Interferon Lambda 3 (IFNL3) Genotyping

Disease Overview

IFNL3 (IL28B), encodes interferon-λ 3 (IFN-λ 3),a member of the type 3 IFN-λ family with antiviral, antiproliferative, and immune modulatory activities. IFN-λs can be induced by viruses and inhibit HCV replication in vitro. Variations within the IFNL3 gene is the strongest pretreatment response predictor in treatment naive Hepatitis C virus genotype 1. The mechanism by which IFNL3 affects antiviral response is not well understood at this time.

Uses for Test

- Estimate genetic risk of abnormal drug metabolism for drugs metabolized by ***IFNL3*** (Peg interferon alpha and ribavirin based regimens).
- Identify genotypes shown to have a drug-gene variant relationship.
- Pharmacogenomic orders may be reviewed by a pharmacist for clinical appropriateness prior to test completion if clinical data is available.

Therapeutic Implications

IFNL3 genotype/phenotype variability is closely linked to viral kinetics and improved sustained virologic response (SVR). The strongest predictor of treatment response to pegylated interferon alpha and ribavirin based regimens for hepatitis C is *IFNL3* genotype. A favorable response (70% chance of SVR after 48 weeks of treatment) is found when a patient displays the CC genotype. A 30 % chance of achieving SVR after 48 weeks is found in patients with CT or TT genotypes.

Treatment Guidelines

The Clinical Pharmacogenetics Implementation Consortium (CPIC) has published dosing guidelines for *IFNL3* genotypes: https://cpicpgx.org/

Test Interpretation

- Clinical sensitivity: drug dependent.
- Analytical sensitivity/specificity: > 99%.

Results

A detailed report is provided. This report is reviewed and signed out by a Laboratory Director. No mutations detected is predictive of *1 functional alleles.

Test Limitations

- Only the targeted *IFNL3* variants will be detected.
- Diagnostic errors can occur due to rare sequence variations.
- Risk of therapeutic failure or adverse reactions with *IFNL3* substrates may be affected by genetic and non-genetic factors that are not detected by this test.
- This result does not replace the need for therapeutic drug or clinical evaluation and monitoring.

Related Tests

- Multiple genes can be involved in drug metabolism, drug activation and drug action on the target tissue. Additional genotyping tests are available for *CYP2C19, CYP2C9, VKORC1, SLCO1B1, TPMT, CYP2D6 ,CYP4F2, CYP2C cluster, CYP3A5* and *DPYD* as individual tests or as a PGx Panel.
- The panel includes a comprehensive medication report based on the genotypes detected.
- Therapeutic drug monitoring and/or metabolic ratios may be useful for evaluating the pharmacokinetics of a particular drug for a patient.

Sample Requirements

- **Collection**
  - Lavender-top tube (EDTA)
  - All specimens should be sent in the original container and should not be aliquoted to another tube
  - The specimen submitted should only be used for this testing and should not be shared with any other testing that would also utilize this specimen type.
- **Specimen**
  - Whole blood, preferred volume: 2 mL to 4 mL (1mL minimum).
- **Stability**
  - Room temp – 72 hours
  - Refrigerated – 7 days
  - Frozen – 7 days
  - Not affected by hemolysis
  - Not affected by lipemia

Tests Involved

- CPT code: 81283
- Lab Test ID: LBOR0177

Test Schedule

- Set up Monday to Friday
- Turn Around Time: 5-7 days

Additional information

- These tests are available through the Sanford Imagenetics program. Contact Sanford Laboratories at (605) 328-5464 or (800) 522-2561 for questions regarding this testing.

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SANFORD Laboratories

Sanfordhealth.org/imagenetics

References

• Beverage JN, Sissung TM, Sion AM, et al: CYP2D6 polymorphisms and the impact on tamoxifen therapy. J Pharm Sci 96:2224-2231, 2007. • Ingelman-Sundberg Magnus, Sim Sarah C, Gomez Alvin, Rodriguez-Antona Cristina : Influence of cytochrome P450 polymorphisms on drug therapies: pharmacogenetic, pharmacoepigenetic and clinical aspects in Pharmacology & therapeutics (2007).• Gardiner Sharon J, Begg Evan J: Pharmacogenetics, drug-metabolizing enzymes, and clinical practice in Pharmacological reviews (2006). • Bernard S, Neville KA, et al. Interethnic differences in genetic polymorphisms in the U.S. Population: clinical implications. The Oncologist. 2006;11(2):126-135 • Weinshilboum Richard: Inheritance and drug response.The New England journal of medicine (2003). • Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for CYP2D6, available along with the 2015 supplement and other relevant resources at www.pharmgkb.org • The human cytochrome P450 (CYP) allele nomenclature database, available at www.cypalleles.ki.se/ • Sistonen Johanna, Sajantila Antti, Lao Oscar, Corander Jukka, Barbujani Guido, Fuselli Silvia in Pharmacogenetics and genomics(2007).