

Multiple Endocrine Neoplasia Type 1 (*MEN1*) Sequencing and Deletion/Duplication

FOR DIAGNOSTIC AND PRESYMPTOMATIC IDENTIFICATION OF MULTIPLE ENDOCRINE NEOPLASIA TYPE 1, MEN1 SYNDROME, MULTIPLE ENDOCRINE ADENOMATOSIS, AND WERMER SYNDROME

Disease Overview

- Multiple endocrine neoplasia type 1 (*MEN1*) syndrome can include the development of multiple endocrine and non-endocrine tumors.
- Common *MEN1*-related endocrine tumors include parathyroid (90–95 percent), pancreatic islet cell (30–80 percent), and pituitary (15–90 percent).
- Non-endocrine tumors include facial angiofibromas, collagenomas, lipomas, meningiomas, ependymomas, and leiomyomas.
- Primary hyperparathyroidism is the most common and often the initial manifestation of *MEN1*.
- Gastrinoma and carcinoid tumors are the most frequent causes of mortality.
- Treatment of *MEN1* is dependent on tumor type and may include surgery and/or drug therapy.
- Recommendations for screening of asymptomatic individuals with a known *MEN1* mutation include routine biochemical testing (i.e., prolactin, calcium, gastrin, and parathyroid hormone) and imaging (i.e., head MRI and abdominal CT or MRI) to identify potential tumors in early stages.

Epidemiology

Prevalence of *MEN1* is approximately one in 30,000.

Genetics

- Autosomal dominant inheritance.
- *MEN1* syndrome is caused by inactivating mutations of the *MEN1* tumor suppressor gene.
- De novo mutation rate is approximately 10 percent.
- Variable expressivity.
- Penetrance is approximately 50 percent by age 20 and greater than 95 percent by age 40.

Indication for Ordering

Diagnostic testing for individuals with clinical and/or biochemical evidence of *MEN1*.

Contraindication for Ordering

If the specific familial mutation has already been identified in a relative, testing can be performed on at-risk family members by ordering Familial Mutation, Targeted Sequencing (ARUP test code 2001961). A copy of the relative's genetic test result is required.

Additional Ordering Note

Please complete the patient history form for *MEN1* and submit with the sample for optimal interpretation of test results.

Interpretation

- Identification of a known pathogenic *MEN1* mutation predicts the presence of *MEN1* syndrome.
- Absence of a pathogenic mutation reduces but does not exclude the possibility that the individual is affected with *MEN1*. Medical management should rely on clinical findings and family history.
- *MEN1* mutations of unknown clinical significance may be detected by this assay.

Methodology

- PCR followed by bidirectional sequencing of the entire coding region and intron-exon boundaries of the *MEN1* gene.
- Multiplex ligation-dependent probe amplification (MLPA) to identify large exonic deletions/duplications in the *MEN1* gene.
- Combined clinical sensitivity for sequencing and deletion/duplication analysis is up to 94 percent. Approximately 90 percent of detectable mutations are sequence variants, while up to 4 percent of causative mutations are large deletions.
- Analytical sensitivity and specificity are 98 percent.

Limitations

- Rare diagnostic errors may occur due to primer- or probe-site mutations.
- Regulatory region and deep intronic mutations will not be detected, and breakpoints of large deletions/duplications will not be determined.
- Genes other than *MEN1* will not be evaluated by this assay.

Related Test

Familial Mutation, Targeted Sequencing (2001961)

References

1. Falchetti A. Genetic screening for multiple endocrine neoplasia syndrome type 1 (MEN-1): when and how. *F1000 Med Rep* 2010;24;2:Pii 14.
2. Falchetti A, et al. Multiple endocrine neoplasia type 1 (MEN1): not only inherited endocrine tumors. *Genet Med* 2009;11(12):825–35.
3. Marini F, et al. Multiple endocrine neoplasia type 1. *Orphanet J Rare Dis* 2006;1:38.
4. Brandi ML, et al. Guidelines for diagnosis and therapy of MEN Type 1 and Type 2. *J Clin Endocrinol Metab* 2001;86(12):5658–71.

Test Information

2005360 **Multiple Endocrine Neoplasia Type 1 (MEN1) Sequencing and Deletion/Duplication**
2005359 **Multiple Endocrine Neoplasia Type 1 (MEN1) Sequencing**
2005346 **Multiple Endocrine Neoplasia Type 1 (MEN1) Deletion/Duplication**

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.

AUTHOR

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