Albinism is a general term used to describe an absence of pigment in the eyes, skin, or hair. Individuals with any of the forms of albinism may have mild to severe oculo-cutaneous clinical manifestations. Ocular hallmarks of all types of albinism include nystagmus, iris translucency, foveal hypoplasia, reduction in visual acuity, and misrouting of the optic nerve fibers at the chiasm (detected by altered visually evoked potentials).

Pathogenic variants in the TYR gene are known to cause autosomal recessive oculocutaneous albinism type 1 (OCA1) which is characterized by the ocular changes found in all types of albinism (see introduction above) along with hypopigmentation of the skin and hair. It is divided into two general subgroups: OCA1A (loss of protein function) and OCA1B (partially active/hypomorphic protein function). Throughout life, individuals with OCA1A have white hair, white skin, blue translucent irides, retinal pigment epithelium cells without melanin, and poor vision. In comparison to OCA1A, individuals with OCA1B can have a milder phenotype with hair and iris color that may darken over time.

Pathogenic variants in the OCA2 gene (previously known as the P gene) are known to cause autosomal recessive oculocutaneous albinism type 2 (OCA2) which is characterized by the ocular changes found in all types of albinism (see introduction above) along with skin and hair pigmentation that ranges from very light to almost normal for a given ethnic background. Vision is stable, usually better than found in OCA1 and may improve in adolescence.

Pathogenic variants in the TYRP1 gene are known to cause autosomal recessive oculocutaneous albinism type 3 (OCA3) which is characterized by the ocular changes found in all types of albinism (see introduction above) along with an accumulation of reddish pigment in the skin and hair.

Pathogenic variants in the SLC45A2 gene (previously called MATP and AIM1) are known to cause autosomal recessive oculocutaneous albinism type 4 (OCA4) which is characterized by the ocular changes found in all types of albinism (see introduction above) along with hypopigmentation of the skin and hair. The clinical presentation of OCA4 and OCA2 are very similar; however, OCA4 has a higher prevalence in the Japanese population.

Pathogenic variants in the GPR143 gene are known to cause X-linked ocular albinism type 1 (OA1, also known as Nettleship-Falls ocular albinism or XLOA) which, in males, is characterized by the ocular changes found in all types of albinism (see introduction above) along with non-progressive vision loss, strabismus, and generally minor skin findings. Carrier females may show a characteristic mosaic pigmentation pattern of the retinal pigment epithelium.

References:
- OMIM
- GeneReviews
- Emory and Rimoin's Principles and Practice of Medical Genetics, 5th Edition

**Genes**

GPR143, LRMDA, OCA2, SLC24A5, SLC45A2, TYR, TYRP1

**Indications**

This test is indicated for:
- Confirmation of a clinical diagnosis of albinism.
- Carrier testing in adults with a family history albinism.

**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: Saliva**

**Specimen Requirements:**
Oragene™ Saliva Collection Kit
Orangene™ 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.

**Type: DNA, Isolated**

**Specimen Requirements:**
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: 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.

**Special Instructions**

Please include fundus photographs, electroretinogram (ERG) findings, visual field findings, and visual acuity, if available, for expert review and clinical correlation with test results.

**Related Tests**

- Eye Disorders: Comprehensive Sequencing and Deletion/Duplication Panels.
- Albinism: Deletion/Duplication Panel.