Use a keyword, test name or number

APOE Alzheimer's Risk

TEST: 504040 CPT: 81401

Expected Turnaround Time	5 - 7 days Turnaround time is defined as the usual number of days from the date of pickup of a specimen for testing to when the result is released to the ordering provider. In some cases, additional time should be allowed for additional confirmatory or additional reflex tests. Testing schedules may vary.
Related Documents	• Sample Report

SPECIMEN REQUIREMENTS

Specimen	Whole blood
Volume	5 mL whole blood **or** 4 buccal swabs
Minimum Volume	0.5 mL **or** two buccal swabs (**Note:** This volume does **not** allow for repeat testing.)
Container	Lavender-top (EDTA) tube (preferred), yellow-top (ACD) tube, **or** buccal swab kit provided by LabCorp.
Storage Instructions	Maintain specimen refrigerated or at room temperature. Stable at room temperature or refrigerated for seven days. Specimen is unstable frozen.
Causes for Rejection	Frozen whole blood samples; quantity not sufficient for analysis; improper container; one buccal swab

TEST DETAILS

Use	This test is to detect the presence of the *APOE4* variant, which is associated with increased risk of late-onset (age >60-65) Alzheimer's disease (AD). Testing may be considered for patients with dementia to supplement information from clinical and other evaluations. This test is not appropriate for children. *APOE* genotype results are E2/E2, E2/E3, E2/E4, E3/E3, E3,E4, or E4/E4. APOE genotyping supplies supplementary information for the clinical diagnosis of Alzheimer's disease. Alzheimer's disease (AD) is the most common form of dementia in the elderly and currently affects more that 5 million Americans. It is a progressive neurodegenerative disorder with brain findings of amyloid plaques containing β-amyloid and neurofibrillary tangles. AD is a complex and heterogeneous disease, influenced by many genetic and environmental factors. An early-onset variety in 1% to 5% of AD cases is autosomal-dominant and caused by rare mutations in known genes, including *PSEN1, PSEN2,* and *APP.* The predominant form of AD is late-onset (age >60-65), which can be familial (15% to 20%) or sporadic. The *APOE4* (E4) variant of apolipoprotein E is strongly associated with risk of late-onset AD. Apolipoprotein E (apoE) has multiple roles, including lipid transport in the blood and the brain. The *APOE4* variant increases the risk for late-onset Alzheimer's disease and may contribute to the pathology of the disease through influence on β-amyloid, inflammation, or other processes. The risk for development of late-onset AD is increased approximately two- to threefold for individuals with one copy of the *APOE4* variant and by approximately 10- to 15-fold for individuals with two copies of the variant (E4/E4 genotype). The *APOE2* variant has some protective effect against development of late-onset AD. The lifetime risk for late-onset Alzheimer's disease is approximately 10% to 12% in the general population, though it is higher in women than men and doubles when there is a first-degree relative with this disorder. The lifetime risk is approximately 9% for individuals negative for *APOE4*, and for individuals with E4/E4 may be as high as 25% for males and 45% for females. Among patients with late-onset AD, the presence of *APOE4* may lead to earlier development of symptoms. However, *APOE4* is neither necessary nor sufficient for the development of Alzheimer's disease. Approximately 30% to 50% of patients with late-onset Alzheimer's disease do not have an *APOE4* allele. *APOE4* is common, with 25% of the general population having one copy and 1% having two copies of this variant. Among patients with late-onset AD, 50% to 70% are positive for *APOE4.*

	The development of late-onset Alzheimer's disease is influenced by many factors other than *APOE4,* including age, gender, family history, level of education, and history of head trauma. Midlife cardiovascular risk factors in individuals with *APOE4* also increase risk for cognitive decline. A number of genetic influences on Alzheimer's development in addition to *APOE4* have also been reported and are under investigation. *APOE4* is also associated with poor outcome to brain trauma, and it can influence therapeutic response to drugs for AD.
Limitations	This is not a diagnostic test. *APOE4* increases risk of late-onset Alzheimer's disease, but many patients with *APOE4* do not develop AD and—of patients with late-onset AD—30% to 50% are negative for *APOE4.* This test was developed, and its performance characteristics determined, by LabCorp. It has not been cleared or approved by the US Food and Drug Administration (FDA).
Methodology	Polymerase chain reaction (PCR) with restriction enzyme digestion and polyacrylamide gel electrophoresis
References	Altmann A, Tian L, Henderson VW, Greicius MD; Alzheimer's Disease Neuroimaging Initiative Investigators. Sex modifies the APOE-related risk of developing Alzheimer disease. *Ann Neurol.* 2014 Apr; 75(4):563-573. PubMed 24623176 Bangen KJ, Beiser A, Delano-Wood L, et al. APOE genotype modifies the relationship between midlife vascular risk factors and later cognitive decline. *J Stroke Cerebrovasc Dis.* 2013 Nov; 22(8):1361-1369. PubMed 23601373 Bird TD. Alzheimer disease overview. In: Pagon RA, Adam MP, Ardinger HH, et al, eds. *GeneReviews.* Seattle, Wash: University of Washington; 2014. PubMed 20301340 Goldman JS, Hahn SE, Catania JW, et al. Genetic counseling and testing for Alzheimer disease: Joint practice guidelines of the American College of Medical Genetics and the National Society of Genetic Counselors. *Genet Med.* 2011 Jun; 13(6)597-605. Erratum: 2011 Aug;13(8):749. PubMed 21577118 Schipper HM. Apolipoprotein E: Implications for AD neurobiology, epidemiology and risk assessment. *Neurobiol Aging.* 2011 May; 32(5):778-790. PubMed 19482376

CPT Statement/Profile Statement