

Narcolepsy (*HLA-DQB1*) Genotyping

*TO PROVIDE SUPPORTING EVIDENCE FOR A DIAGNOSIS OF
NARCOLEPSY IN A SYMPTOMATIC INDIVIDUAL*

Disease Overview

- Narcolepsy is a sleep disorder characterized by invalidating excessive daytime sleepiness and cataplexy (the sudden loss of muscle tone triggered by strong emotions). Additional sleep abnormalities seen in individuals with narcolepsy include disturbed nighttime sleep, sleep paralysis, and hypnagogic hallucinations (occurring in the period between sleep and wakefulness).
- Narcolepsy is generally diagnosed in adulthood but has been reported in children.
- HLA-DQB1*06:02* is strongly associated with narcolepsy, but the *HLA-DQB1*06:02* allele by itself is not sufficient to cause narcolepsy.

Epidemiology

- Approximately one in 2,000 individuals is affected with narcolepsy.
- The incidence of *HLA-DQB1*06:02* varies by ethnicity but appears important for the development of narcolepsy across all populations.

Genetics

- Narcolepsy is multi-factorial, having both a genetic and environmental component; familial cases are rare.
- More than 99 percent of Caucasians with narcolepsy and cataplexy have the *HLA-DQB1*06:02* allele, compared to 15–25 percent of the general Caucasian population.
- HLA-DQB1*06:02* is also strongly associated with narcolepsy in Japanese, African-American, Korean, and Hispanic populations.

Indications for Ordering

- Individuals with a clinical diagnosis of narcolepsy.
- Individuals with an uncharacterized sleep disorder.

Contraindication for Ordering

Prenatal testing.

Interpretation

- Identification of the *HLA-DQB1*06:02* allele is supportive of a clinical diagnosis of narcolepsy but does not by itself establish a diagnosis.
- If the *HLA-DQB1*06:02* allele is not identified, a diagnosis of narcolepsy is reduced but not eliminated.

Methodology

- PCR with melting-curve analysis.
- Clinical sensitivity and specificity are 85–95 percent and less than 1 percent, respectively.

Limitations

- This test will not differentiate between heterozygosity (one copy) and homozygosity (two copies) of the *HLA-DQB1*06:02* allele.
- Rare diagnostic errors may occur due to primer-site mutations.
- Alleles other than *HLA-DQB1*06:02* will not be identified.
- Other genetic and non-genetic factors that influence narcolepsy are not evaluated.

Related tests

- CBC with Platelet Count & Automated Differential (0040003)
- Glucose, Plasma or Serum (0020024)
- Drug of Abuse 9 Panel, Urine-Screen Only (0090453)
- Drug Screen (non-forensic), Urine, Qualitative (0090500)
- Melatonin (0098816)

References

- Hor, et al. Genome-wide association study identifies new HLA class II haplotypes strongly protective against narcolepsy. *Nat Genet* 2010; 42:786–90.
- Mignot, et al. Complex HLA-DR and –DQ interactions confer risk of narcolepsy-cataplexy in three ethnic groups. *Am J Hum Genet* 2001;68:686–99.
- Watson, et al. Does narcolepsy symptom severity vary according to *HLA-DQB1*0602* allele status? *Sleep* 2010;33:29–35.
- Roh, et al. Association of HLA-DR and –DQ genes with narcolepsy in Koreans. *Hum Immunol* 2006;67:749–55.

Test Information

2005023 Narcolepsy (*HLA-DQB1*06:02*) Genotyping

For specific collection, transport, and testing information, refer to the ARUP website at www.aruplab.com.

For information on test selection, ordering, and interpretation, refer to ARUP Consult® at www.arupconsult.com.