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
SA00059534	SAMPLEREPORT, BTKS A		1966-06-10	F	47
Order Number	**Client Order Number**	**Ordering Physician**	**Report Notes**		
SA00059534	SA00059534	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

This individual was shown to have the following mutation in the BTK gene: splice site substitution in intron 16, c.1631+1G>T, g.100496273, p.?

BTK Full Gene Interpretation

MCR

The patient was found to have a pathogenic variation in the BTK gene - a splice site substitution located in the donor splice site of intron 16. Five prediction programs indicate that this variation would result in the loss of a splice donor. This mutation has been previously reported in BTKBase, a database of BTK mutations in XLA patients and female carriers (g. 66846 using the old numbering in BTKBase). While the consequence of this mutation is unpredictable, it is highly likely that this would result in skipping of exon 16. The BTK genetic result appears to correlate with the available clinical information of hypogammaglobulinemia and recurrent infections. No information is available on presence or absence of peripheral B cells or intracellular Btk protein. Recommend Btk protein evaluation by flow cytometry (test #89011) to determine impact of this mutation on Btk protein and for genotype-phenotype correlation.

This result would be consistent with a diagnosis of X-linked Agammaglobulinemia (XLA) for this male patient.

Since a mutation has been identified in the BTK gene in this individual, genetic testing for this 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 on-line test catalog at mayomedicallaboratories.com for information about how to order the "BTK Gene, Known Mutation" (89306).

The Btk gene has 19 exons, 18 of which are coding and produce an approximately 77kD protein. There are over 600 mutations reported in the BTK gene, including missense, nonsense, frameshift, deletions, insertions and splice-site mutations. 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.

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

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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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

BTK, Full Gene Sequencing MCR

Performed

Received: 03 Jul 2013 13:32 **Reported:** 04 Sep 2013 11:27

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