MEN 2 and FMTC Mutations, Exons 10, 11, and 13-16

Clinical Use
- Screen at-risk individuals for MEN 2 and FMTC
- Diagnose MEN 2 and FMTC
- Differentiate between familial and sporadic MTC

Reference Range
Negative (no mutations detected)

Interpretive Information
Mutation present
- FMTC and/or MEN 2A
- MEN 2B

Clinical Background
Multiple endocrine neoplasia type 2 (MEN 2) is an autosomal dominant syndrome associated with a high risk of medullary thyroid carcinoma (MTC). The MEN 2A subtype is associated with hyperparathyroidism, and both MEN 2A and MEN 2B subtypes are associated with an increased risk for pheochromocytoma. MEN 2B is further characterized by mucosal neuromas on the lips and tongue and in the gastrointestinal tract.

Over 95% of MEN 2A cases and over 85% of familial MTC (FMTC) cases have a germline mutation in 1 of 5 conserved cysteine residues encoded in exon 10 or 11 of the RET proto-oncogene. A point mutation in exon 16 is present in over 95% of MEN 2B cases. Other mutations in these exons and in exons 13, 14, and 15 have also been associated with MEN 2.

Once the mutation in an affected family member has been identified, testing of first-degree relatives allows presymptomatic identification of those at risk for MEN 2 and prophylactic treatment. Correlation between specific mutations and aggressiveness of MTC may aid in appropriately timing prophylactic thyroidectomy and pheochromocytoma screening. Genetic testing is recommended for all individuals with MTC since RET mutations have been detected in 1% to 20% of those who appear to have sporadic MTC (ie, those without a known family history of MEN 2).

Method
- Polymerase chain reaction (PCR) and semi-automated DNA sequencing
- Analytical specificity: mutations in exons 10, 11, 13, 14, 15, and 16 of the RET proto-oncogene

Specimen Requirements
5 mL room temperature whole blood
3 mL minimum

Collect blood in a lavender-top (EDTA) or yellow-top (ACD solution B) tube. Alternatively, submit amniotic fluid, bone marrow, tissue biopsy (eg, dissected CVS) or extracted DNA.