MAYO CLINIC LABORATORIES

Test Definition: NAT2Q

N-Acetyltransferase 2 (NAT2) Genotype, Varies

Overview

Useful For

Identifying patients who may be at risk for altered metabolism of drugs that are substrates of arylamine *N*-acetyltransferase type 2, including isoniazid

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
CULFB	Fibroblast Culture for Genetic Test	Yes	No
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
MATCC	Maternal Cell Contamination, B	Yes	No

Testing Algorithm

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
- Pharmacogenomic Association Tables
- Multiple Genotype Test List
- Informed Consent for Genetic Testing (Spanish)

Method Name

Real-Time Polymerase Chain Reaction (PCR) with Allelic Discrimination Analysis

NY State Available

Yes

Specimen

Specimen Type

Varies

Specimen Required

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

Submit only 1 of the following specimens:

Specimen Type: Whole blood
Container/Tube: Lavender top (EDTA)
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: Extracted DNA
Container/Tube:
Preferred: Screw Cap Micro Tube, 2mL with skirted conical base
Acceptable: Matrix tube, 1mL

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. If not ordering electronically, complete, print, and send 1 of the following with the specimen:
-Neurology Specialty Testing Client Test Request (T732)
-Therapeutics Test Request (T831)

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
Arylamine *N*-acetyltransferase type 2 (NAT2) is a highly polymorphic phase 2 metabolic enzyme that conjugates hydrazine derivatives and aromatic amine drugs with acetyl-groups.(1) NAT2 also is involved in the acetylation and activation of some procarcinogens.(1,2)

Individuals acetylate drugs at different rates by NAT2 and are described as having slow, intermediate, or rapid (fast) acetylator phenotypes. Some studies, which have examined diversity of *NAT2* haplotypes among individuals of different ethnicities hypothesize that the NAT2 slow acetylator phenotype was positively selected for in the transition from hunter-gatherer or nomadic lifestyle to an agricultural or pastoral lifestyle.(3) The prevalence of slow acetylator phenotypes increases with decreasing distance to the equator. Near the equator, up to 80% of individuals may be slow acetylators, while in some more northern countries, as few as 10% of the population may have the slow acetylator

phenotype.

A number of drugs are metabolized by NAT2 including procainamide, dapsone, nitrazepam, hydralazine, sulfasalazine, amifampridine, and isoniazid.(4) Isoniazid is used to treat and prevent tuberculosis and is still used as a primary treatment agent. Adverse reactions with isoniazid, which include nausea, drug-induced hepatitis, peripheral neuropathy, and sideroblastic anemia, are associated more often with a slow NAT2 acetylator phenotype. These individuals may require a lower dose to avoid adverse reactions.(4) Of note, acetaminophen is a significant NAT2 inhibitor.

The *NAT2* gene contains a single intronless exon of 870 base pairs and encodes 290 amino acids. *NAT2* is highly polymorphic and contains at least 16 known single nucleotide variants and 1 single base pair deletion. These genetic variants are combined into 36 known haplotypes or alleles. Each individual haplotype is predictive of either a rapid (fast) or slow acetylator phenotype. Individuals with 2 rapid haplotypes are predicted to be rapid (normal) metabolizers, while those with 1 rapid and 1 slow haplotype are intermediate metabolizers, and those with 2 slow haplotypes are poor metabolizers.(5,6) Studies with patients who have different acetylator haplotypes have correlated the ratio of plasma N-acetylisoniazid/isoniazid drug concentrations with haplotypes, with slow and intermediate acetylators having lower ratios than rapid acetylators.(7) In March 2024, PharmVar announced the launch of the NAT2 webpage and made important changes to the NAT2 nomenclature.(9) This report uses legacy NAT2 nomenclature.(10)

NAT2 genotype results are used to predict metabolizer phenotypes, as indicated in the Table. Note that the reference allele for *NAT2* is *4 in the legacy nomenclature.(10) If no variants are detected, the default genotype and phenotype reported are *4/*4 and rapid acetylator phenotype, respectively.

Table. NAT2 alleles and function per legacy nomenclature(10)

***NAT2* allele**	**Predicted acetylator phenotype**
**4*	Rapid (normal)
**5*	Slow
**6*	Slow
**7*	Slow
**10*	Slow, but may be substrate dependent
**12D*	Slow
**14*	Slow
**17*	Slow
**19*	Slow

Reference Values

An interpretive report will be provided.

Interpretation

An interpretive report will be provided. The wild-type (normal) genotype for *NAT2* is *4. This is the most commonly occurring allele in some, but not all, ethnic groups.(8)

Individuals are classified as being slow, intermediate, or rapid (fast) acetylators depending on their diplotypes. Slow acetylators have 2 slow haplotypes, rapid acetylators have 2 rapid (fast, normal) haplotypes, and intermediate acetylators have one of each.

The genotype, with associated star alleles, is assigned using standard allelic nomenclature as described by the Human *NAT2* Alleles (Haplotypes) Database (https://nat.mbg.duth.gr/Human_NAT2_alleles.htm).(10)

For additional information regarding pharmacogenomic genes and their associated drugs, see Pharmacogenomic Associations Tables. This resource also includes information regarding enzyme inhibitors and inducers, as well as potential alternate drug choices.

Drug-drug interactions and drug-metabolite inhibition must be considered when adjusting medication dosage. It is important to interpret the results of testing and dose adjustments in the context of hepatic and renal function and patient age. For applicable medications, therapeutic drug monitoring is useful to verify that the drug concentration is within the therapeutic range.

Cautions

Rare variants (ie, polymorphisms) may be present that could lead to false-negative or false-positive results. If results obtained do not match the clinical findings (phenotype), additional testing should be considered.

Samples may contain donor DNA if obtained from patients who received non-leukocyte reduced blood transfusions or allogeneic hematopoietic stem cell transplantation. Results from samples obtained under these circumstances may not accurately reflect the recipient's genotype. For individuals who have received blood transfusions, the genotype usually reverts to that of the recipient within 6 weeks. For individuals who have received allogeneic hematopoietic stem cell transplantation, a pretransplant DNA specimen is recommended for testing.

NAT2 genetic test results in patients who have undergone liver transplantation may not accurately reflect the patient's arylamine *N*-acetyltransferase type 2 (NAT2) status.

This method may not detect all variants that result in altered NAT2 activity. Therefore, absence of a detectable variant does not rule out the possibility that a patient has altered NAT2 metabolism due to other *NAT2* variants that cannot be detected with this method. Furthermore, when 2 or more variants are identified, the cis-/trans-status (whether the variants are on the same or opposite chromosomes) is often not known; therefore, multiple haplotypes may be provided.

Clinical Reference

1. Salazar-Gonzalez RA, Doll MA, Hein DW. Human arylamine N-acetyltransferase 2 genotype-dependent protein expression in cryopreserved human hepatocytes. Sci Rep. 2020;10(1):7566
2. Meyer UA. Polymorphism of human acetyltransferases. Environ Health Perspect. 1994;102 Suppl 6(Suppl 6):213-216
3. McDonagh EM, Boukouvala S, Aklillu E, Hein DW, Altman RB, Klein TE. PharmGKB summary: very important pharmacogene information for N-acetyltransferase 2. Pharmacogenet and Genomics. 2014;24(8):409-425
4. Hein DW, Millner LM. Arylamine N-acetyltransferase acetylation polymorphisms: paradigm for pharmacogenomic-guided therapy- a focused review. Expert Opin Drug Metab Toxicol. 2021;17(1):9-21
5. Sabbagh A, Darlu P. Inferring haplotypes at the *NAT2* locus: the computational approach. BMC Genet. 2005;6:30
6. Leff MA, Fretland AJ, Doll MA, Hein DW. Novel human N-acetyltransferase 2 alleles that differ in mechanism for slow acetylator phenotype. J Biol Chem. 1999;274(49):34519-34522
7. Chen B, Li JH, Xu YM, Wang J, Cao XM. The influence of NAT2 genotypes on the plasma concentration of isoniazid and acetylisoniazid in Chinese pulmonary tuberculosis patients. Clin Chim Acta. 2006;365(1-2):104-108
8. Lin HJ, Han CY, Lin BK, Hardy S. Ethnic distribution of slow acetylator mutations in the polymorphic

N-acetyltransferase (NAT2) gene. Pharmacogenetics. 1994;4(3):125-134
9. PharmVar: Pharmacogene Variation Consortium. Updated December 2, 2025. Accessed January 22, 2026. Available at www.pharmvar.org/gene/NAT2
10. Human NAT2 alleles (haplotypes). Updated May 2024. Accessed January 22, 2026. Available at https://nat.mbg.duth.gr/Human_NAT2_alleles.htm

Performance

Method Description
Genomic DNA is extracted from whole blood or saliva. Genotyping for NAT2 alleles is performed using a polymerase chain reaction (PCR)-based 5'-nuclease assay. Fluorescently labeled detection probes anneal to the target DNA. PCR is used to amplify the section of DNA that contains the variant. If the detection probe is an exact match to the target DNA, the 5'-nuclease polymerase degrades the probe, the reporter dye is released from the effects of the quencher dye, and a fluorescent signal is detected. Genotypes are assigned based on the allele-specific fluorescent signals that are detected.(Unpublished Mayo method)

PDF Report
No

Day(s) Performed
Varies

Report Available
3 to 8 days

Specimen Retention Time
Whole blood: 25 days (if available); Saliva: 30 days (if available); Extracted DNA: 3 months

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.

Test Definition: NAT2Q

N-Acetyltransferase 2 (NAT2) Genotype, Varies

CPT Code Information

81479-Unlisted molecular pathology procedure

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
NAT2Q	NAT2 Genotype, V	101141-0

Result ID	Test Result Name	Result LOINC® Value
616425	NAT2 Genotype	101142-8
616426	NAT2 Phenotype	101143-6
616427	Interpretation	69047-9
616428	Additional Information	48767-8
616430	Method	85069-3
616429	Disclaimer	62364-5
616431	Reviewed By	18771-6