Test Definition: IL28Q

Interleukin 28B (IL28B) Variant (rs12979860), Varies

Overview

Useful For

Predicting responsiveness of genotype 1 hepatitis C viral infections to combined pegylated-interferon and ribavirin-based therapies

Special Instructions

- Informed Consent for Genetic Testing
- 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

Multiple genotype tests can be performed on a single specimen after a single extraction. See Multiple Genotype Test List for a list of tests that can be ordered together.

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

Submit only 1 of the following specimens:

Specimen Type: Whole blood
Container/Tube:
Preferred: Lavender top (EDTA)
Acceptable: None
Specimen Volume: 3 mL
Collection Instructions:
1. Invert several times to mix blood.
2. Send whole blood specimen in original tube. **Do not aliquot**.
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 is met, the preferred volume of blood must be submitted. Testing may be canceled if DNA requirements are inadequate.

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
Specimen Volume: 100 mcL
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) 1year /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 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

Individuals with hepatitis C virus (HCV) genotype 1 infections have variable responses to treatment with pegylated-interferon and ribavirin combination therapy. Some individuals will respond to treatment with sustained viral response, while other patients have poor response and fail to achieve sustained viral clearance.

Response to pegylated-interferon and ribavirin combination therapy in HCV genotype 1-infected individuals has been found to be closely associated with a single-nucleotide variant (SNV), designated rs12979860, located 3 kilobases upstream from the interleukin 28B gene locus (*IL28B*, *a*lso known as *IFNL3*) present on human chromosome 19.

HCV genotype 1-infected individuals with the CC genotype, as compared to either the CT or TT genotypes, of this SNP in *IL28B* have approximately 2- to 3-fold greater rates of sustained viral response to combined pegylated-interferon and ribavirin therapy.(1) Similar increases in sustained viral response rates were observed across various racial groups, including European Americans (95% CI, 1.8- to 2.3-fold), African Americans (95% CI, 1.9- to 4.7-fold), and Hispanics (95% CI, 1.4- to 3.2-fold).(1) The CC genotype has also been associated with a 3-fold increase in rate of spontaneous clearance of HCV.(2,4) The SNV in *IL28B* is only one of many factors that can influence response rates to pegylated-interferon and ribavirin combination therapy in HCV genotype 1 infection, and the SNV genotype result should be interpreted in the context of other clinical factors present in a given patient.

Frequency of the rs12979860 C allele varies across different racial and ethnic groups. The rs12979860 C variant is most frequently present in individuals from East Asia (allele frequency >0.9) and least common in individuals of African origin (allele frequency 0.2-0.5).(2) In a recent US-based study, the favorable CC genotype was observed in 37% of Whites, 29% Hispanics, and 14% of African Americans tested.

The mechanism by which the *IL28B* genotype mediates response to pegylated-interferon and ribavirin combination therapy among HCV genotype 1-infected individuals is not yet understood and is the subject of intense ongoing research. The impact of the *IL28B*-related alteration on response rates in patients infected with HCV genotypes other than genotype 1 is still being investigated.

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

Rare variants 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-leukoreduced 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.

For liver transplant patients, the *IL28B* genotype of the recipient and the donor are independent predictors of sustained virologic response with combined pegylated-interferon and ribavirin therapy.(3)

This test does not detect variants other than the rs12979860 single-nucleotide variant.

Clinical Reference

1. Ge D, Fellay J, Thompson AJ, et al. Genetic variation in IL28B predicts hepatitis C treatment-induced viral clearance. Nature. 2009;461(7262):399-401
2. Thomas DL, Thio CL, Martin MP, et al. Genetic variation in IL28B and spontaneous clearance of hepatitis C virus. Nature. 2009;461(7265):798-801
3. Charlton MR, Thompson A, Veldt BJ, et al. Interleukin-28B polymorphisms are associated with histological recurrence and treatment response following liver transplantation in patients with hepatitis C virus infection. Hepatology. 2011;53(1):317-324
4. Thompson AJ, Muir AJ, Sulkowski MS, et al. Interleukin-28B polymorphism improves viral kinetics and is the strongest pretreatment predictor of sustained virologic response in genotype 1 hepatitis C virus. Gastroenterology. 2010;139(1):120-9.e18. doi:10.1053/j.gastro.2010.04.013

Performance

Method Description

Genomic DNA is extracted from whole blood or saliva. Genotyping for the *IL28B* single nucleotide variant 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

Test Definition: IL28Q

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Day(s) Performed
Monday through Friday

Report Available
3 to 7 days

Specimen Retention Time
Whole blood, saliva swab: 2 weeks (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.

CPT Code Information
81283

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
IL28Q	IL28B Genotype, V	60279-7

Result ID	Test Result Name	Result LOINC® Value
610145	IL28B Genotype	60279-7
610146	IL28B Phenotype	In Process
610147	Interpretation	69047-9
610148	Additional Information	48767-8
610149	Method	85069-3
610150	Disclaimer	62364-5
610151	Reviewed by	18771-6