

MECP2–Related Disorders

MECP2–Related Disorders:

- Classic Rett syndrome
- Variant Rett syndrome
- Severe neonatal encephalopathy
- Nonsyndromic X-linked intellectual disability
- *MECP2* duplication syndrome

Pathogenic variants in the *MECP2* gene have broad phenotypic variability. Classic Rett syndrome primarily affects females and is characterized by a period of normal development followed by rapid regression of language and motor skills by two years of age. Atypical variants of Rett syndrome also primarily affect females and have been described in individuals with clinically suspected but molecularly unconfirmed Angelman syndrome, intellectual disability with spasticity or tremor, mild learning disabilities, and autism. Pathogenic variants in *MECP2* have also been identified in intellectually normal and mildly impaired women, presumably due to non-random X-inactivation.

In males, *MECP2* pathogenic variants classically present with severe neonatal encephalopathy with early lethality. A few males have been reported with typical and variant Rett syndrome and nonsyndromic intellectual disability.

Some individuals have duplications of *MECP2* rather than pathogenic sequence variants or deletions. This causes a distinct *MECP2* duplication syndrome characterized by infantile hypotonia, severe intellectual disability, poor speech development, progressive spasticity, recurrent respiratory infections, and seizures. *MECP2*-duplication syndrome is thought to be 100% penetrant in males. Some females have been described with features of *MECP2* duplication syndrome, but most are asymptomatic carriers.

Indications:

- Diagnostic testing in females with suspected Rett syndrome or variant Rett syndrome
- Diagnostic testing in males with severe neonatal encephalopathy or features of *MECP2* duplication syndrome
- Diagnostic testing in selected individuals with molecularly unconfirmed but clinically suspected Angelman syndrome, intellectual disability, or autism
- Prenatal diagnosis in families with an identified pathogenic *MECP2* variant
- Carrier testing in relative of a patient with a *MECP2*-related disorder.

Testing Methodology:

PCR-based sequencing of the coding regions and their exon/intron boundaries of the *MECP2* gene. *MECP2* deletion/duplication analysis is performed by multiple ligation-dependent probe amplification (MLPA).

Sensitivity:

Clinical Sensitivity: PCR-based sequencing of the coding regions and their exon/intron boundaries of the *MECP2* gene detects ~80% patients with classic Rett syndrome and ~40% of atypical Rett syndrome. Large deletions account for 8% of classic Rett syndrome and 3% of atypical Rett syndrome. Of those who do not have a pathogenic variant identified by sequence analysis, approximately 30% with classic Rett syndrome and 7% with atypical Rett syndrome have large deletions.

Analytical Sensitivity: The sensitivity of PCR-based DNA sequencing is over 99% for the detection of nucleotide base changes, small deletions and insertions in the regions analyzed. Mutations in regulatory regions

or other untranslated regions are not detected by this test. Multiple exon deletions, large insertions, genetic recombination events and rare, primer site mutations are not be identified by this methodology.

Specimen:

At least 3mLs of whole blood in a lavender top (EDTA) tube or 6 cytobrushes. Label tube with patient's name, birth date, and date of collection.

Turn-Around Time:

28 days.

COST:

Please call 1-866-450-4198 for current pricing, insurance preauthorization or with any billing questions.

CPT CODES:

- **MECP2 sequence analysis:** 81302
- **MECP2 deletion/duplication analysis:** 81304
- **Family specific analysis:** 81403

Results:

Each test report includes a detailed interpretation of the genetic findings, the clinical significance of the result, and specific recommendations for clinical management and additional testing, if warranted. Results will be reported to the referring physician or health care provider as specified on the test requisition form.

Shipping Instructions:

Please enclose **test requisition** with sample.

All information must be completed before sample can be processed.

Place samples in styrofoam mailer and ship at room temperature by overnight Federal Express to arrive Monday through Saturday.

Ship to:

Cytogenetics and Molecular Genetics Laboratories
3333 Burnet Avenue NRB 1042
Cincinnati, OH 45229
513-636-4474