BLOODCENTER of WISCONSIN

*Doing more good than you know*

January 26, 2009

MEMO

Blood Services
Medical Services
Diagnostic Laboratories
Blood Research Institute

TO: Customers and Colleagues

FROM: Michael Janasik
Account Manager, Diagnostic Laboratories

RE: New ELA2 Gene Sequencing Assay Available

BloodCenter of Wisconsin's Molecular Diagnostics Laboratory now offers an ELA2 Gene Sequencing Test. We are very pleased about this addition to our menu of tests for laboratory evaluation of patients with congenital and cyclic neutropenia.

Identification of a mutation in the *ELA2* gene confirms a diagnosis of congenital or cyclic neutropenia. Mutations in *ELA2* have been reported in 90-100% of cyclic neutropenia patients and 38-80% of congenital neutropenia patients.

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**_ELA2_-Related Neutropenia Sequence Analysis**

Method: PCR amplification and bi-directional DNA sequence analysis
Sample: 5 ml EDTA (lavender top) whole blood
Shipping: Room Temperature
Requisition: Molecular Diagnostics Testing
TAT: 2-3 weeks CPT Codes: 83891, 83892 x 5, 83898 x 5, 83904 x 5, 83912

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Contact Us: For additional information, contact Mike Janasik at (414) 937-6290 or Michael.Janasik@bcw.edu

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# *ELA2*-RELATED NEUTROPENIA SEQUENCE ANALYSIS

*BloodCenter of Wisconsin offers DNA sequencing of the ELA2 gene for diagnosis of congenital and cyclic neutropenia.*

## BACKGROUND:

*ELA2*-related neutropenia includes congenital and cyclic neutropenia. Both are characterized by recurrent fever, infections and inflammation of the mouth, skin and pharynx. Diagnosis of these disorders is based on clinical findings and serial measurement of the absolute neutrophil count (ANC). Cyclic neutropenia is distinguished from congenital neutropenia by regular oscillations of the ANC and generally milder infectious complications.

Identification of a mutation in the *ELA2* gene confirms a diagnosis of congenital or cyclic neutropenia. *ELA2*-related neutropenia is inherited in an autosomal dominant manner. *ELA2* is the only gene known to cause these disorders. Mutations in *ELA2* have been reported in 90-100% of cyclic neutropenia patients and 38-80% of congenital neutropenia patients. The mutation detection rate is highest in patients with the classic clinical symptoms defining these disorders.

## REASONS FOR REFERRAL:

- Confirmation of diagnosis
- Evaluation of family members
- Prenatal diagnosis

## METHOD:

PCR amplification and bi-directional DNA sequence analysis is performed. The complete coding region and slice junction of each exon is compared to the reference sequence, and the functional implications of sequence variations are characterized using the *ELA2* mutation database[1].

## LIMITATIONS:

Analytical sensitivity is >99%. Rare polymorphisms within primer or probe regions may interfere with detection of gene variants. Large deletions or duplications and novel mutations that are outside the regions sequenced will not be detected. Clinical sensitivity is 90-100% for cyclic neutropenia patients and 38-80% for congenital neutropenia.

[1] http://bioinf.uta.fi/ELA2base/index.php?content=pub/IDbases

REPORTABLE RANGE:
Sequence variations are reported as heterozygous or homozygous and are classified according to the following system:

I. Sequence variation is previously reported and is a recognized cause of the disorder
II. Sequence variation is previously unreported and is of the type which is expected to cause the disorder.
III. Sequence variation is previously unreported and is of the type which may or may not be causative of the disorder
IV. Sequence variation is previously unreported and is probably not causative of disease.
V. Sequence variation is previously reported and is a recognized neutral variant.
VI. Sequence variations that are not known or expected to be causative of disease, but have been found to be associated with a clinical presentation.

Known polymorphisms are not reported but are available upon request.

SPECIMEN REQUIREMENTS:
5 ml EDTA (lavender top) whole blood.
Contact the laboratory to discuss prenatal sample requirements.

TESTING SCHEDULE:
Turnaround time is 21 days.

SHIPPING REQUIREMENTS:
Ship on an ice pack or at room temperature. Place the specimen and the requisition into plastic bags and seal. Insert into a Styrofoam container, seal and place into a sturdy cardboard box, and tape securely. Ship the package in compliance with your overnight carrier guidelines. Label with the following address:

Client Services/Hemostasis Reference Laboratory
BloodCenter of Wisconsin
638 N. 18th St.
Milwaukee, WI 53233
Phone: 800-245-3117, ext. 6250

*ELA2*-Related Neutropenia Sequence Analysis:
CPT Codes: 83891, 83892 x 5, 83898 x 5, 83904 x 5, 83912

REFERENCES:
Dale, DC, ELA2-Related Neutropenia (2008) GeneReviews, http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part=cyclic-n

November 2008