Proportionate Short Stature/Small for Gestational Age: Deletion/Duplication Panel

**Test Code:** MD010
**Turnaround time:** 2 weeks
**CPT Codes:** 81228 x1, 81406 x1

**Condition Description**

Short stature is defined as a height less than two standard deviations from the mean for a given age and gender (i.e. height is less than the third percentile on standard growth curves). Based on the clinical presentation, short stature can be broken down into three subcategories: small for gestational age (SGA), non-SGA proportionate short stature, and disproportionate short stature (e.g. skeletal dysplasias). SGA, which is sometimes called intrauterine growth restriction (IUGR), is used to describe a fetal weight below the 10th percentile when controlled for gender and gestational age. It can also be used to describe a newborn whose birth weight is below the 10th percentile. Short stature can have either a non-genetic or a genetic etiology. Examples of non-genetic causes of short stature are malnutrition, infections, growth hormone deficiency and chronic diseases such as kidney disease and congenital heart disease. Examples of genetic causes of short stature are chromosome abnormalities such as Turner syndrome (45,X), epigenetic abnormalities such as aberrant methylation at 11p15.5 and uniparental disomy, as well as autosomal dominant, autosomal recessive and X-linked genetic defects. Short stature due to genetic causes can be an isolated finding or part of the clinical spectrum of a genetic syndrome.

Please note that this panel only includes testing for SGA and non-SGA proportionate short stature subcategories and does not include testing for disproportionate short stature (e.g. skeletal dysplasias).

In addition, this panel does not include testing for growth hormone deficiency, which may be an integral part of the workup for an individual with short stature.

**References:**

**Genes**

ATRX, BLM, BTK, CREBBP, CUL7, DHCR7, EP300, ERCC6, ERCC8, FGD1, GH1, GHR, GHHR, GLI2, HESX1, IGF1, IGF1R, INSR, KDM6A, KMT2D, KRAS, LHX3, NBN, NIPBL, PITX2, POU1F1, PRNP, PTPN11, RAF1, ROR2, RPS6KA3, SHOX, SMARCAL1, SMC1A, SMC3, SOS1, SOX2, SOX3, SRCAP, STAT5B, TBCE, THR8, TRIM37, WRN

**Indications**

This test is indicated for:

- Individuals with a clinical diagnosis of proportionate short stature.

**Methodology**

**Deletion/Duplication Analysis:** DNA isolated from peripheral blood is hybridized to a gene-targeted CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes that cover the entire genomic region.

Please note that a “backbone” of probes across the entire genome are included on the array for analytical and quality control purposes. Rarely, off-target copy number variants causative of disease may be identified that may or may not be related to the patient's phenotype. Only known pathogenic off-target copy number variants will be reported. Off-target copy number variants of unknown clinical significance will not be reported.

**Detection**

**Deletion/Duplication Analysis:** Detection is limited to duplications and deletions. The CGH array will not detect point or intronic mutations. Results of molecular analysis must be interpreted in the context of the patient's clinical and/or biochemical phenotype.
Specimen Requirements

Submit only 1 of the following specimen types

Type: Whole Blood

Specimen Requirements:

In EDTA (purple top) tube:
Infants (2 years): 3-5 ml
Older Children & Adults: 5-10 ml.

Specimen Collection and Shipping: Ship sample at room temperature with overnight delivery.

Type: Isolated DNA

Specimen Requirements:

In microtainer: 10 ug

Isolation using the Qiagen™ Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping: Refrigerate until time of shipment in 100 ng/ul of TE buffer. Ship sample at room temperature with overnight delivery.

Related Tests

- Individual sequencing analysis is available for the SHOX, NIPBL, SMC1A, CREBBP, EP300, DHCR7, KMT2D, PTPN11, RAF1, KRAS, SOS1, and FGD1 genes.
- Variations of this panel are available if previous genetic testing has been performed. These include:
  - PSS/SGA Panel: Comprehensive
  - PSS/SGA Panel: EmArray Cyto + SNP & NGS
  - PSS/SGA Panel: Russell-Silver Panel & NGS
  - PSS/SGA Panel: NGS
- A next generation sequencing panel is also available for Noonan syndrome and related disorders.
- Custom diagnostic mutation analysis (KM) is available to family members if mutations are identified by targeted mutation testing or sequencing analysis.
- Proportionate Short Stature/Small for Gestational Age sequencing panels.