Peutz-Jeghers Syndrome: STK11 Gene Deletion/Duplication

Test Code: VM
Turnaround time: 2 weeks
CPT Codes: 81404 x1

Condition Description

Peutz-Jeghers syndrome (PJS) is an autosomal dominant condition characterized by the association of gastrointestinal polyposis and mucocutaneous pigmentation. Peutz-Jeghers-type hamartomatous polyps are most common in the small intestine (in order of prevalence: in the jejunum, ileum, and duodenum) but can also occur in the stomach and large bowel. Gastrointestinal polyps can result in chronic bleeding and anemia and cause recurrent obstruction and intussusception requiring repeated laparotomies and bowel resections. Variable expressivity is common; some affected individuals in families with PJS may have only polyps or perioral pigmentation.

The age at onset for symptoms from polyps is variable, with some individuals developing symptoms within the first few years of life. Significant inter familial variability is observed in the age at which polyps are first observed, suggesting that the natural history of polyps in a family may be a predictor of severity for offspring. In studies from MD Anderson Cancer Center, the median age at first GI symptoms was ten years, while the median age at first polypectomy was 13 years. A report from Korea indicated a mean age of onset for GI symptoms of 12.5 years. In a review of 32 kindreds with PJS, laparotomy for bowel obstruction was performed in 30% of individuals by age ten years and in 68% by age 18 years.

Mucocutaneous hyperpigmentation presents in childhood as dark blue to dark brown macules around the mouth, eyes, and nostrils, in the perianal area, and on the buccal mucosa. Hyperpigmented macules on the fingers are common. The macules may fade in puberty and adulthood. Individuals with Peutz-Jeghers syndrome are at increased risk for malignancies (colorectal, gastric, pancreatic, breast, and ovarian cancers). Females are at risk for sex cord tumors with annular tubules (SCTAT), a benign neoplasm of the ovaries, and adenoma malignum of the cervix, a rare aggressive cancer. Males occasionally develop calcifying Sertoli cell tumors of the testes, which secrete estrogen and can lead to gynecomastia.

The diagnosis of Peutz-Jeghers syndrome is based on clinical findings. In individuals with a clinical diagnosis of PJS, molecular genetic testing of the STK11(LKB1) gene(19p13.3) reveals disease-causing mutations in approximately 100% of individuals who have a positive family history and approximately 90% of individuals who have no family history of PJS.

About 50% of probands have an affected parent and about 50% have no family history of PJS, but the proportion of cases caused by de novo gene mutations is unknown as the frequency of subtle signs of the disorder in parents has not been thoroughly evaluated and molecular genetic data are insufficient. Parents of affected individuals with no known family history of PJS should be evaluated clinically, and with molecular genetic testing if a disease-causing STK11 mutation has been identified in the proband.

The risk to the offspring of a proband with a positive family history is 50%. The risk to offspring of a proband with a negative family history is 50% if the proband tests positive for a pathogenic STK11 mutation. The risk to offspring of a proband with no family history of PJS who tests negative for an STK11 mutation remains unknown.

Click here for the GeneTests summary on this condition.

Genes

STK11

Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of PJS in individuals who have tested negative for sequence analysis
- Individuals at-risk for PJS due to family history who have tested negative for sequence analysis

Methodology

DNA isolated from peripheral blood is hybridized to a CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes which cover the entire genomic region.

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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

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

* Preferred specimen type: Whole Blood

Type: Whole Blood

Specimen Requirements:

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

Specimen Collection and Shipping: Refrigerate until time of shipment. Ship sample within 5 days of collection at room temperature with overnight delivery.

Type: Saliva

Specimen Requirements:

Oragene™ Saliva Collection kit (available through EGL) used according to manufacturer instructions.

Specimen Collection and Shipping: Store sample at room temperature. Ship sample within 5 days of collection at room temperature with overnight delivery.

Special Instructions

Submit copies of diagnostic biochemical test results with the sample, if appropriate. Contact the laboratory if further information is needed.

Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside of Emory Genetics Laboratory, please submit a copy of the sequencing report with the test requisition.

Related Tests

- Sequencing analysis of the STK11 gene is available (VL) and is required before deletion/duplication analysis.
- Prenatal testing is available to individuals who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.