Duchenne/Becker Muscular Dystrophy
Indication-Specific Gene Panel

including: sequencing and high resolution deletion/duplication analysis

PANEL DESCRIPTION:
Dystrophinopathies are muscular conditions caused by mutations in DMD, the gene responsible for an essential structural protein in the muscular system called dystrophin. The incidence of Duchenne muscular dystrophy is thought to be approximately 1 in 3,600 male live births. The incidence of all dystrophinopathies or the number of affected females is unknown. This panel is designed to detect both small-scale deletions or duplications and sequence-based mutations within DMD known to be associated with dystrophinopathies.

PANEL OVERLAP:
The gene on this panel is also included on our Autism | Intellectual Disability | Multiple Anomalies Panel.

PANEL DETAILS:
- This panel includes both high resolution deletion/duplication analysis and sequencing of the gene specified.
  - Deletion/duplication analysis is performed using a high resolution, custom microarray platform designed to target the gene of interest at the exon level.
  - Sequencing is performed using a customized next generation sequencing library. Analysis includes the coding exons of the DMD gene plus ten bases into the introns and untranslated regions (5' and 3'). Sanger sequencing is performed to confirm variants suspected or confirmed to be pathogenic.
- Detection rates are limited to the gene specified; this test does not provide whole genome analysis.

RECOMMENDED TESTING STRATEGY:
Tests below can be ordered individually, however a tiered testing strategy is recommended. Our laboratory’s Comprehensive Testing for dystrophinopathies includes the following two tests:

**Targeted Deletion/Duplication Analysis**
- Deletions and duplications involving the DMD gene are a more common cause of Duchenne Muscular Dystrophy and Becker Muscular Dystrophy than sequence variations. Del/dup analysis can identify partial or whole gene deletions and duplications in the associated gene.

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Detection</th>
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<tbody>
<tr>
<td>Duchenne Muscular Dystrophy (DMD)</td>
<td>50-65% deletions involving DMD</td>
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<tr>
<td></td>
<td>5-10% duplications involving DMD</td>
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<td></td>
<td>20-35% sequence variants in DMD</td>
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<tr>
<td>Becker Muscular Dystrophy (BMD)</td>
<td>65-70% deletions involving DMD</td>
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<tr>
<td></td>
<td>10-20% duplications involving DMD</td>
</tr>
<tr>
<td></td>
<td>10-20% sequence variants in DMD</td>
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**Next Generation Sequencing**
- If no pathogenic aberrations are detected del/dup analysis, NGS is performed.

DISORDERS INCLUDED IN THIS PANEL:
  - Duchenne muscular dystrophy (DMD)
  - Becker muscular dystrophy (BMD)
  - DMD-related dilated cardiomyopathy
INDICATIONS FOR TESTING:
- Developmental delay
- Gross motor delay or loss of motor skills
- Low muscle tone
- Calf hypertrophy
- Abnormal gait
- Dilated cardiomyopathy
- Elevated serum CK
- Skeletal muscle biopsy showing decreased dystrophin quantity

SPECIMEN COLLECTION & TRANSPORT:
Complimentary test kits are available upon request, but are not required.

SAMPLE TYPE and REQUIREMENTS:
- blood: 3 - 5 ml whole blood in an EDTA tube (purple top)
  - newborn minimum requirement: 1 - 3 ml
- buccal swab: 2 swabs
- extracted DNA: 70 ng/µg with a total yield of 7-10 µg (in TE) in a DNA microcentrifuge tube
  - *When submitting extracted DNA for genetic testing, nucleic isolation must have occurred in a CLIA-certified laboratory or a laboratory meeting equivalent requirements as determined by the CAP and/or CMS.

SHIPPING:
- Maintain and ship samples at room temperature.
- Coordinate transport for sample to be received in our laboratory within 24-48 hours of collection.
  - LOCAL: Call 402-559-5070 (option 1)
  - OUT OF AREA: Prior to shipment, please fax the completed test request form to 402-559-7248, including the FedEx® airbill tracking number.
    - Saturday delivery MUST be checked when sending FedEx® on Friday.
    - Please include Internal Billing Reference # 3155070600 on the FedEx® airbill.
    - Ship To: Human Genetics Laboratory – Zip 5440
      - UNMC Shipping & Receiving Dock
      - 601 S. Saddle Creek Road
      - Omaha, NE 68106

FORMS FOR TESTING: The following forms can be downloaded via our website.
- Required: Postnatal Test Request Form
- Optional: Informed Consent for Genetic Testing

POTENTIAL TEST RESULTS:
Once a variant is confirmed, our laboratory team interprets this information in conjunction with the patient’s clinical findings and the scientific literature in order to classify a finding. There are three possible results:
- A normal result indicates that sequencing or deletion/duplication analysis of the genes analyzed did not find any pathogenic mutations or variants of uncertain clinical significance (or no clinically-significant chromosome anomalies were identified by microarray analysis).
- An abnormal (or pathogenic) result indicates that a pathogenic mutation was identified (or microarray analysis identified a genomic dosage anomaly [deletion or duplication] or ROH that likely provides an explanation for the individual’s clinical findings). Any available information regarding the phenotype associated with that mutation will accompany the technical details on the report.
- In some cases, the clinical significance of an identified sequence variant (or chromosomal anomaly detected by microarray) may not be well understood. These variants (anomalies) will be reported as variants of uncertain clinical significance (UCS). Any available information about the molecular characteristics of the genetic change and the relationship of the genetic change to
phenotype will be included on the report. Over time, as more patients are reported, a variant of uncertain clinical significance may be revised to an informative result, and a revised report will be generated.

- Parental testing may be recommended in order to classify the result as *de novo* or familial for the purpose of recurrence risk calculation.

**TURNAROUND TIME:** For all sample types, results are typically available in 4 - 5 weeks.

**BILLING:** Our laboratory offers patient/self-pay, insurance (including Medicare/Medicaid), and client/institution billing options. Verifying coverage requirements or obtaining preauthorization PRIOR TO OR AT THE TIME OF SPECIMEN COLLECTION is often necessary. We provide preauthorization services upon request by calling 402-559-5070 (option 3); the following form is helpful for obtaining the information required by insurance providers and can be downloaded via our website.

- Insurance Preauthorization Request

In some circumstances, a test may be warranted even though insurance coverage is denied or not guaranteed. For these situations, we request the following form be signed by the patient and submitted with the sample. This helps inform patients of their potential financial responsibility, should the costs of genetic testing not be paid by their insurance provider.

- Advanced Beneficiary Notice of Noncoverage (ABN) – required when billing Medicare

**CPT CODES:**

- Targeted Deletion/Duplication Analysis: 81161
- Next Generation Sequencing: 81408

**PRICING:** For current costs contact the laboratory billing staff at 402-559-5070 (option 3).

**GENE LIST:**

| DMD |

**REFERENCES:**


updated 3-12-2019