Endocrine Disorders: Sequencing Panel

Test Code: MM290
Turnaround time: 6 weeks
CPT Codes: 81407 x1, 81405 x1, 81406 x1

Condition Description

The Endocrine Disorders Panel primarily tests for two broad categories of endocrine disorders: (1) disorders of sexual development (DSD) and hormone production, and (2) transient or permanent neonatal diabetes mellitus (NDM) and maturity onset diabetes of the young (MODY). DSD may manifest in infancy with ambiguous genitalia or at puberty when atypical sexual development occurs. DSD include such things as hypogonadotropic hypogonadism (with or without anosmia), premature ovarian failure or ovarian dysgenesis, and congenital adrenal hyperplasia. DSD are important to diagnose early for proper treatment and management of these conditions. NDM and MODY are genetically heterogeneous disorders. A molecular genetic diagnosis is critical, since some monogenic diabetes can be treated with sulfonylureas, instead of requiring life-long insulin therapy.

References:
- Bonnefond et al., 2010 PLoS ONE 5(10):e13630.
- Hughes et al., 2013 Endocrine abstracts 33: P48.

Genes

ABCC8, AGPAT2, AKT2, BLK, BMP15, BSLCL2, CAV1, CHD7, CIDEA, CJS2, CYP17A1, CYP19A1, EIF2AK3, FGF8, FGFR1, FGFA, FOXP3, FSHR, GATA4, GCK, GDF3, GLI3, GNRH1, GNRHR, HADH, HNF1A, HNF1B, HNF4A, IER3IP1, INS, INSR, KCNJ11, KISS1, KISS1R, KLF11, LHCGR, LMNA, NEUROD1, NOBOX, NR0B1, NR5A1, NSMF, PAX4, PDX1, POR, PPARG, PROK2, PROKR2, PSMC3IP, PTF1A, RFX6, SLC2A2, TAG3, TACR3, TBC1D4, WFS1, ZMPSTE24

Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of disorders of sexual development.
- Confirmation of a clinical diagnosis of disorders of hormonal imbalance.
- Confirmation of a clinical diagnosis of neonatal diabetes mellitus.
- Confirmation of a clinical diagnosis of mature onset diabetes of the young.

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 meant 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

Submit only 1 of the following specimen types

Type: Saliva

Specimen Requirements:
Oragene™ Saliva Collection Kit
Orangene™ 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.

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: 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.

Related Tests

- Maturity Onset Diabetes of the Young Panel
- Endocrine Disorders: Deletion/Duplication Panel