Courtagen
DIAGNOSTICS LABORATORY

Courtagen's epiSEEK®

Actionable Results

Results from the epiSEEK® Comprehensive Epilepsy and Seizure Disorder panel can have immediate implications for treatment.

Disorder/Syndrome	Gene	Implications for Treatment
Alper's-Huttenlocher and other POLG-related disorders	**POLG**	Avoid valproic acid, which can induce or accelerate liver disease
Creatine deficiency syndromes	**GAMT, GATM**	Oral creatine (GAMT, AGAT)
Dravet syndrome, and other SCN1A-related disorders	**SCN1A**	Valproate, clobazam, stiripentol, levetiracetam, topiramate. Avoid phenytoin, carbamazepine, and lamotrigine
Glucose transporter type 1 deficiency syndrome	**SLC2A1**	Seizures typically respond to a ketogenic diet
Pyridoxal 5'-phosphate-dependent epilepsy	**PNPO**	Seizures respond to treatment with supplemental pyridoxal 5-phosphate (PLP)
Pyridoxine-dependent epilepsy. Folinic-acid responsive seizures.	**ALDH7A1**	Seizures respond to treatment with supplemental pyridoxine and/or folinic acid
Lafora disease	**EPM2A, EPM2B(NHLRC1)**	Avoid phenytoin, lamotrigine, carbamazepine, and oxcarbazepine
Unverricht-Lundborg disease	**CSTB**	Avoid sodium channel blockers and GABAergic drugs, which can increase myoclonus, dementia, and ataxia

Examples of Treatment Indications

1) Sequence informs glucose transporter 1 deficiency syndrome (GLUT1 DS). Children who are not able to move glucose to the brain due to a genetic defect in glucose transporters in both the BBB and astrocytes are identifiable with panel sequencing. The only treatment is the ketogenic diet, and is reported to work well [1-4] in patients suffering from this condition. The spectrum of GLUT1 deficiency continues to expand rapidly, largely due to the availability of the genetic test SLC2A1 (solute carrier family 2, member 1). This genetic testing is much simpler and safer to obtain than the more invasive lumbar puncture previously required for diagnosis.

2) Rare mutations in SYNGAP1 can cause a seizure disorder with loss of expressive language and developmental delay[5]. Both static and progressive encephalopathies associated with SYNGAP1 mutations carry important implications for diagnostic testing. The ketogenic diet may be helpful in regaining some of the expressive language loss.

3) Creatine synthesis disorders are identifiable with sequencing. Half of the body's daily requirement of creatine is synthesized by the enzyme AGAT and GAMT. A specific creatine transporter, CTI, encoded by the X-linked gene, facilitates the uptake into tissues. In the case of creatine synthesis disorders, treatment with oral creatine can improve seizures and neurological function. The X-linked creatine transport disorders are not significantly amenable to therapy. Sequencing can reveal which patients are treatable[6].

4) Courtagen's epiSEEK® Comprehensive Next Generation Sequencing panel also uniquely includes calcium genes known to influence Dravet Syndrome [7, 8].

Courtagen's Unmatched Customer Support

Turn Around Time: 4-6 weeks. Results are delivered in weeks, not months.

Saliva Sample: DNA for sequencing is reliably extracted from a single saliva sample. No blood draw or muscle biopsy required. (Blood and tissue are accepted, as requested.)

Insurance Assistance: Courtagen works with patients, physicians, and insurance carriers to pre-approve each test. Courtagen will bill the insurance company and is willing to handle an appeal process as needed.

Genetic Counselors: Available to address your questions regarding Courtagen test results.

Clinical Experience: Courtagen's Medical Director, Laboratory Director, and variant science team have over 25 years of experience in the treatment and genetic interpretation of neurological and metabolic disorders.

Reports: Utilizing Courtagen's customized Zypher® informatics pipeline and thorough clinical evaluation, each report is provided in a concise format with interpretation and recommendations for consideration.

References

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6. Yu, J.Y. & Pearl, P.L. Metabolic causes of epileptic encephalopathy. *Epilepsy research and treatment* **2013**, 124934 (2013).

7. Ohmori, I. et al. CACNA1A variants may modify the epileptic phenotype of Dravet syndrome. *Neurobiol Dis* **50**, 209-217 (2013).

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