Melanoma-Pancreatic Cancer: **CDKN2A** Gene Deletion/Duplication

**Test Code:** VO  
**Turnaround time:** 2 weeks  
**CPT Codes:** 81228 x1

### Condition Description

Members of families with melanoma-pancreatic cancer syndrome (also known as familial atypical multiple-mole melanoma (FAMMM) syndrome) inherit a predisposition to develop multiple atypical cutaneous nevi (> 50), although not all patients with melanoma in these families display this phenotype. These families also appear to be at increased risk of other malignancies, particularly adenocarcinoma of the pancreas. A melanoma family apparently predisposed to pancreatic cancer was reported first in 1968, and a number of additional families have been identified subsequently. Several studies of melanoma-pancreatic cancer syndrome families have found an excess of nonmelanoma malignancies compared with the expected frequency of these malignancies in the general population. The risk of developing malignant disease in these families appears to be increased 10-fold to 40-fold, and the cumulative risk of pancreatic cancer, the second most common cancer in the syndrome, has been estimated at 17% by age 75 years. In addition, these families may be at increased risk of developing other carcinomas, including breast tumors, lung tumors, sarcoma, and digestive tract tumors.

The most common known mutation in these melanoma-prone families involves the **CDKN2A** gene on chromosome 9p21. **CDKN2A** encodes p16, a low-molecular-weight protein that inhibits the cyclin D1-cyclin dependent kinase complex (CDK4). If it is not inhibited, the CDK4 complex, in turn, phosphorylates the retinoblastoma protein, allowing a cell to progress through the G1 phase of the cell cycle. Thus, p16 acts as a tumor suppressor protein, and mutations in **CDKN2A** can result in unregulated cell growth and neoplastic progression. Germ line **CDKN2A** mutations have been detected in up to 25% of melanoma-prone families worldwide.

**Reference**


### Genes

**CDKN2A**

### Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of melanoma-pancreatic cancer syndrome in individuals who have tested negative for sequence analysis
- Individuals at-risk for melanoma-pancreatic cancer syndrome 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. 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) 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\textsuperscript{TM} 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 EGL Genetics, please submit a copy of the sequencing report with the test requisition.

---

### Related Tests

- Sequencing analysis of the *CDKN2A* gene is available (VN) 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.