## Condition Description

Dyskeratosis congenita (DKC) is a bone-marrow failure syndrome characterized by:

- early onset of cutaneous hyperpigmentation
- nail dystrophy
- hyperkeratotic palms
- hypotrichosis
- continuous lacrimation due to atresia of the lacrimal ducts
- poor dentition
- oral leukoplakia

Other symptoms include:

- thrombocytopenia
- anemia
- testicular atrophy
- Hodgkin disease
- pancreatic adenocarcinoma
- deafness

Reports on various families with individuals with the condition also include features such as:

- prenatal and postnatal growth retardation
- mental retardation
- elevated immunoglobulin levels
- gastrointestinal hemorrhage from mucosal ulcerations
- intracranial calcifications
- nutmeg-like cirrhosis of the liver

Bone marrow failure has been reported in approximately 50% of cases of DKC, and in some patients symptoms related to aplastic anemia may precede the diagnosis of DKC. In 70% of cases, pancytopenia is the cause of death. Males are affected in a pattern consistent with X-linked recessive inheritance. Variability in the age of onset, severity of bone marrow failure, and range of congenital abnormalities has been observed. Mutations in the \(DKC1\) gene (Xq28) have been shown to cause DKC.

Mutations in \(DKC1\) also cause Hoyeraal-Hreidarsson syndrome (HHS), which is a more severe form of dyskeratosis congenita. Hoyeraal-Hreidarsson syndrome is a multisystem disorder affecting males and is characterized by:

- aplastic anemia
- immunodeficiency
- microcephaly
- cerebellar hypoplasia
- growth retardation

HHS may be a severe form of DKC in which affected individuals pass away before characteristic mucocutaneous features develop.

The protein product of the \(DKC1\) gene, dyskerin, is associated with small nucleolar RNA6s and with human telomerase RNA. The pathology of DKC is consistent with compromised telomerase function leading to a defect in telomere maintenance, which may limit the proliferative capacity of human somatic cells in epithelia and blood. Most mutations causing dyskeratosis congenita are missense mutations, although noncoding mutations have been described. In one study, mutations in the \(DKC1\) gene were detected in 21 of 37 families with dyskeratosis congenital. In another study, sequence variations were detected in 10 of 25 families. In a third study, four mutations were identified in five males with presumed X-linked dyskeratosis congenita.

For patients with suspected X-linked dyskeratosis congenita, 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.

Please [click here](#) for the OMIM summary on this condition.

### Genes

- **DKC1**

### Indications

This test is indicated for:

- Confirmation of a clinical/biochemical diagnosis of X-linked dyskeratosis congenita in an individual in whom sequencing analysis was negative.
Carrier testing in adult females with a family history of X-linked dyskeratosis congenita in whom sequencing analysis was negative.

**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™ 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**

Please submit copies of diagnostic biochemical test results along 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**

- X-Linked Dyskeratosis Congenita: **DKC1 Gene Sequencing (SV)** is required before deletion/duplication analysis.
- X-Linked Mental Retardation: **64-Gene Deletion/Duplication (OL)**.
- Prenatal testing is available to couples who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.

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