

PLEC-related Epidermolysis Bullosa: PLEC Gene Deletion/Duplication

Test Code: DPLEC

Turnaround time: 2 weeks

CPT Codes: 81228 x1

Condition Description

Epidermolysis Bullosa with Muscular Dystrophy (EB-MD)

Approximately 50 cases of epidermolysis bullosa-muscular dystrophy (EB-MD) have been reported worldwide. Blistering occurs early and is generally mild. Muscular dystrophy may not appear until later childhood, adolescence, or in some cases adulthood, and can cause immobility and eventually death later in life. Mutations have been described throughout the *PLEC* (also known as *PLEC1*) gene (8q24). Inheritance is autosomal recessive.

Epidermolysis Bullosa with Pyloric Atresia (EB-PA)

Epidermolysis bullosa with pyloric atresia (EB-PA) is characterized by fragility of the skin and mucous membranes, manifest by blistering with little or no trauma; congenital pyloric atresia; and ureteral and renal anomalies (dysplastic/multicystic kidney, hydronephrosis/hydronephrosis, ureterocele, duplicated renal collecting system, absent bladder). The course of EB-PA is usually severe and often lethal in the neonatal period. Although most affected children succumb as neonates, those who survive may have severe blistering with formation of granulation tissue on the skin around the mouth, nose, fingers, and toes, and internally around the trachea. However, some affected individuals have little or no blistering later in life. Additional features shared by EB-PA and the other major forms of EB include congenital localized absence of skin (aplasia cutis congenita), milia, nail dystrophy, scarring alopecia, hypotrichosis, and contractures.

Because the clinical features of all types of epidermolysis bullosa (EB) overlap significantly, examination of a skin biopsy by transmission electron microscopy (TEM) and/ or immunofluorescent antibody/antigen mapping is usually required to establish the diagnosis. The three genes known to be associated with EB-PA are *ITGB4* (~80% of EB-PA), *ITGA6* (~5%), and *PLEC* (~15%).

EB-PA is inherited in an autosomal recessive manner.

Epidermolysis Bullosa Simplex, Onga Type

Epidermolysis bullosa simplex, Onga type has been observed in one Norwegian and one German family with autosomal dominant inheritance. It is a result of the site-specific missense p.Arg2110Trp mutation in *PLEC*. A single lethal case of autosomal recessive EBS resulting from *PLEC* mutations has also been described, as has a case of EBS with severe mucous membrane involvement as a result of mutations in *PLEC*.

For patients with suspected *PLEC*-related EB, 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: [Epidermolysis Bullosa with Pyloric Atresia](#)
- OMIM #612138: [Epidermolysis Bullosa Simplex with Pyloric Atresia](#)
- OMIM #226670: [Epidermolysis Bullosa Simplex with Muscular Dystrophy](#)
- OMIM #131950: [Epidermolysis Bullosa Simplex, Onga Type](#)

Genes

[PLEC](#), PLEC1

Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of *PLEC*-related epidermolysis bullosa in individuals who have tested negative for sequence analysis
- Carrier testing in adults with a family history of *PLEC*-related epidermolysis bullosa 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.

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

Type: DNA, Isolated

Specimen Requirements:

Microtainer

3µg

Isolation using the Perkin Elmer™ Chemagen™ 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

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

- Sequence analysis of the *PLEC* gene is available and is required before deletion/duplication analysis.
- [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 to adults who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.