Fanconi Anemia Type B: FANCB Gene Sequencing

Condition Description

Fanconi anemia (FA) is characterized by physical abnormalities. Approximately 60-75% of affected individuals have variable physical abnormalities which may include short stature, abnormal skin pigmentation, skeletal anomalies, and ear or eye abnormalities. Other features include heart defects, hearing loss, developmental delay, hypogonadism, and genitourinary tract abnormalities.

FA is diagnosed by the detection of chromosomal aberrations in cells that have been cultured with a DNA interstrand cross-linking agent. There are at least 15 genes that are responsible for the known FA complementation groups. Mutations in the FANCB gene (Xp22.31) (OMIM# 300515), which are responsible for FA complementation group B (FA-B) (OMIM# 300514), account for 2% of FA cases. FA-B cases are the only X-linked form of FA and mainly affect males. Females can be heterozygote carriers at risk for having a child with X-linked FA. Carriers are found to have 100% skewing of X inactivation.

This testing is for sequence analysis of the FANCB gene only.

For patients with suspected FA-B, sequence analysis is recommended as the first step in mutation identification. For patients in whom mutations are not identified by full gene sequencing, deletion/duplication analysis is appropriate.

References:
- GeneReviews
- OMIM #300514: Fanconi anemia complementation group B
- OMIM# 300515: FANCB gene

Genes

FANCB

Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of Fanconi Anemia Type B.
- Carrier testing in adults with a family history of Fanconi Anemia Type B.

Methodology

PCR amplification of 8 exons contained in the FANCB gene is performed on the patient’s genomic DNA. Direct sequencing of amplification products is performed in both forward and reverse directions, using automated fluorescence dideoxy sequencing methods. The patient's gene sequences are then compared to a normal reference sequence. Sequence variations are classified as mutations, benign variants unrelated to disease, or variations of unknown clinical significance. Variants of unknown clinical significance may require further studies of the patient and/or family members. This assay does not interrogate the promoter region, deep intronic regions, or other regulatory elements, and does not detect large deletions.

Detection

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 will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's clinical and/or biochemical phenotype.

Analytical Sensitivity: ~99%

Specimen Requirements

Submit only 1 of the following specimen types

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.

Related Tests

- Deletion/duplication analysis of the FANCB gene by CGH array is available for those individuals in whom sequence analysis is negative.
- Custom diagnostic mutation analysis (KM) is available to family members if mutations are identified by targeted mutation testing or sequencing analysis.
- Prenatal testing is available only for known familial mutations to individuals who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.
- X-Linked Intellectual Disability panels are available for 30, 60, and 90 genes.