Biotinidase Deficiency (BTD) Sequencing

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Biotinidase deficiency (BTD), a disorder that affects approximately 1 in 60,000 individuals, is caused by biallelic pathogenic variants in the *BTD* gene.[1] Specific variants are associated with the degree of deficiency, either partial or profound. Molecular testing of the *BTD* gene may be useful if enzymatic testing suggests BTD.

Deficiency in biotinidase enzymatic activity impairs the body's ability to recycle and reuse the vitamin biotin, resulting primarily in neurologic and dermatologic manifestations.[2,3] Timely diagnosis is important. Early identification and treatment of BTD can prevent and even reverse some symptoms, whereas untreated BTD may result in permanent neurologic, visual, and hearing impairment.[2,4] Refer to the ARUP Consult Biotinidase Deficiency topic for additional information about screening and laboratory testing for this condition.

Featured ARUP Testing

Biotinidase Deficiency (BTD) Sequencing 3004424

Method: Massively Parallel Sequencing

Molecular DNA test to confirm a diagnosis of BTD when biotinidase enzymatic activity is low

If a familial sequence variant has been previously identified, targeted sequencing for that variant may be appropriate; refer to the Laboratory Test Directory for additional information.

Disease Overview

Incidence

- Carrier frequency: 1/120[5]
- Variants confer[5]:
  - Profound BTD in 1/~137,000
  - Partial BTD in 1/~110,000
  - Profound and partial BTD (combined incidence) in 1/~61,000

Symptoms

- Profound BTD (<10% of normal biotinidase activity)[3]:
  - Seizures
  - Developmental delay
  - Hypotonia
  - Ataxia
  - Vision problems
  - Hearing loss
  - Alopecia
  - Rashes
- Partial BTD (10-30% of normal biotinidase activity)[3]
  - Mild forms of symptoms associated with profound BTD may manifest under stress (e.g., surgery or infection).[5]

Screening

- Newborn screening for BTD is performed across the United States.[3]
- Confirmatory testing following an abnormal newborn screen includes evaluation of enzyme activity in serum and may include molecular testing of the *BTD* gene.[3]

Refer to the American College of Medical Genetics and Genomics Biotinidase Deficiency algorithm for more information.[6]

Genetics

Gene

BTD (NM_001370658)

Inheritance

Autosomal recessive

Genotype-Phenotype Correlation

Most pathogenic variants in BTD cause complete or near-complete loss of enzymatic activity. However, p.Asp444His is a common variant associated with a milder phenotype.[5]

Test Interpretation

Clinical Sensitivity

99%

Analytic Sensitivity

For massively parallel sequencing:

Variant Class	Analytic Sensitivity (PPA) Estimate[a] (%)	Analytic Sensitivity (PPA) 95% Credibility Region[a] (%)
SNVs	99.2	96.9-99.4
Deletions, 1-10 bp	93.8	84.3-98.2
Deletions, 11-44 bp	99.9	87.8-100
Insertions, 1-10 bp	94.8	86.8-98.5
Insertions, 11-23 bp	99.9	62.1-100

[a]Gene included in this test is a subset of a larger methods-based validation from which the PPA values are derived.

bp, base pairs; PPA, positive percent agreement; SNVs, single nucleotide variants

Results

Variant(s) Detected	Clinical Significance
2 pathogenic *BTD* gene variants identified on opposite chromosomes	Predicts a diagnosis of BTD
1 severe and 1 mild *BTD* gene variant identified	Predicts partial BTD
1 copy of a pathogenic *BTD* gene variant identified	Predicts that individual is at least a carrier of BTD
No pathogenic gene variants detected by sequencing	Likelihood is reduced that the individual is a carrier of or affected by BTD

Limitations

- Diagnostic errors may occur due to rare sequence variations.

- Large deletions and duplications are not detected.
- Deep intronic and promoter variants will not be detected.
- A negative result does not exclude a diagnosis of BTD.
- The following exon is not sequenced due to technical limitations of the assay:
  - *BTD* (NM_000060) exon 1

References

1. National Organization for Rare Disorders (NORD). Rare Disease Database: biotinidase deficiency. Published 2019; accessed Feb 2021.

2. Hayek W, Dumin Y, Tal G, et al. Biotinidase deficiency: a treatable neurological inborn error of metabolism. *Isr Med Assoc J*. 2019;21(3):219-221.

3. Strovel ET, Cowan TM, Scott AI, et al. Laboratory diagnosis of biotinidase deficiency, 2017 update: a technical standard and guideline of the American College of Medical Genetics and Genomics. *Genet Med*. 2017;19(10).

4. Wolf B. Biotinidase deficiency should be considered in individuals thought to have multiple sclerosis and related disorders. *Mult Scler Relat Disord*. 2019;28:26-30.

5. Wolf B. Biotinidase deficiency. In: Adam MP, Ardinger HH, Pagon RA, et al, eds. *GeneReviews.* University of Washington, Seattle. Last update Jun 2016; accessed Feb 2021.

6. American College of Medical Genetics and Genomics. Biotinidase deficiency [algorithm]. Reaffirmed Feb 2026; accessed Sep 2026.

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