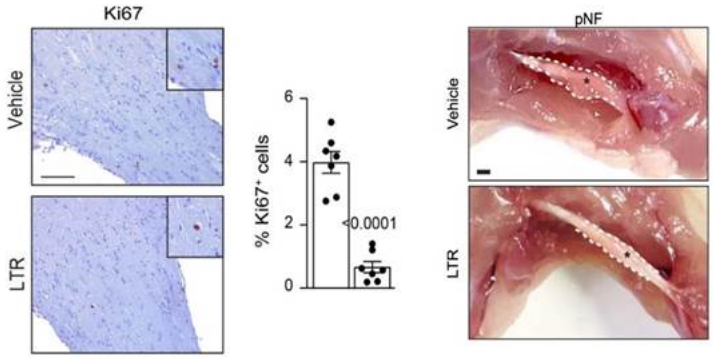
Published Date: 5/13/2025

Value Proposition: *A novel approach to repurposing FDA-approved anti-epileptic drugs to treat brain and nerve tumors associated with neurofibromatosis type I, offering a faster, cost-effective pathway to address an urgent unmet medical need.*

Technology Description

Neurofibromatosis type 1 (NF1) individuals have a lifetime predisposition to develop central nervous system (gliomas) and peripheral nervous system (neurofibromas) tumors. While surgery, standard chemotherapy, and targeted therapy (MEK inhibitors) are employed, these approaches have potential long-term effects on the developing brain and may not be easily tolerated by young patients. Additionally, it is not clear how long to treat individuals with MEK inhibitors and whether stopping therapy will cause the tumors to accelerate their growth (rebound). Better defining the mechanisms that support NF1-associated tumor growth is critical to finding novel therapeutic targets.

The research team at Washington University School of Medicine, led by Dr. David Gutmann, has discovered a link between neuronal excitation and the expression of paracrine factors that are indispensable for both NF1-associated glioma and plexiform neurofibroma growth. By normalizing neuronal excitation using pharmacological agents that activate the HCN channel, both NF1-associated CNS and PNS tumor progression was reduced.



Stage of Research

In vivo demonstration of the mechanism of action. Potential repurposing of existing FDA-approved anti-seizure compounds to both prevent tumor progression and inhibit tumor growth. Potential use of excitability and circulating paracrine factors as disease biomarkers.

Left: Administration of lamotrigine (LTR) reduced the progression of the optic pathway glioma mouse model based on a tumor-specific biomarker (Ki67). Right: Similarly, LTR attenuated the lesion growth of a plexiform neurofibroma (pNF) mouse model.

Applications

- Therapeutic intervention for NF1-associated tumors.

Key Advantages

- The novel mechanism of action is independent of RAS signaling and therefore may synergize with other drugs targeting NF1 tumors.
- Doses at or below the levels used for seizure indications appear sufficient for anti-tumor response.

Patents

US patent application pending, see US20230190758A1

Related Web Links: David Gutmann; Gutmann Lab, related publications