Interpretation
This individual possesses a DNA sequence alteration in the Notch3 gene that is a known CADASIL-associated mutation. Therefore, this individual is likely to be affected with, or predisposed to developing, CADASIL, due to the gain or loss of a cysteine residue within one of the EGF-like repeats of the Notch3 receptor. 1,2,4-6

Technical Results
DNA variant 1: Transversion T > G
Nucleotide position: 3029
Codon position: 984
Amino acid change: Phenylalanine > Cysteine
Variant type: Disease-associated mutation

Comments
Sequencing of this individual’s Notch3 gene demonstrated a DNA sequence alteration that has been previously reported as a CADASIL-associated mutation. Therefore, this individual is likely to be affected with, or predisposed to, developing CADASIL that may lead to recurrent transient ischemic attacks, migraines and strokes. 1,2,4-6

This analysis may also have detected other types of sequence alterations as listed in the Technical Results section, a common occurrence for an analysis of this scope. In the context of the known CADASIL associated mutation detected here, the presence of additional variants is of reduced significance. For further explanation, please consult the glossary at the end of this report.

CADASIL is an autosomal dominant disease. Family members may be at risk for possessing or inheriting this mutation. Athena recommends genetic counseling for this individual and his or her family members. Please contact Athena Client Services at 1-866-AthenaDX for a genetic counselor in your area and further information on family member testing.

BACKGROUND
The Notch3 gene is composed of 33 exons encoding 2,321 amino acids. CADASIL mutations are characterized by the gain or loss of a cysteine residue located within the 23 exons (exons 2 through 24) encoding for the 34 epidermal growth factor (EGF)-like repeat domains of the Notch3 receptor. 1-3 These highly stereotyped missense mutations have been found to cause CADASIL in over 90% of patients. 2,6 No other types of mutations have been associated with CADASIL. In approximately 10% of CADASIL patients the cause of the disease has not been uncovered.

The accuracy of mutation detection by the analyses performed here was determined to be greater than 99% by Athena Diagnostics, Inc.

CADASIL is an adult-onset hereditary syndrome characterized by recurrent transient ischemic attacks and strokes. 1-6 Mutations within the Notch3 gene have been identified as the underlying genetic defect associated with the disorder. 1,2 It has been postulated that the molecular