Test Definition: AIHL

Aminoglycoside-Induced Hearing Loss, Targeted Variant Testing, Droplet Digital PCR, Varies

Overview

Useful For

Identification of individuals who may be at risk for aminoglycoside-induced hearing loss (AIHL)

Establishing a diagnosis of late-onset sensorineural hearing loss associated with aminoglycoside exposure

Identifying mitochondrial variants associated with AIHL, allowing for predictive testing of at-risk family members

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
CULAF	Amniotic Fluid Culture/Genetic Test	Yes	No
_STR1	Comp Analysis using STR (Bill only)	No, (Bill only)	No
_STR2	Add'l comp analysis w/STR (Bill Only)	No, (Bill only)	No
CULFB	Fibroblast Culture for Genetic Test	Yes	No
MATCC	Maternal Cell Contamination, B	Yes	No

Genetics Test Information

This test detects 2 mitochondrial gene *RNR1* (MT-RNR1) variants, m.1555A>G and m.1494C>T, which are the most common variants associated with aminoglycoside induced ototoxicity.

Testing Algorithm

Cultured fibroblast specimens:

For cultured fibroblast specimens, a fibroblast culture will be performed at an additional charge. If viable cells are not obtained, the client will be notified.

Cord blood:

For cord blood specimens that have an accompanying maternal blood specimen, maternal cell contamination studies will be performed at an additional charge.

Special Instructions

- Informed Consent for Genetic Testing
- Informed Consent for Genetic Testing (Spanish)
- Molecular Genetics: Hereditary Hearing Loss Patient Information

Highlights
This test uses droplet digital polymerase chain reaction to evaluate for the presence of 2 mitochondrial variants associated with aminoglycoside-induced hearing loss.

Method Name
Droplet Digital Polymerase Chain Reaction (ddPCR)

NY State Available
Yes

Specimen

Specimen Type
Varies

Ordering Guidance
The preferred genetic test for diagnosis in individuals with suspicion of syndromic or non-syndromic hereditary hearing loss is AHLP / AudioloGene Hearing Loss Panel, Varies.

Specimen Required
Patient Preparation: A previous hematopoietic stem cell transplant from an allogenic donor will interfere with testing. For information about testing patients who have received a hematopoietic stem cell transplant, call 800-533-1710.

Submit only 1 of the following specimens:

Specimen Type: Whole blood
Container/Tube: Lavender top (EDTA) or yellow top (ACD)
Specimen Volume: 3 mL
Collection Instructions:
1. Invert several times to mix blood.
2. Send whole blood specimen in original tube. **Do not aliquot**.
3. Whole blood collected postnatal from an umbilical cord is also acceptable. See Additional Information
Specimen Stability Information: Ambient (preferred) 4 days/Refrigerated 4 days/Frozen 4 days
Additional Information:
1. Specimens are preferred to be received within 4 days of collection. Extraction will be attempted for specimens received after 4 days, and DNA yield will be evaluated to determine if testing may proceed.
2. To ensure minimum volume and concentration of DNA are met, the requested volume must be submitted. Testing may be canceled if DNA requirements are inadequate.
3. For postnatal umbilical cord whole blood specimens, maternal cell contamination studies are recommended to ensure test results reflect that of the patient tested. A maternal blood specimen is required to complete maternal cell contamination studies. Order MATCC / Maternal Cell Contamination, Molecular Analysis, Varies on both the cord blood

and maternal blood specimens under separate order numbers.

Specimen Type: Saliva
Patient Preparation: Patient should not eat, drink, smoke, or chew gum 30 minutes prior to collection.
Supplies:
DNA Saliva Kit High Yield (T1007)
Saliva Swab Collection Kit (T786)
Container/Tube:
Preferred: High-yield DNA saliva kit
Acceptable: Saliva swab
Specimen Volume: 1 Tube if using T1007 or 2 swabs if using T786
Collection Instructions: Collect and send specimen per kit instructions.
Specimen Stability Information: Ambient (preferred) 30 days/Refrigerated 30 days
Additional Information: Saliva specimens are acceptable but not recommended. Due to lower quantity/quality of DNA yielded from saliva, some aspects of the test may not perform as well as DNA extracted from a whole blood sample. When applicable, specific gene regions that were unable to be interrogated will be noted in the report. Alternatively, additional specimen may be required to complete testing.

Specimen Type: Blood spot
Supplies: Card-Blood Spot Collection (Filter Paper) (T493)
Container/Tube:
Preferred: Collection card (Whatman Protein Saver 903 Paper)
Acceptable: PerkinElmer 226 filter paper or blood spot collection card
Specimen Volume: 2 to 5 Blood spots
Collection Instructions:
1. An alternative blood collection option for a patient older than 1 year is a fingerstick. For detailed instructions, see How to Collect a Dried Blood Spot Sample.
2. Let blood dry on the filter paper at ambient temperature in a horizontal position for a minimum of 3 hours.
3. Do not expose specimen to heat or direct sunlight.
4. Do not stack wet specimens.
5. Keep specimen dry.
Specimen Stability Information: Ambient (preferred)/Refrigerated
Additional Information:
1. Blood spot specimens are acceptable but not recommended. Multiple extractions will be required to obtain sufficient yield for supplemental analysis, and there is significant risk for test failure due to insufficient DNA.
2. Due to lower concentration of DNA yielded from blood spot, some aspects of the test may not perform as well as DNA extracted from a whole blood sample. When applicable, specific gene regions that were unable to be interrogated will be noted in the report. Alternatively, additional specimen may be required to complete testing.
3. For collection instructions, see Blood Spot Collection Instructions
4. For collection instructions in Spanish, see Blood Spot Collection Card-Spanish Instructions (T777)
5. For collection instructions in Chinese, see Blood Spot Collection Card-Chinese Instructions (T800)

Specimen Type: Cultured fibroblasts

Source: Skin or tissue
Container/Tube: T-25 flask
Specimen Volume: 2 Flasks
Collection Instructions: Submit confluent cultured fibroblast cells from a skin or tissue biopsy. Cultured cells from a prenatal specimen will not be accepted.
Specimen Stability Information: Ambient (preferred) <24 hours/Refrigerated <24 hours
Additional Information:
1. Specimens are preferred to be received within 24 hours of collection. Culture and extraction will be attempted for specimens received after 24 hours and will be evaluated to determine if testing may proceed.
2. A separate culture charge will be assessed under CULFB / Fibroblast Culture for Biochemical or Molecular Testing. An additional 3 to 4 weeks are required to culture fibroblasts before genetic testing can occur.

Specimen Type: Extracted DNA
Container/Tube:
Preferred: Screw Cap Micro Tube, 2 mL with skirted conical base
Acceptable: Matrix tube, 1 mL
Collection Instructions:
1. The preferred volume is at least 100 mcL at a concentration of 75 ng/mcL.
2. Include concentration and volume on tube.
Specimen Stability Information: Frozen (preferred) 1 year/Ambient/Refrigerated
Additional Information: DNA must be extracted in a CLIA-certified laboratory or equivalent and must be extracted from a specimen type listed as acceptable for this test (including applicable anticoagulants). Our laboratory has experience with Chemagic, Puregene, Autopure, MagnaPure, and EZ1 extraction platforms and cannot guarantee that all extraction methods are compatible with this test. If testing fails, one repeat will be attempted, and if unsuccessful, the test will be reported as failed and a charge will be applied. If applicable, specific gene regions that were unable to be interrogated due to DNA quality will be noted in the report.

Forms

1. **New York Clients-Informed consent is required.** Document on the request form or electronic order that a copy is on file. The following documents are available:
-Informed Consent for Genetic Testing (T576)
-Informed Consent for Genetic Testing (Spanish) (T826)
2. Molecular Genetics Hereditary Hearing Loss Patient Information
3. If not ordering electronically, complete, print, and send a Therapeutics Test Request (T831) with the specimen.

Specimen Minimum Volume

See Specimen Required

Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Varies		

Clinical & Interpretive

Clinical Information

Aminoglycosides (tobramycin, streptomycin, and gentamicin, etc) are a group of broad-spectrum antibiotics commonly prescribed for infections caused by gram-negative bacteria. In the United States, approximately 4 million courses of aminoglycosides are administered each year with approximately 2% to 5% of treated patients developing clinically significant hearing loss. Mitochondrial gene *RNR1* (MT-RNR1) variants m.1555A>G and m.1494C>T are the most common variants associated with aminoglycoside-induced ototoxicity. Hearing loss associated with aminoglycoside exposure can occur even after a single dose and may be bilateral, irreversible, and often severe to profound. Avoidance of aminoglycoside antibiotics reduces the risk of developing hearing loss for individuals carrying one of these 2 variants.

The severity and onset of hearing loss in individuals with the associated disease-causing mitochondrial variants range from profound congenital deafness to mild to moderate late-onset hearing loss. Evidence demonstrates that this variance can often be explained by variant load in an individual. In contrast to variants in nuclear genes, which are present in either 0, 1, or 2 copies, mitochondrial variants can be present in any fraction of the total organelles, a phenomenon known as heteroplasmy. Penetrance of hearing loss without exposure to aminoglycosides is thought to be a function of the degree of heteroplasmy, with a correlation between higher fraction of altered mitochondria and higher penetrance. Hearing loss is believed to be 100% penetrant in homoplasmic individuals who receive aminoglycoside antibiotics.

Reference Values

An interpretive report will be provided.

Interpretation

The interpretive report includes an overview of the findings as well as the associated clinical significance.

Cautions

Clinical Correlations:
Test results should be interpreted in context of clinical findings, family history, and other laboratory data. Misinterpretation of results may occur if the information provided is inaccurate or incomplete.

If testing was performed because of a clinically significant family history, it is often useful to first test an affected family member. Detection of a reportable variant in an affected family member would allow for more informative testing of at-risk individuals.

Technical Limitations:
This assay will not detect all variants or genes that cause mitochondrial nonsyndromic hearing loss and deafness. Therefore, the absence of a detectable variant does not rule out the possibility that an individual is a carrier of or affected with mitochondrial non-syndromic hearing loss and deafness.

Some individuals who are a carrier or have a diagnosis of mitochondrial nonsyndromic hearing loss and deafness may have a variant that is not identified by this assay. The absence of a variant, therefore, does not eliminate the possibility of a hereditary hearing loss disorder. For predictive testing of asymptomatic individuals, it is important to first document the presence of a gene variant in an affected family member.

Of note, absence of the mitochondrial variants MT-RNR1 m.1494C>T or MT-RNR1 m.1555A>G does not rule out the presence of these variants below the limits of detection of this assay (<5% heteroplasmy).

Rare alterations exist that could lead to false-negative or false-positive results. If results obtained do not match clinical findings, additional testing should be considered.

Clinical Reference

1. Gao Z, Chen Y, Guan MX. Mitochondrial DNA mutations associated with aminoglycoside induced ototoxicity. J Otol. 2017;12(1):1-8
2. Krause KM, Serio AW, Kane TR, Connolly LE. Aminoglycosides: An overview. Cold Spring Harb Perspect Med. 2016;6(6):a027029
3. Qian Y, Guan MX. Interaction of aminoglycosides with human mitochondrial 12S rRNA carrying the deafness-associated mutation. Antimicrob Agents Chemother. 2009;53(11):4612-4618
4. Usami S, Nishio S. Nonsyndromic hearing loss and deafness, mitochondrial. In: Adam MP, Feldman J, Mirzaa GM, et al, eds. GeneReviews [Internet]. University of Washington, Seattle; 2004. Updated June 14, 2018. Accessed November 20, 2025. Available at www.ncbi.nlm.nih.gov/books/NBK1422/

Performance

Method Description

This test is a droplet digital polymerase chain reaction method for the detection of MT-RNR1 m.1494C>T and MT-RNR1 m.1555A>G associated with aminoglycoside-induced hearing loss. Variant nomenclature is based on the following GenBank Accession number (build GRCh37 [hg19]): NC_012920.1.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

1 to 7 days-Specimens must arrive in the performing laboratory by 12 p.m. for the report to be available 1 day from specimen receipt.

Specimen Retention Time

Whole blood: 28 days (if available); Saliva: 30 days (if available); Extracted DNA: 3 months; Blood spots: 1 year (if

available)

Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Main Campus

Fees & Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

81401

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
AIHL	Aminoglycoside-Induced Hearing Loss	101633-6

Result ID	Test Result Name	Result LOINC® Value
609786	Specimen	31208-2
609787	Source	31208-2
609788	Result Summary	50397-9
609789	Result	82939-0
609790	Interpretation	69047-9
609791	Additional Information	48767-8
609792	Method	85069-3
609793	Disclaimer	62364-5
609794	Released By	18771-6