## Congenital Obesity: Sequencing Panel

**Test Code:** MM600  
**Turnaround time:** 6 weeks  
**CPT Codes:** 81406 x1, 81408 x1, 81403 x1, 81404 x1

### Condition Description

Congenital obesity is the excessive accumulation and storage of fat in the body that is present during infancy and/or childhood. Obesity may be diagnosed as an isolated clinical finding or as a part of syndromic findings. Monogenic forms of childhood obesity are very rare. Mutations in only a few genes controlling appetite and metabolism are known to cause the development of severe obesity in early childhood. EGL offers testing for syndromic and nonsyndromic single-gene causes of congenital obesity; predisposition and susceptibility genes are not included in this testing.

Syndromic causes of congenital and early-onset obesity on this panel include:

- Albright hereditary osteodystrophy
- Alstrom syndrome
- Bardet-Biedl syndrome
- Borjeson-Forssman-Lehmann syndrome
- Cohen syndrome
- Schaaf-Yang syndrome (also called Prader-Willi-like syndrome)
- Leptin deficiency
- Leptin receptor deficiency
- MC4R (melanocortin 4 receptor) deficiency

### References:

6. OrphaNet available at [http://www.orpha.net/].

### Genes

ALMS1, ARL6, BBS1, BBS10, BBS12, BBS2, BBS4, BBS5, BBS7, BBS9, CEP290, GNAS, LEP, LEPR, MAGEL2, MC4R, MKKS, MKS1, NR0B2, NTRK2, PCSK1, PHF6, POMC, SDCCAG8, SIM1, TRIM32, TTC8, VPS13B, WDPCP

### Indications

The test is indicated for:

- Individuals with a clinical or suspected diagnosis of congenital obesity.

### Methodology

**Next Generation Sequencing:** In-solution hybridization of all coding exons is performed on the patient's genomic DNA. Although some deep intronic regions may also be analyzed, this assay is not mean to interrogate most promoter regions, deep intronic regions, or other regulatory elements, and does not detect single or multi-exon deletions or duplications. Direct sequencing of the captured regions is performed using next generation sequencing. The patient's gene sequences are then compared to a standard reference sequence. Potentially causative variants and areas of low coverage are Sanger-sequenced. Sequence variations are classified as pathogenic, likely pathogenic, benign, likely benign, or variants of unknown significance. Variants of unknown significance may require further studies of the patient and/or family members.

### Detection

**Next Generation Sequencing:** Clinical Sensitivity: Unknown. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations cannot be detected by this analysis. Large deletions/duplications will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's clinical/biochemical phenotype.

**Analytical Sensitivity:** ~99%.

### Specimen Requirements

Disclaimer: This information is confidential and subject to change without notice. It may not be reproduced in whole or part unless authorized in writing by an authorized EGL representative.
Type: Whole Blood (EDTA)

Specimen Requirements:
EDTA (Purple Top)
Infants and Young Children (2 years of age to 10 years old): 3-5 ml
Older Children & Adults: 5-10 ml
Autopsy: 2-3 ml unclotted cord or cardiac blood

Specimen Collection and Shipping:
Ship sample at room temperature for receipt at EGL within 24 hours of collection. Do not refrigerate or freeze.

Type: DNA, Isolated

Specimen Requirements:
Microtainer
8µg
Isolation using the Perkin Elmer™Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

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

Type: Saliva

Specimen Requirements:
Oragene™ Saliva Collection Kit
Oragene™ Saliva Collection Kit used according to manufacturer instructions. Please contact EGL for a Saliva Collection Kit for patients that cannot provide a blood sample.

Specimen Collection and Shipping:
Please do not refrigerate or freeze saliva sample. Please store and ship at room temperature.