MAYO CLINIC
Mayo Medical Laboratories

1-800-533-1710

BTKS

Bruton Tyrosine Kinase (BTK) Genotype, Full Gene Sequence

Patient ID	Patient Name		Birth Date	Gender	Age
SA00059533	SAMPLEREPORT, BTKS N		1966-06-10	F	47
Order Number	**Client Order Number**	**Ordering Physician**	**Report Notes**		
SA00059533	SA00059533	Client, Client			
Account Information		**Collected**			
C7028846 DLMP Rochester		27 Jun 2013 00:00			

BTK, Full Gene Sequence

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BTK Full Gene Result

MCR

A mutation was NOT detected in the BTK gene.

BTK Full Gene Interpretation

MCR

No heterozygous pathogenic variations or variants of unknown significance (VUS) were identified in the BTK gene for this female patient, which would be consistent with carrier status for X-linked agammaglobulinemia (XLA). There are over 600 mutations reported in the BTK gene, including missense, nonsense, frameshift, deletions and insertions. The full-gene sequencing method can identify 92% of mutations within the BTK gene. However, 8% of mutations, which include large deletions, duplications or rearrangements cannot be detected by this method, but could potentially be identified by Btk flow cytometry due to absent Btk protein. This female patient had normal Btk protein in B cells and monocytes, however, the flow cytometry assay may not be sensitive to identify all carrier females based on protein expression alone. This result strongly decreases the likelihood, but does not conclusively rule out carrier status for X-linked Agammaglobulinemia (XLA) for this female patient. Some individuals who are suspected carriers of XLA and have involvement of the BTK gene may have mutations that are not identified by the described testing methodology, as described above. It is often helpful to test an obligate carrier or an affected family member. Identification of the mutation in this family would allow for more direct testing and risk assessment of at risk individuals. If this patient is the mother of a child affected with XLA, there is a small (<5%) risk that she carries the familial BTK mutation in a population of cells in the germline (germline mosaicism). This status would not be identified with the described testing methodology. Individuals with germline mosaicism are at increased risk for passing the mutation to future offspring. Correlation with family history recommended.

ADDITIONAL INFORMATION

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 Iorio 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 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.

If the patient has had an allogeneic blood or marrow transplant or a recent (i.e. less than 6 weeks from time of sample collection) heterologous blood transfusion these results may be inaccurate due to the presence of donor DNA. Laboratory developed test.

Reviewed By

MCR

Jamie Bruflat

Performing Site Legend

Code	Laboratory	Address
MCR	Mayo Clinic Dept. of Lab Med and Pathology	200 First Street SW, Rochester, MN 55905

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BTK, Full Gene Sequencing MCR

Performed

Received: 03 Jul 2013 13:32 **Reported:** 04 Sep 2013 11:25

Performing Site Legend

Code	Laboratory	Address
MCR	Mayo Clinic Dept. of Lab Med and Pathology	200 First Street SW, Rochester, MN 55905