MAYO CLINIC

1-800-533-1710

BTK Gene, Full Gene Analysis

BTKSG

PATIENT NAME				ORDER NUMBER
TESTRNV, IMPLEMENTATION				**M702000285**
PATIENT ID X100407758	DATE OF BIRTH 02/19/1968	AGE 54 Y	SEX Male	REQUESTED BY ATLAS TEST
COLLECTED 2/2/2023, 8:33 AM	RECEIVED 2/7/2023, 3:03 PM	REPORTED 2/24/2023, 4:17 PM		
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TEST DESCRIPTION

Evaluation of BTK gene associated with X-linked agammaglobulinemia

SPECIMEN

WB Whole Blood

RESULT SUMMARY

Pathogenic Variant Detected

RESULT

Gene (Transcript)	Variant	Zygosity	Classification
BTK (NM_000061.2)	c.1921C>T p.Arg641Cys (p.R641C) ChrX(GRCh37):g.100604932G>A	Hemizygous	Pathogenic

The following hemizygous PATHOGENIC variant was detected:
BTK (NM_000061.2), chrX(GRCh37):g.100604932G>A, c.1921C>T, p.Arg641Cys (p.R641C)

INTERPRETATION

BTK c.1921C>T (p.Arg641Cys), PATHOGENIC
The hemizygous c.1921C>T (p.Arg641Cys) missense variant in the BTK gene (MIM:300300) is classified as pathogenic. The BTK gene encodes Bruton tyrosine kinase (BTK), a protein essential for the development and maturation of B cells. Pathogenic variants in this gene are associated with X-linked agammaglobulinemia (XLA). This variant has previously been reported in multiple male individuals with a diagnosis of X-linked Agammaglobulinemia (XLA) (1-7). This residue (p.Arg641) has been identified as important for stabilizing protein structure, and other variants have been detected at this residue (p.Arg641His and p.Arg641Gly) (2,3,8). This variant is absent from large control databases (9,10). The finding of a pathogenic BTK variant is supportive of a diagnosis of XLA for this individual but should be correlated with clinical findings. Appropriate screening and/or management strategies should be considered.

This result should be interpreted in the context of clinical findings, family history, and other laboratory testing.

Consultation with a genetics professional is recommended for interpretation of this result and to determine whether reproductive risk assessment and familial testing may be of benefit to this family. Genetic testing for family members is available by ordering FMTT / Familial Mutation, Targeted Testing for the specific variant(s) detected. Please contact the laboratory at 1-800-533-1710 or the online test catalog at www.mayocliniclabs.com for information about FMTT.

REFERENCES:
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METHOD

Next generation sequencing (NGS) and/or Sanger sequencing was performed to test for the presence of variants in coding regions and intron/exon boundaries of the gene analyzed. The human genome reference GRCh37/hg19 build was used for sequence read alignment. At least 99% of the bases are covered at a read depth >30X. Sensitivity is estimated at >99% for single nucleotide variants, >94% for indels up to 39 base pairs, >95% for deletions up to 75 base pairs and insertions up to 47 base pairs. NGS and/or a PCR-based quantitative method was performed to test for the presence of deletions and duplications in the gene analyzed. See the Genes Analyzed field for a list of gene(s) tested.

There may be regions of genes that cannot be effectively evaluated for sequencing or deletion and duplication analysis as a result of technical limitations of the assay, including regions of homology, high GC content, and repetitive sequences. Confirmation of select reportable variants was performed by alternate methodologies based on internal laboratory criteria. See www.mayocliniclabs.com (TEST ID BTKSG) for details regarding genes with regions not routinely covered.

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GENES ANALYZED

BTK

DISCLAIMER

Clinical Correlations
An online research opportunity called GenomeConnect (genomeconnect.org), a project of ClinGen, is available for the recipient of this genetic test. This patient registry collects de-identified genetic and health information to advance the knowledge of genetic variants. Mayo Clinic is a collaborator of ClinGen. This may not be applicable for all tests.

If testing was performed because of a clinically significant family history it is often useful to first test an affected family member. Detection of a reportable variant(s) in an affected family member would allow for more informative testing of at risk individuals.

To discuss the availability of further testing options or for assistance in the interpretation of these results, Mayo Clinic Laboratory genetic counselors can be contacted at 1-800-533-1710.

Technical Limitations
Next generation sequencing may not detect all types of genomic variants. In rare cases, false negative or false positive results may occur. The depth of coverage may be variable for some target regions, but assay performance below the minimum acceptable criteria or for failed regions will be noted. Given these limitations, negative results do not rule out the diagnosis of a genetic disorder. If a specific clinical disorder is suspected, evaluation by alternative methods can be considered.

There may be regions of genes that cannot be effectively evaluated for sequencing or deletion and duplication analysis as a result of technical limitations of the assay, including regions of homology, high GC content, and repetitive sequences. Confirmation of select reportable variants was performed by alternate methodologies based on internal laboratory criteria.

Additionally, low level mosaic variants may not be detected.

This test is not designed to differentiate between somatic and germline variants. If there is a possibility that any detected variant is somatic, additional testing may be necessary to clarify the significance of results.

Reclassification of Variants Policy
See www.mayocliniclabs.com (TEST ID BTKSG) for information regarding the laboratory's policy for reclassification of variants.

Variant Evaluation
Variant curation is performed using published ACMG-AMP recommendations as a guideline. Other gene-specific guidelines may also be considered. Variants classified as benign or likely benign are not reported.

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Results from in silico evaluation tools may change over time and should be interpreted with caution and professional clinical judgment.

TEST CLASSIFICATION

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

RELEASED BY

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