CLARITAS GENOMICS

Hemophagocytic Lymphohistiocytosis (HLH) Region of Interest

Rapid genetic analysis for patients with HLH and HLH-associated macrophage activation syndrome (MAS)

Key Features

1 Expert Design
Evaluates 20 genes related to inherited forms of HLH and HLH-associated MAS

2 Rapid Expansion to a Clinical Exome
If no pathogenic variant is uncovered, providers may order expansion into the Claritas Clinical Exome

3 Access to Exome Data
Interactive variant browsing via the WuXi NextCODE™ platform and access to exome data via a secure download of VCF and BAM files

Report Features

- All sequence variants are orthogonally or sanger confirmed
- Includes companion deletion/duplication analysis when ordered

Test Characteristics

- Orthogonal sequencing is carried out using Illumina NextSeq™ and Thermo Fisher Ion Proton™ systems to generate a variant list
- Assesses protein coding sequences of targeted genes and 10 bp of adjacent intronic sequences
- Detects SNVs, insertions, and deletions less than 10 bp
- >100x mean coverage on both platforms; >98% at 20x**
- Adding the companion deletion/duplication analysis can increase detection rate of the assay (Note: not all genes are covered by deletion/duplication analysis).
- Trios are encouraged, but not required
- More information on methodology is available at Chennagiri et al., *Orthogonal NGS for High Throughput Clinical Diagnostics*, Sci Rep 6, 24650 (2016).

**Data for the Claritas Clinical Exome

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Turnaround Time

- 6 – 8 weeks

Clinical Features of HLH

- HLH is a life-threatening immunodeficiency that may be genetic (sometimes referred to as familial HLH [FHLH] or "primary HLH") or acquired ("secondary HLH").
- HLH results when the body over-produces certain immune cells in an uncontrolled hyperfinlammatory response.
- Symptoms of HLH often present within the first months of life with 70% of familial cases due to genetic factors occurring before one year of age.
- Symptoms include fever, enlarged liver or spleen, skin rash, lymph node enlargement, breathing problems, easy bruising, abnormal bleeding, kidney or heart problems, neurologic abnormalities and an increased risk for leukemia or lymphoma.
- Laboratory findings may include cytopenia (low blood cell count), elevated triglycerides or low levels of fibrinogen, hemophagocytosis, decreased or absent natural killer (NK) cell activity, high levels of ferritin in the blood and/or elevated CD25 (IL-2r) blood levels.

Indications For Testing

- Symptoms of HLH due to genetic factors can be difficult to distinguish from acquired HLH. Molecular testing has value in making a diagnosis of HLH and detecting cases due to genetic factors which can also have implications for other family members.
- Patient with suspected HLH (multiple symptoms consistent with the disorder)
- More than one family member with HLH symptoms that are not explainable by acquired factors, or MAS is suspected and symptoms are consistent.

https://rarediseases.info.nih.gov/diseases/6589/hemophagocytic-lymphohistiocytosis
https://www.histio.org/hemophagocyticsyndromes#.WOzBbojytaR

Innovative Approach to Results

Saves time and money by minimizing sequential testing	Orthogonal technologies enable the most accurate and comprehensive results	Independent platforms provide superior sensitivity and specificity	Immediate confirmation of variants reduces turnaround time	Variant interpretation performed by credentialed Genetic Counselors and Medical Directors

Support Services

Our Genetic Counselors and Medical Directors are ready to answer your questions about genetic testing

Result Types	No variant reported	Pathogenic variant reported	Variant of uncertain clinical significance reported
Next Steps	Connect with an expert to discuss next steps	**Access the Interpretive Genomic Services, a network of genetic specialists and researchers**	Parental testing when applicable

Providers may request raw data in the form of BAMs and VCFs, or via access in the NextCODE interactive platform

How to Order

1 Download and complete the requisition form
www.claritasgenomics.com

2 Obtain the patient's sample

Whole blood
- ROI only: 0.5-3cc
- ROI with Del/Dup Analysis: 2-5cc
- EDTA (preferred), NaCitrate, or ACD

Extracted DNA
- 10µg at 50ng/µL

Saliva
- Contact Client Services for sample requirements

3 Prepare the sample for shipment
- Complimentary kits are available for samples shipped within the United States and include a prepaid airbill
- Order kits at www.claritasgenomics.com

4 Ship overnight for receipt Monday through Friday

Claritas Genomics
Attn: Specimen Processing
99 Erie Street
Cambridge, MA 02139

Connect to The Claritas Network

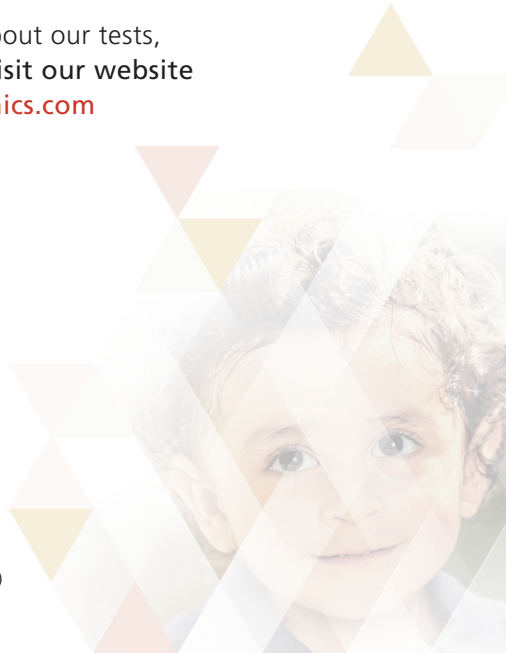
Access the Interpretive Genomics Services at Boston Children's Hospital, which provides consultation with experts in genes and/or phenotypes

Take advantage of partnerships and save on send-out costs

Questions or Comments? We Want to Hear From You.

Email us at clientservices@claritasgenomics.com
Call us at 617.553.5880
Toll-Free at 855.373.9003
Fax at 617.553.5842

For more information about our tests, products and services, **visit our website** at www.claritasgenomics.com



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