Diamond Blackfan Anemia Gene Sequencing Panel

Genes Tested:

EPO	*GATA1*	*RPL11*	*RPL15*	*RPL18*
RPL26	*RPL27*	*RPL31*	*RPL35*	*RPL35A*
RPL5	*RPL9*	*RPS10*	*RPS15*	*RPS15A*
RPS17	*RPS19*	*RPS24*	*RPS26*	*RPS27*
RPS27A	*RPS28*	*RPS29*	*RPS7*	*TSR2*

Disorder:

Diamond Blackfan anemia (DBA) is an inherited bone marrow failure syndrome caused by defects of ribosome biogenesis. DBA is characterized by infantile or early childhood onset red cell anemia, although growth retardation and congenital malformations are common features. Approximately 30% to 50% of patients have congenital malformations of the limbs, head, face, heart, and/or genitourinary system. Individuals with DBA are at increased risk of developing hematopoetic malignancies as well as solid tumors, including acute myeloid leukemia and osteogenic sarcoma. The phenotypic spectrum of Diamond Blackfan anemia is broad, and symptoms can vary markedly between affected individuals, even between family members. X-linked thrombocytopenia with or without anemia and secondary to pathogenic variants in *GATA1* is included in this panel because of its phenotypic overlap with DBA.

Genetics:

Diamond Blackfan anemia is a genetically heterogeneous disorder, and is inherited in an autosomal dominant pattern. Approximately 45% of cases are inherited from an affected parent and 55% are isolated cases. DBA shows incomplete penetrance, therefore some individuals with pathogenic variants do not meet diagnostic criteria, but may be at increased risk of developing malignancies. *GATA1* and *TSR2* pathogenic variants are inherited in an X-linked pattern.

Indications:

Diamond Blackfan Anemia Panel by NGS

Confirmation of diagnosis in a patient with the following symptoms:

- Classic DBA: normochromic macrocytic anemia in the absence of other cytopenias, reticulocytopenia, normal marrow cellularity with a paucity of erythroid precursors, age of onset less than one year
- Non-classic DBA: macrocytosis, elevated erythrocyte adenosine deaminase activity, or elevated HbF with mild or absent anemia, short stature or congenital anomalies consistent with DBA, adult onset of symptoms of DBA

Gene Specific Sequencing:

- Confirmation of genetic diagnosis in a patient with DBA and in whom a specific genetic diagnosis is suspected

Variant Specific Analysis:

- Presymptomatic testing of at-risk family members for medical management and prior to bone marrow donation
- Prenatal diagnosis of an at-risk fetus, after confirmation of variant(s) in the parent(s) and by prior arrangement only.

Specimen:

At least 3 mLs whole blood in a lavender top (EDTA) tube or saliva in an Oragene saliva kit. Please call 513-636-4474 for a free saliva collection kit.

Note: For post-transplant patients, we accept pre-transplant samples or post-transplant skin fibroblasts ONLY (blood, saliva, and cytobrushes are not accepted). Culturing of skin fibroblasts is done at an additional charge.

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changing the outcome together

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Testing Methodology:

Diamond Blackfan Anemia panel by NGS: This test is performed by enrichment of the coding exons, flanking intronic and untranslated regions (5' and 3'), as well as known pathogenic variants (HGMD 2018.4) in the promoter and deep intronic regions of the genes specified above using oligonucleotide probe hybridization followed by next-generation sequencing with >50X coverage at every target base. All pathogenic and likely pathogenic variants, as well as variants of unknown (indeterminate) significance, as determined bioinformatically, are confirmed by Sanger sequencing. Regions with <50X will be filled in by Sanger sequencing. A detailed non-coding variant list is available upon request.

Gene specific sequencing: PCR-based sequencing of the entire coding region and intron/exon boundaries of the specified gene and selected known pathogenic variants in the promoter and deep intronic regions.

Variant specific analysis: Sanger sequencing following PCR amplification of the targeted variant(s) of the specified gene.

Test Sensitivity:

Analytical Sensitivity: The sensitivity of DNA sequencing is over 99% for the detection of nucleotide base changes, small deletions and insertions in the regions analyzed.

Limitations: Variants in the regulatory regions and non-reported variants in the untranslated regions may not be detected by this test. Large deletions/ duplications, large insertions and other complex genetic events will not be identified using sequencing methodology.

Note: Single gene sequencing and targeted variant analysis is also available for all genes on the Diamond Blackfan Anemia Panel. Deletion/duplication is available for many of the genes on this panel. For further details, visit: www.cincinnatichildrens.org/deldup.

Turn-Around Time:

- DBA NGS Panel: up to 6 weeks
- Single gene sequencing: up to 28 days

CPT Codes:

- **Diamond Blackfan Anemia Panel by NGS:** 81443
- **Single gene sequencing, targeted variant analysis, and deletion/duplication:** call for information.

Please call 1-866-450-4198 for current pricing, insurance preauthorization or with any billing questions.

Results:

Results will be reported to the referring physician or health care provider as specified on the test requisition.

Shipping Instructions:

Please enclose **test requisition** with sample.
All information must be completed before sample can be processed.

Place samples in styrofoam mailer and ship at room temperature by overnight Federal Express to arrive Monday through Friday.

Ship to:

Cytogenetics and Molecular Genetics Laboratories
3333 Burnet Avenue NRB 1042
Cincinnati, OH 45229
513-636-4474

References:

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