CPAL
Central Pennsylvania Alliance Laboratory

Technical Bulletin
No. 61

April 16, 2007

Hepatitis C Virus (HCV) Genotyping

Contact:
Dr. Jeffrey Wisotzkey, 717-851-1422
Technical Director, CPAL

Effective Date: May 1, 2007

Mnemonic: HCV GENO

Specimen: K-3/K-2 EDTA Plasma (2.0ml). Freeze within 4 hours. Short term storage (-18°C to -29°C). Long term storage, stable up to 12 months at -70°C.

Reference Range: Patients referred for HCV genotyping must have detectable HCV viral loads. Results will be reported as type 1,2,3,4,5 or 6. On rare occasion, a "mixed" genotype may be detected and will be reported as such.

Summary: The hepatitis C virus (HCV) has been classified into at least 6 distinct genotypes. The most prevalent genotypes in our geographic region are types 1 and 2. Classification of the HCV genotype is based on the primary nucleic acid (RNA) sequence of the viral genome. Diagnostic assays have been developed to determine the specific viral genotype. These methodologies include RNA (DNA) sequencing, LiPA (hybridization) and other methods that directly interrogate the nucleic acid sequence of the viral genome to specifically identify the genotype present in a clinical specimen.

HCV genotyping should be performed on all HCV infected persons prior to treatment in order to determine duration of therapy and likelihood of response[1]. Overall response rates vary according to genotype. In prospective treatment studies, genotype is the strongest predictor of response[1]. Patients with genotype 1 are typically less effectively treated with IFN-α, typically requiring twice the dose and duration of treatment, whereas genotypes 2 and 3 are more likely to respond to INF- α[2]. Sustained virological response rates (SVR) were higher in patients who have genotype 2 or genotype 3 HCV infections, lower pretreatment

HCV RNA levels, younger ages, lower body weights and the absence of bridging fibrosis and cirrhosis[1].

HCV genotype analysis is performed at CPAL using the Invader® HCV Genotyping reagents developed by Third Wave Technologies, Inc. This assay, like others, targets the 5'Non-coding (5'-NC) region of the HCV viral genome to determine the genotype. The assay utilizes the cleavase enzyme and fluorescence resonance energy transfer technologies, combined with automated, computerized data analysis to generate specific genotype identifications.

As with all laboratory results and disease conditions, treatment decisions should be made in conjunction with all clinical information, including HCV genotype, viral load, clinical history and other relevant clinical parameters. In addition, it is possible, on rare occasion, for a patient to be infected with more than one HCV type. Often times, the minor species is not detected by HCV genotyping assays. In cases of potential treatment failures/poor response, the presence of additional HCV types should be considered and may be detected upon subsequent testing, following initial treatment.

Subtyping

This laboratory does not provide HCV subtype data. With currently available drug regimens for therapeutic use in HCV infections, all published and accepted guidelines for management of hepatitis C recommend the use of standard genotyping, not subtyping to assist in determining the duration of therapy. The use of subtyping is not recommended for patient therapy purposes and should only be used for epidemiological purposes. In addition, currently there are no sufficiently accurate methods for generating subtype identification.

Analyte Specific Reagents Disclaimer

The HCV genotyping assay is derived from Invader® HCV Genotyping Analyte Specific Reagents (ASRs). Each HCV Genotype report will contain the following regulatory statement to reflect this fact.

This test was developed and its performance characteristics determined by the Central Pennsylvania Alliance Laboratory, York, PA. It has not been cleared or approved by the U.S. Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary. This test is used for clinical purposes. It should not be regarded as investigational or for research. This laboratory is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88) as qualified to perform high complexity clinical laboratory testing.

1. Strader, DB, T Wright, DL Thomas and LB Seeff. Diagnosis, Managemnt, and Treatment of hepatitis C. AASLD Practice Guideline. *Hepatology* 2004: 39: pp1147-1171.

2. McHutchinson, JG, SC Gordon, ER Schiff et al. Interferon Alfa-2b alone or in combination with ribavirin as initial treatment for chronic hepatitis C. *NEJM* 1998;339:1485-92.