FIRST IN CLASS

Whole genome sequencing, transcriptome and DNA methylation

Our First in Class test offers a comprehensive, short-read (SR) whole genome sequencing with free reflex to a SR transcriptome and/or Infinium MethylationEPIC microarray for interpretation and classification of some variants.

This test is for patients with complex phenotypes, uninformative or inconclusive prior testing or for patients requiring quick test results to guide clinical management.

The turnaround time for First in Class is 4-6 weeks. Rapid testing is also available with a preliminary report in 7 days and final report in 10-14 days.

Alamya Health integrates multiple data streams to provide meaningful results to support healthcare providers in caring for their patients and family members. These data include sequence and reflex test 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. The test considers disease-associated variants reported in HGMD® and ClinVar as well as variants with minor allele frequency (MAF) of less than 1% in gnomAD database.

- **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 ~20%. At this time, balanced translocations are not reported.

- **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 variants of unknown significance (VUS) and identifies variants with the potential to alter splicing. Transcriptome analysis assesses the potential impact of such variants and their role in clinical presentation.

- **Infinium MethylationEPIC microarrayy**
  Assessment of genomic DNA methylation will be used to guide interpretation of variants in genes that encode epigenetic regulators and that could be associated with the clinical findings. Our First in Class uses Infinium MethylationEPIC microarray testing to focus on genes with well-established epigenetic signatures (see table below) that may indicate the presence of pathogenic variants.

Conditions with methylation signatures currently detected by our Infinium MethylationEPIC microarray*

Intellectual developmental disorder with autism and macrocephaly: *CHD8* gene	CHARGE syndrome: *CHD7* gene	Rahman syndrome: *HIST1H1E* gene
Intellectual developmental disorder, autosomal dominant 7: *DYRK1A* gene	Au-Kline syndrome: *HNRNPK* gene	Koolen-de Vries syndrome: *KANSL1* gene
Kleefstra syndrome 1: *EHMT1* gene	Kleefstra syndrome 2: *KMT2C* gene	Kabuki syndrome type 1: *KMT2D* gene
Sotos syndrome: *NSD1* gene	Bohring-Opitz syndrome: *ASXL1* gene	Kabuki syndrome type 2: *KDM6A* gene
Nicolaides-Baraitser syndrome: *SMARCA2* gene	Shashi-Pena syndrome: *ASXL2* gene	Down syndrome: chromosome 21 trisomy
Floating-Harbor syndrome: *SRCAP* gene	Weaver syndrome: *EZH2* gene	Chromosome 16p11.2 deletion syndrome, AUTS14A: 16p11.2 deletion
Developmental delay, hypotonia, musculoskeletal defects, and behavioral abnormalities: *SRCAP-upstream*	Cohen Gibson syndrome: *EED* gene	Chromosome 7q11.23 duplication syndrome: 7q11.23 duplication
Coffin-Siris syndrome 1: *ARID1B* gene	Imagawa-Matsumoto syndrome: *SUZ12* gene	Williams-Beuren syndrome: 7q11.23 deletion
KBG syndrome: *ANKRD11* gene	Dystonia 28, childhood onset: *KMT2B* gene	DiGeorge syndrome: 22q11 deletion
Developmental disorder and epileptic encephalopathy 94: *CHD2* gene	Congenital heart defects, dysmorphic facial features, and intellectual developmental disorder: *CDK13* gene	

* This signature listing is updated quarterly upon determination of robust epigenetic signatures.

Transcriptome sequencing and the Infinium MethylationEPIC microarray are currently used to generate clarifying or supporting evidence and are not yet approved as independent diagnostic assays.

Payment information

For testing ordered for patients residing in the US, institutional billing will be utilized for testing on inpatients.
For testing requests outside of the US, please contact: orders@alamyahealth.com or call (628) 203 -5690.
Private pay is also available for US-based and international patients.

Visit our website at alamyahealth.com for more information on our First in Class test.