Narcolepsy (HLA-*DQB1*) Genotyping

**Indications for Ordering**

Aid in diagnosis of narcolepsy

**Test Description**

Polymerase chain reaction with melting-curve analysis to detect the HLA-DQB1*06:02 allele

**Tests to Consider**

Genetic testing
- Narcolepsy (HLA-DQB1*06:02) Genotyping 2005023
  - May help rule out narcolepsy when clinical history and sleep studies are inconclusive

Evaluation to rule out other treatable disorders may include
- CBC with Platelet Count and Automated Differential 0040003
- Glucose, Plasma or Serum 0020024
- Drugs of Abuse 9 Panel, Urine – Screen Only 0090453
- Drug Screen (Nonforensic), Urine, Qualitative 0090500
- Melatonin 0098816

**Disease Overview**

Prevalence – 1/2,000 affected with narcolepsy

Incidence
- HLA-DQB1*06:02 allele
  - Varies by ethnicity
  - Caucasians
    - 15% of general population has HLA-DQB1*06:02 allele
    - 99% with narcolepsy and cataplexy have HLA-DQB1*06:02 allele
  - Also strongly associated with narcolepsy in other populations (Japanese, African Americans, Koreans, Hispanics)

Age of onset
- Narcolepsy is generally diagnosed in adulthood
- Has been reported in children

**Symptoms**

- Narcolepsy is a sleep disorder
  - Excessive daytime sleepiness
  - Cataplexy
    - Sudden loss of muscle tone triggered by strong emotions
  - Disturbed nighttime sleep
  - Sleep paralysis
  - Hypnagogic hallucinations
    - Occurs in the period between sleep and wakefulness
  - Diagnosis is based on clinical symptoms

**Genetics**

Gene – HLA-DQB1

Variant – HLA-DQB1*06:02
- Cause of narcolepsy is multifactorial
  - Both genetic and environmental components
  - Familial cases are rare

**Test Interpretation**

Sensitivity/specificity
- Clinical sensitivity – 85-95%
- Clinical specificity – <1%
- Analytical sensitivity/specificity – 99%

Results
- Positive
  - HLA-DQB1*06:02 allele detected
    - Supportive of a clinical diagnosis of narcolepsy
    - Does not by itself establish a diagnosis
- Negative
  - HLA-DQB1*06:02 allele not detected
    - Diagnosis of narcolepsy is less likely but not eliminated

Limitations
- Does not differentiate between heterozygosity and homozygosity of the HLA-DQB1*06:02 allele
- Diagnostic errors can occur due to rare primer-site variations
- Alleles other than HLA-DQB1*06:02 will not be identified
- Other genetic and nongenetic factors that influence narcolepsy are not evaluated