MAYO CLINIC
Mayo Medical Laboratories

# Laboratory Service Report 1-800-533-1710

| Patient Name | Patient ID | Age | Gender | Order # |
|---|---|---|---|---|
| TESTING,89742 | | | | W2935054 |
| **Ordering Phys** | | **DOB** | | |
| **Client Order #** W2935054 | **Account Information** C7999998-STUSTEST 200 FIRST STREET SW ROCHESTER, MN 55901 (507)266-5730 | **Report Notes** | | |
| **Collected** 10/15/2009 06:00 | | | | |
| **Printed** 10/16/2009 15:13 | | | | |

| Test | Flag | Results | Unit | Reference Value | Perform Site* |
|---|---|---|---|---|---|
| **Rapid DNA Extraction** | | REPORTED 10/15/2009 13:14 | | | |
| Comment | | See Comment | | | MCR |
| Genomic DNA was extracted. | | | | | |

**BTK Full-gene Panel, B** REPORTED 10/15/2009 13:14

BTK, Full Gene Sequence

BTK Full Gene Result MCR

This individual was shown to have the following mutation in the BTK gene:
This female patient has been shown to have a missense mutation in exon 17 of the Btk gene, g. 67501, c.1778 (A>AT), p. 549, D>V that results in a change to the amino acid valine at position 549. This mutation appears to be a novel mutation and has not been previously reported in the Btk mutation database - BTKBASE. Furthermore, this patient has an intronic variation in intron 2, g. 46348, IVS-2 +11, C>CT with no change in amino acid within the intronic region. However, this variation has been reported in the BTKBASE as a disease-causing variation. The female patient has normal protein expression by flow cytometry but the presence of 2 variations, one reported to be pathogenic and the other a novel missense mutation very likely confirms her as a carrier for X-Linked agammaglobulinemia (XLA). Therefore, any symptomatic male relatives of this patient should be evaluated for the presence of these variations within the Btk gene by ordering the Btk known mutation test and reporting the specific mutations at the time of test ordering. Further, this patient should receive appropriate genetic counseling regarding her carrier status for XLA.
Concentrations of 3-O-methyldopa, neopterin and tetrahydrobiopterin in cerebrospinal fluid were within our reference ranges. The concentrations of homovanillic acid and 5-hydroxyindoleacetic acid were below our reference ranges. Although the exact cause for the low values is not known it is possible that this patient might respond to dopaminergic or serotoninergic agents if the clinical symptoms agree with a possible defect in this area of metabolism.
PLEASE NOTE: the 5-methyltetrahydrofolate value was at the bottom end of our reference range. We are aware of patients that have had similar values in whom neurological symptoms have improved following initiation of folinic acid therapy.

BTK Full Gene Interpretation MCR

This result is consistent with carrier status for X-linked Agammaglobulinemia (XLA) for this female.

Since the familial mutation has been identified in the BTK gene in this female, genetic testing for this

***Performing Site Legend on Last Page of Report***



* Report times for Mayo performed tests are CST/CDT

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specific mutation in symptomatic male family members
and/or female relatives of childbearing age is
recommended. Please contact the laboratory at
1-800-533-1710 or the online test catalog at
mayomedicallaboratories.com for information about how to
order the "BTK Gene, Known Mutation" (89306)

Reviewed By MCR

Patient report reviewed and interpreted by Dr. Roshini S.Abraham.
Fluorescent DNA sequence analysis was used to test for
the presence of mutations in the 19 exons and exon-intron
boundaries of the BTK gene that are associated with the
diagnosis of X-linked Agammaglobulinemia (XLA).

We predict that a small percentage of individuals who
have a diagnosis of XLA may have a mutation that is not
identified by the methods described above.

The presence of a BTK mutation does not necessarily
confirm a diagnosis of XLA. Clinical correlation
recommended. Please see: Graziani S, Di Matteo G, Benini
L, Di Cesare S, Chiriaco M, Chini L, Chianca M, De lorio
F, La Rocca M, Iannini R, Corrente S, Rossi P, Moschese
V. Identification of a Btk mutation in a
dysgammaglobulinemic patient with reduced B cells: XLA
diagnosis or not? Clinical Immunology. 2008; 128: 322-8.
And also: Fleisher T and Notarangelo L. What does it take
to call it a pathogenic mutation? Clinical Immunology.
2008; 128, 285-6.

A genetic consultation may be of benefit.

A list of common polymorphisms identified for this
patient is available from the lab upon request.

CAUTIONS:
Rare polymorphisms exist that could lead to false
negative or positive results. If results obtained do not
match the clinical findings, additional testing should be
considered.

Test results should be interpreted in the context of
clinical findings, family history, and other laboratory
data. If the full gene sequencing does not match the
clinical impression, the results of the BTK flow

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| cytometry analysis (89011, Bruton's Tyrosine Kinase (BTK), Protein Expression, Flow Cytometry, Blood) should be evaluated for protein expression. Large deletions or rearrangements not detected by the sequence based assay will affect protein expression, and the absence of BTK protein on monocytes can be determined by flow cytometry. | | | | | |
| BTK, Full Gene Sequencing | | | | | |
| Sequencing | | Performed | | | MCR |
| Btk Protein Flow, B | | Normal Expression | | | MCR |
| Normal expression of BTK in monocytes and B cells, does not appear to be consistent with XLA. If clinical evidence for XLA is present, suggest Btk genotyping (89307) to confirm that no Btk mutations are present since approximately 30% of Btk mutations can affect protein function but maintain normal protein expression. | | | | | |
| Analyte Specific Reagent | | | | | |
| This test was developed and its performance characteristics determined by Laboratory Medicine and Pathology, Mayo Clinic. This test has not been cleared or approved by the U.S. Food and Drug Administration. | | | | | |

* Performing Site:

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|---|---|---|
| MCR | Mayo Clinic Dpt of Lab Med & Pathology<br>200 First St SW Rochester, MN 55905 | Lab Director: |