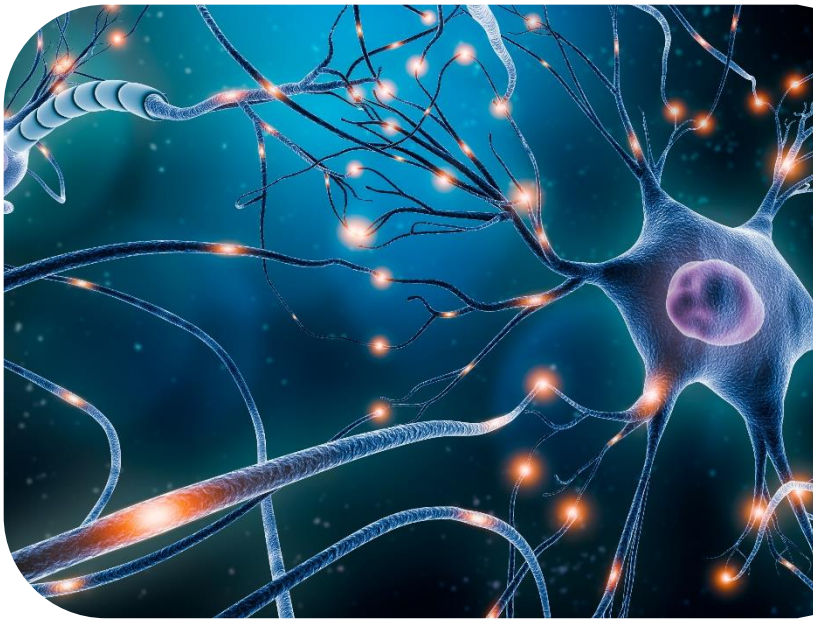
>> Epilepsy

Epilepsy is one of the most common neurological disorders worldwide and is characterized by reoccurring seizures of varying severity. Groundbreaking research is unraveling the complexities of seizure activity and paving the way to novel therapeutics—and sensitive functional assays are needed to evaluate these potential antiepileptics. Axion's Maestro multielectrode array (MEA) platform is enabling scientists to characterize epilepsy and other neurological diseases, both to gain a better understanding of pathogenic mechanisms as well as insight into efficacy of potential therapeutics.



Learn how the Maestro can support epilepsy research with **these selected publications:**

Chronic neuronal activation leads to elevated lactate dehydrogenase A through the AMP-activated protein kinase/hypoxia-inducible factor-1α hypoxia pathway

Alexander Ksendzovsky, Muznabanu Bachani, et al. Brain Communications. (2022)

Changes in neural metabolism have been associated with epilepsy, which is hypothesized to be an adaptation to meet increased energy demands from hyperactivity. Using both human tissue samples and rat cortical neurons, researchers assess the link between neural activity and metabolism, specifically the upregulation of lactate dehydrogenase A.

Highlights:

- Lactate dehydrogenase A is upregulated in human epileptic tissue samples.
- Maestro Pro provides an *in vitro* epilepsy model via culture in low Mg^{2+} conditions to corroborate the effects of neural activity on LDHA upregulation.
- This upregulation of LDHA is abolished via tetrodotoxin (TTX) treatment, suggesting an activity-dependent change in expression.

Read more >>

IDH-mutated gliomas promote epileptogenesis through D-2-hydroxyglutarate-dependent mTOR hyperactivation

Armin Mortazavi, Islam Fayed, et al. Neuro-Oncology. (2022)

Seizures present as a common comorbidity with IDH-mutant glioma and are often resistant or unresponsive to medical intervention. Researchers use human patient cortical tissue samples and neuron-glia co-cultures to explore potential mechanisms underlying glioma-associated epilepsy.

Highlights:

- Using a transwell glioma co-culture model on MEAs, neurons exhibit increased seizure-like activity in the presence of IDH-mutant glioma cells compared to wild-type glioma cells—an effect abrogated by IDH inhibition.
- LDHA is upregulated in patient epileptic tissue, reflecting increased activity and metabolic demand.
- mTOR pathway activation via D-2-HG treatment promotes increased neural activity and metabolic changes, suggesting a potential epileptogenic mechanism in IDH-mutant glioma patients.

Read more >>

Postoperative risk of IDH mutant glioma-associated seizures and their potential management with IDH mutant inhibitors

Michael R. Drumm, Wenxia Wang, et al. The Journal of Clinical Investigation. (2023)

Postoperative seizures often remain a symptom for patients with IDH-mutant gliomas, and this tumor-associated epilepsy (TAE) can result in additional complications and increased risk of tumor recurrence. IDH inhibitors are evaluated using *in vitro* and *in vivo* models, and patients are studied to explore postoperative TAE risk factors.

Highlights:

- Using MEA, neural cultures treated with D2HG exhibit increased neural activity, as described previously, and this effect is dependent upon the presence of astrocytes.
- Either D2HG treatment or integration of IDH-mutant glioma cells into cortical spheroids also promotes increased activity, which is reversed by treatment with mutant IDH inhibitors.
- Mutant IDH inhibition is also effective in *in vivo* models, suggesting potential therapeutic value.

Read more >>

Epilepsy in a mouse model of GNB1 encephalopathy arises from altered potassium (GIRK) channel signaling and is alleviated by a GIRK inhibitor

Sophie Colombo, Haritha P. Reddy, et al. Frontiers in Cellular Neuroscience. (2023)

GNB1 mutations cause a neurodevelopmental disorder characterized by a variety of symptoms, including intellectual impairment, developmental delay, and epilepsy. Researchers developed an *in vivo* model of GNB1 encephalopathy and assessed primary mutant neurons to characterize disease phenotypes and evaluate the therapeutic potential of ethosuximide, an antiepileptic drug.

Highlights:

- GNB1-mutant mice display developmental delay, cognitive impairment, and hyperexcitability.
- Primary GNB1-mutant neurons exhibit increased burst frequency and duration indicative of a seizurogenic phenotype.
- Ethosuximide treatment rescues these effects, suggesting potential therapeutic efficacy.

Read more >>