Dementia Test

DISORDER ALSO KNOWN AS
Alzheimer disease, frontotemporal dementia
*Samples from individuals younger than 18 years of age will not be accepted. See below for additional details.

TEST GENE LIST
APP, DCTN1, GRN, MAPT, PRNP, PSEN1, PSEN2, SQSTM1, TARDBP, TREM2, TYROBP

CLINICAL FEATURES
Dementia is a term that describes a group of symptoms associated with cognitive and/or behavioral changes that interfere with the ability to perform everyday activities.[1] The core mental functions that may be affected include memory, communication, personality, behavior, reasoning, judgement, and visual perception.[1]Dementia from all causes, occurs in 5-7% of adults over 60 years of age.[2] Alzheimer's disease (AD) and frontotemporal dementia (FTD) are the two most common types of dementia.[3] AD accounts for 60-80% of dementia, and is the most common cause of dementia in North America and Europe.4Most AD patients first develop symptoms after 65 years of age, while <10% of patients present with early-onset AD.[3] FTD is more commonly observed in patients younger than 65 years, with symptoms including progressive behavioral and language changes.[3] Other genetic conditions such as Parkinson's disease and amyotrophic lateral sclerosis can also present with symptoms of dementia.

INHERITANCE PATTERN/GENETICS
Some forms of dementia are thought to be multifactorial, resulting from the interactions of environmental and genetic factors.[5]However, distinct, inherited forms of dementia have been documented.[5]Individuals with a family history of dementia and a young age of onset are more likely to have an inherited form of dementia.[6]The Dementia panel at GeneDx includes analysis of 11 genes associated with inherited forms of dementia. The complete list of genes and associated disorders is included in the table below. Dementia is most often inherited in an autosomal dominant manner, however autosomal recessive inheritance also occurs. Symptoms and age of onset can vary between and within families, and reduced penetrance has been described.[6] A clinical diagnosis of dementia is based on medical and family history, neurological and neuropsychological evaluations, neuropathological studies, and exclusion of other disorders with similar clinical presentations.[1]However, clinical evaluation alone may not be sufficient to distinguish the various genetic causes of dementia given their phenotypic and genetic heterogeneity. The Dementia gene panel at GeneDx can assist in confirming a clinical diagnosis, defining a specific type of dementia, or aiding in the development of a comprehensive medical plan including symptom management and recurrence risk assessment.

*Dementia is an adult onset disorder for which there is currently no specific medical intervention that, if initiated in childhood, would alter the clinical course. Therefore, in accordance with policy and position statements from the American College of Medical Genetics (ACMG)[7,8], American Society of Human Genetics (ASHG)[9], and the American Academy of Pediatrics[8], samples from individuals younger than 18 years of age will not be accepted for this testing.

TEST METHODS
Using genomic DNA from the submitted specimen, the complete coding regions and splice site junctions of the genes on this panel are enriched using a proprietary targeted capture system developed by GeneDx for next-generation sequencing. The enriched targets are simultaneously sequenced with paired-end reads on an Illumina platform. Bi-directional sequence reads are assembled and aligned to reference sequences based on NCBI RefSeq transcripts and human genome build GRCh37/UCSC hg19. After gene specific filtering, data are analyzed

to identify sequence variants. Alternative sequencing methods are used to analyze regions with inadequate sequence data. Reportable variants include pathogenic variants, likely pathogenic variants, and variants of uncertain significance. Likely benign and benign variants, if present, are not routinely reported, but are available upon request.

TEST SENSITIVITY

The technical sensitivity of sequencing is estimated to be >99% at detecting single nucleotide events. It will not reliably detect deletions greater than 20 base pairs, insertions or rearrangements greater than 10 base pairs, or low-level mosaicism. For the genes on this panel, sequencing but not deletion/duplication analysis, is performed. The hexanucleotide repeat expansion in the *C9orf72* gene is not performed as part of the Dementia Panel.

REFERENCES:

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