FIRST IN CLASS

Whole Genome Sequencing targeted for NICU

Alamya Health offers rapid, comprehensive, short-read whole genome and mitochondrial genome sequencing for a patient or for a patient and parents (trios).

Initial results are available in 7 days. To guide the interpretation of variants of uncertain significance and/or to confirm variant pathogenicity, this competitively priced multi-modal testing approach may include reflex to short-read transcriptome and/or Infinium Methylation Epic microarray at no additional cost.

Alamya Health reports incorporate multiple data streams to provide meaningful results to support healthcare providers in caring for their patients and family members. These data include the above sequence and reflex data as well as patient phenotype, familial inheritance patterns, and knowledge mined from the literature and curated databases.

Sequencing

The First in Class Genome is sequenced using a NovaSeq 6000 in a CAP/CLIA certified laboratory. Disease-associated variants reported in HGMD® and ClinVar as well as variants with minor allele frequency (MAF) of less than 1% in gnomAD database are considered.

Copy Number Variants (CNV), Single Nucleotide Variants (SNV), and Indels

The overall sensitivity for SNV and Indels is 99.86% and 99.39%, respectively. Sensitivity for detection of insertions (as opposed to duplications) is currently at approximately 20%. At this time, balanced translocations are not reported. Variants of relevance identified by next generation sequencing (NGS) are continuously and individually validated for quality; those variants meeting internal QC criteria (based on extensive validation processes) are not validated by Sanger sequencing. All reported CNVs are confirmed by qPCR.

- **Uniparental Disomy (UPD)**
  UPD and parental origin are analyzed based on homozygosity and haplotype analysis.

- **Mitochondrial Genome**
  Mitochondrial genome sequencing generally achieves an average read depth of >3,000x and a minimum acceptable read depth of 500x.

- **Transcriptome**
  RNA-seq, also known as transcriptome sequencing, improves the diagnostic rate depending on the clinical phenotype and tissue sample. RNA-seq aids in prioritizing and resolving VUSs. For variants with the potential to alter splicing and to cause the clinical presentation, transcriptome analysis assesses the impact of the variants.

- **Infinium MethylationEPIC microarray**
  Assessment of genomic DNA methylation guides interpretation of variants in genes that encode epigenetic regulators and that could be associated with the clinical findings. This approach focuses on genes with well-established epigenetic signatures and for which the signature can indicate the presence of pathogenic variants. Alamya Health uses the Infinium MethylationEPIC microarray testing to assess these epigenetic signatures. This signature listing is updated quarterly upon determination of robust epigenetic signatures.

Au-Kline syndrome: HNRNPK gene	Down syndrome: chr21 trisomy	KBG syndrome: ANKRD11 gene (moderate effect size signature)
Autism spectrum: 16p11.2 deletion	Dup7 syndrome: 7q11.23 duplication	Kleefstra syndrome: EHMT1 gene or 9q34 deletion
Autism spectrum: CHD8 gene	DYRK1A syndrome: DYRK1A gene	Nicolaides-Baraitser syndrome: SMARCA2 gene
Bohring-Opitz syndrome: ASXL1 gene	Floating-Harbor syndrome: SRCAP gene	Sotos syndrome: NSD1 gene
CHARGE syndrome: CHD7 gene	Imagawa-Matsumoto syndrome: SUZ12 gene	Weaver syndrome: EZH2 gene
Cohen Gibson syndrome: EED gene	Kabuki syndrome type 1: KMT2D gene	Williams syndrome: 7q11.23 deletion
Developmental delay, hypotonia, musculoskeletal defects, and behavioral abnormalities: SRCAP gene	Kabuki syndrome type 2: KDM6A gene	

Transcriptome sequencing and the Infinium MethylationEPIC microarray are currently used to generate clarifying or supporting evidence and are not yet accredited or licensed as independent diagnostic assays. Classification of gene variants using data generated by either or both of these tests are based on our current understanding of RNA splicing/expression and distinct DNA methylation profiles that can be associated with variants in the specific gene. Such variants may be reclassified over time based on reliable new information.

Payment information

For testing ordered in patients residing in the US, institutional billing will be implemented. For testing requests outside of the US, please contact: sales@alamyahealth.com or call (628) 252-5243.