Hereditary Periodic Fever Syndromes Panel: Sequencing and CNV Analysis

**Test Code:** MM180  
**Turnaround time:** 6 weeks  
**CPT Codes:** 81402 x1, 81479 x1

### Condition Description

Hereditary periodic fever syndromes (HPFS) is a group of familial autoinflammatory disorders with heterogeneous genetic causes. There are seven types of HPFS that have been characterized. Clinical features continue to be used reliably to assign patients to this general disease category. Identification of the precise genetic defect is important to permit carrier testing and early prenatal diagnosis. Molecular analysis is likely to expand the clinical spectrum of HPFS and may also provide data relevant to prognosis and future therapeutic intervention. HPFS is a very rare disorder. Although each HPFS presents with particular symptoms, globally they share intermittent, apparently unprovoked episodes of fever and inflammation. HPFS can be inherited in an autosomal dominant or autosomal recessive manner.

### References:

- OMIM

### Genes

ELANE, LPIN2, MEFV, MKV, NLRP3, PSTPIP1, TNFRSF1A

### Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of hereditary periodic fever syndromes.  
- Carrier testing in adults with a family history of hereditary periodic fever syndromes.

### 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.

**Copy Number Analysis:** Comparative analysis of the NGS read depth (coverage) of the targeted regions of genes on this panel was performed to detect copy number variants (CNV). The accuracy of the detected variants is highly dependent on the size of the event, the sequence context and the coverage obtained for the targeted region. Due to these variables and limitations a minimum validated CNV size cannot be determined; however, single exon deletions and duplications are expected to be below the detection limit of this analysis.

### Detection

**Clinical Sensitivity:** Unknown. Pathogenic variants in the promoter region, some pathogenic variants in the introns and other regulatory element pathogenic variants cannot 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 for sequence variant detection is ~99%.

**Copy Number Analysis:** The sensitivity and specificity of this method for CNV detection is highly dependent on the size of the event, sequence context and depth of coverage for the region involved. The assay is highly sensitive for CNVs of 500 base pairs or larger and those containing at least 3 exons. Smaller (< 500 base pairs) CNVs and those that involving only 1 or 2 exons may or may not be detected depending on the sequence context, size of exon(s) involved and depth of coverage.

### 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 72 hours of collection. Do not freeze.

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**Type: DNA, Isolated**

**Specimen Requirements:**
- Microtainer
- 8 µg
- 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**

- Hereditary Periodic Fever Syndromes: Deletion/Duplication Panel