DNA Sequence Analysis of Genes Related to Functional Disorders

Genes associated with metabolism, physiological function, and neurologic development are factors in functional symptoms and disease

Functional disorders encompass a wide range of phenotypes that can present with diverse and multi-system symptomatology. A functional disorder is a medical condition that impairs the normal function of a bodily process, but where the body or associated organs appear normal under examination, imaging, laboratory values, or other standard studies. The occurrence of multiple functional symptoms in one individual suggests a genetic condition as the underlying cause. The theraSEEK™ panel includes a curated selection of genes primarily associated with genetic disorders that present with functional symptoms, and also genes in metabolic and physiologic pathways of interest. In addition to determining a genetic diagnosis, this panel can identify genetic risk factors for multifactorial functional disease.

Genetic testing using Next Generation Sequencing is a valuable tool for obtaining a definitive diagnosis in the patient, thereby providing insight to the prognosis, treatment choices, and recurrence risks for the family. Importantly, understanding the genetic basis of the patient’s condition can assist the clinician in developing a targeted personalized treatment plan, which may include medication, nutritional interventions, supplements, and other therapies or avoidance of certain agents.

theraSEEK™: A selection of 299 genes encompassing:

- Metabolism and physiological functions (amino acids, carbohydrates/glucose, cell signaling, cofactors, metals, select drugs, extracellular matrix, fatty acid oxidation, glycosylation, heme, ion channels, lipids, lysosomes, neurotransmitters, organic acids, peroxisomes, purines/pyrimidines, transcription/translation, urea cycle);
- Metabolic pathways (antioxidant, biopterin, coenzyme Q10, folate, methionine, transsulfuration);
- Neurological development and function;
- Mitochondrial function (electron transport chain, mtDNA replication, morphology).
- In addition to full sequencing for rare genetic disease-causing variants, the test includes a SNP analysis for common variants associated with biochemical pathways. Physicians will receive the genetic analysis report, plus a separate SNP analysis report with 60 SNPs, and a data file with over 1,100 SNPs.

Indications for Testing

- Migraine headache
- Chronic pain conditions (joint, bone, myalgia)
- Gastrointestinal conditions (dysmotility, intermittent diarrhea or constipation, abdominal pain, recurrent vomiting, nausea, GERD)
- Fatigue/exercise intolerance
- Autonomic dysfunction (dizziness, POTS, arrhythmias)
- Psychiatric / mood disorders (depression, anxiety, schizophrenia)
- Neuropathy/sensory deficits
- Autistic spectrum disorder with additional functional symptoms
- ADHD and other behavioral conditions
- Abnormal movement (tics, tremor, dyskinesia, restless legs)
- Sleep disturbance
Performance

This test was designed to sequence the exons and canonical splice sites (+/-1,2) of a panel of 299 genes that can inform meaningful treatment options for genetic disorders involving functional disease symptoms (e.g. CDCA treatment for patients with pathogenic variants in the CYP27A1 gene, presenting with headaches, muscle weakness, chronic fatigue, alternating constipation and diarrhea). Genomic DNA is extracted from the submitted sample (typically saliva), and captured with an inversion probe method for the genes specific to this panel. The captured targets are sequenced on an Illumina MiSeq sequencing system with 250bp paired-end reads. Panel-specific sequencing coverage, specificity, and sensitivity are listed below:

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<tbody>
<tr>
<td>Mean depth of coverage</td>
<td>&gt;400</td>
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<tr>
<td>Sensitivity</td>
<td>98.4%</td>
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<tr>
<td>Specificity</td>
<td>99.9%</td>
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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; however, blood and muscle tissue are accepted. No charge saliva kits are provided, no charge phlebotomy services are offered.

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.

Courtagen Care Financial Assistance Program: Provides financial assistance to patients based on demonstrated financial need. A qualified applicant may be asked to contribute between $0 and a maximum cost sharing of $200 depending on determination of financial need.

Online Portal: A secure physician online portal is available for ordering genetic tests and accessing patient reports when completed. Immediate results can also be faxed.

Genetic Counselors: Available to address physician’s questions regarding Courtagen test results. Contact us at clinical@courtagen.com.

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 ZiPhyr® informatics pipeline and thorough clinical evaluation, each report is provided in a concise format with interpretation and recommendations for consideration.

Data and DNA Security: Advanced IT solutions safeguard patient records and financial information. In the laboratory, Courtagen de-identifies patient and test records and uses the proprietary method of DREAM PCR to provide exceptional lab decontamination.

Required forms

Courtagen Test Requisition (completed and signed by ordering clinician)
Patient Clinical Information (Clinic visit note preferred and/or symptom checkoff sheet)
Signed Patient Consent (on the Courtagen Test Requisition or Consent Form provided in the saliva kit)
Photocopy front & back of all insurance cards (including subscriber date of birth)