RETT SYNDROME
MECP2 GENE SEQUENCING

Rett syndrome (OMIM 312570) is an X-linked disorder caused by mutations in the MECP2 gene (OMIM 300005). Classic Rett syndrome typically affects females, and is characterized by normal development for the first 6 to 18 months of life, followed by regression in language and motor skills. Cognitive impairment is present. The hallmark of classic Rett syndrome is the development of repetitive, stereotypic hand movements with loss of purposeful hand movements. Additional features include acquired microcephaly, seizures, autistic features, teeth grinding, impaired sleeping patterns, and breathing disturbances.

Mutations in MECP2 are associated with other disorders that have variable phenotypes. Atypical Rett syndrome typically affects females. Characteristics include impairment of hand skills, speech, and other communication skills. Developmental regression is seen, although recovery of social interactions may occur. Acquired microcephaly is typically present, and other features of classical Rett syndrome may or may not be seen. Atypical Rett syndrome is variable in its course and age of onset. Non-progressive mild mental retardation has also been described in females with MECP2 mutations.

Mutations in MECP2 are associated with severe neonatal encephalopathy (OMIM 300673) in males. Males may also present with “PPM-X syndrome” (OMIM 300055) which is characterized by severe mental retardation, psychosis, pyramidal signs, macro-orchidism, and Parkinsonian features.

Testing: Testing is performed by sequencing the entire coding region of MECP2, including untranslated exon 1, coding exons 2 through 4, surrounding intronic regions, and the 3’ untranslated region. This will detect point mutations, small deletions, and small insertions. For females, the assay will not detect a partial or whole gene deletion. For males, a partial or whole gene deletion may appear as failure to amplify a region of the gene.

A negative test result does not rule out a diagnosis of Rett syndrome. This assay will detect mutations in about 80% of individuals with classic Rett syndrome and in about 40% of individuals with atypical Rett syndrome. Large deletions, which would not be detected by this assay, account for about 8% of classic Rett syndrome and about 3% of atypical Rett syndrome.

Turnaround time: 10-14 days

CPT codes and cost: 83890(x1) 83898 (x4) 83904 (x13) 83912 (x1) $ 685

BILLING: We do not bill third party payers (insurance companies) for samples received from external sources. The person or institution (e.g., Clinical Lab; Send-out Lab; Physician Office) sending the sample is responsible for full payment of the invoices within 30 days of receipt of the invoice. If the patient is on Medical assistance, please contact the lab prior to sample submission. Direct patient billing will be accepted only when a valid credit card form is received with the patient sample.

Online resources:
International Rett Syndrome Foundation - http://www.rettsyndrome.org/
OMIM entries
Credit Card Billing Information

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<td>Work:</td>
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<th>Card holder signature:</th>
<th>Authorized payment amount:</th>
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For Direct Patient Billing
Prepayment for the testing services is required prior to beginning our testing. Please complete this form and include this paperwork with the shipment of the patient sample.

Billing questions can be addressed to: Denise Axsmith
Senior Budget/Financial Analyst
Nemours/A.I. duPont Hospital for Children
daxsmith@nemours.org
Phone: 302.651.6802
Fax: 302.651.6881
Facsimile Verification Form

Name of Facility receiving Fax: ________________________________

Name of Physician/Lab receiving Fax: ________________________________

Street Address: __________________________________________________________

City __________________________ State: ______

Fax Number: ________________________________
(to which lab results and/or patient information may be sent)

Phone Number: ________________________________

By signing this Facsimile Verification Form, I validate the accuracy of the above information and assume responsibility for assuring that the Fax machine is in a location which will maintain confidentiality of all reports transmitted by the Molecular Diagnostics Laboratory of the Alfred I. duPont Hospital for Children, to the above fax number.

Authorized Contact Person: ____________________________________________

Signature: __________________________ Date: ______________

Title: ________________________________

In our continuing efforts to maintain patient confidentiality, the Molecular Diagnostics Laboratory of the Alfred I. duPont Hospital for Children requests you to verify the fax number only once (for this patient sample and for future patient reports) from your medical practice or institution and to assure that all faxes regarding patient information are received in a secure location in accordance with HIPAA regulations.

Please complete this Facsimile Verification Form and fax back to 302.651.6795. If you have any questions regarding this form please contact Susan Kirwin, Assistant Director of The Molecular Diagnostics Laboratory, at 302.651.6775.

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