CARDIOFACIOCUTANEOUS SYNDROME, MAP2K2-RELATED: MAP2K2 GENE SEQUENCING

**Test Code:** SMAP2
**Turnaround time:** 4 weeks
**CPT Codes:** 81479 x1

**Condition Description**
Cardiofaciocutaneous (CFC) syndrome is characterized by features in three primary systems: cardiac, craniofacial, and ectodermal; however, other systems may be involved as well. Cardiac abnormalities can include pulmonic stenosis and other valve dysplasias, septal defects, hypertrophic cardiomyopathy, and rhythm disturbances. Individuals with CFC syndrome have a distinctive craniofacial appearance. Ectodermal features include skin findings, such as xerosis, hyperkeratosis, ichthyosis, keratosis pilaris, ulerythema oophorogenes, eczema, pigmented moles, palmoplantar hyperkeratosis; hair findings such as sparse, curly, fine or thick, woolly, or brittle hair, and possible absent eyelashes and eyebrows; and the nails may be dystrophic or fast growing. Cognitive delay (ranging from mild to severe) is seen in all affected individuals. Neoplasias have been reported in some individuals with CFC.

There are four genes known to be associated with CFC. Mutations in the BRAF gene account for ~75% of cases, MAP2K1 and MAP2K2 account for ~25% of cases, and KRAS accounts for <2% of cases. CFC syndrome is inherited in an autosomal dominant manner; however, most cases of CFC syndrome arise de novo.

Please note that this test is for the MAP2K2 (19p13.3) gene only.

For patients with suspected MAP2K2-related CFC syndrome, 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 #601263: MAP2K2 gene
- OMIM #115150: CFC syndrome

**Genes**
MAP2K2

**Indications**
This test is indicated for:
- Confirmation of a clinical diagnosis of MAP2K2-related CFC syndrome.
- Carrier testing in adults with a family history of MAP2K2-related CFC syndrome.

**Methodology**
PCR amplification of 11 exons contained in the MAP2K2 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: Mutations in the MAP2K1 and MAP2K2 genes account for ~25% of cases. 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

* 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

Disclaimer: This information is confidential and subject to change without notice. It may not be reproduced in whole or part unless authorized in writing by an authorized EGL representative.
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.

### Related Tests

- Deletion/duplication analysis of the MAP2K2 gene by CGH array is available for those individuals in whom sequence analysis is negative.
- Sequence and deletion/duplication analysis are also available for the KRAS and BRAF genes.
- 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.