MedGenome Labs Ltd.
Sy No 94/1C and 94/2, Tower-1, Veerasandra Village, Attibele Hobli,
Electronic City, Phase-1, Bangalore, Karnataka, 560100.

MEDGENOME

DNA TEST REPORT – MEDGENOME LABORATORIES

Full Name / Ref No:	**Sharmaine De Silva**	Order ID/Sample ID:	**1650199/9786674**
Date of Birth / Age:	73 years	Sample Type:	Peripheral Blood in EDTA
Gender:	Female	Date of Sample Collection:	19-02-2026
Referring Clinician:	Dr. Mahendra Perera, Aegle Omics Private Limited - Colombo	Date of Sample Receipt: Date of Order: Date of Report:	21-02-2026 23-02-2026 02-03-2026
Test Requested:	**UGT1A1 repeat analysis [MGM076]**		

CLINICAL DIAGNOSIS / SYMPTOMS / HISTORY

The subject is being evaluated for *UGT1A1*28* variation in promoter region of *UGT1A1* gene.

RESULTS

EXPANDED REPEAT PATTERN DETECTED

Result summary

Gene (Transcript) #	Location	Variant	Zygosity	Disease (OMIM)	Inheritance
UGT1A1 (+) (ENST00000360418)	Promoter region	(c.-55_-54insTA); *UGT1A1*28*	Heterozygous	Gilbert Syndrome / Crigler-Najjar syndrome type 2	Autosomal recessive

CLINICAL CORRELATION AND VARIANT INTERPRETATION

A heterozygous 2 bp insertion of TA nucleotides [c.-55_-54insTA], leading to 7 TA repeats [A (TA)$_7$TAA] in the promoter region of *UGT1A1* gene, was detected in this patient.

This variation is generally known as *UGT1A1*28*. The *UGT1A1* promoter region with six TA repeats [A(TA)$_6$TAA] is considered as normal, while TA repeats of more than six numbers of results in decreased transcriptional activity of *UGT1A1* gene, which encodes for bilirubin-UGT enzyme (1, 2). Reduced bilirubin-UGT enzyme expression slows the rate of glucuronidation of unconjugated bilirubin and it builds up in the body, causing mild hyperbilirubinemia.

***Inheritance:** Gilbert syndrome is generally considered to be an autosomal recessive disorder (3). However, there have been cases of heterozygosity and compound heterozygosity reported in patients with Gilbert syndrome, particularly among the Asian population (4, 5).

Gilbert Syndrome (OMIM# 143500) is caused by homozygous, compound heterozygous, or heterozygous variations in *UGT1A1* gene. The *UGT1A1*28* variation, along with other external factors like non-*UGT1A1* variations, hepatic transport abnormalities, occult hemolysis and stress induced induction of heme oxygenase are also reported in the pathogenesis of Gilbert syndrome (6).

Crigler-Najjar syndrome type 2 (OMIM# 606785), is caused by UGT1A1*28 variation in homozygous condition along with a *UGT1A1* structural variation in heterozygous condition. Hence the expanded TA repeat pattern observed in the *UGT1A1* promoter of this subject needs to be carefully correlated with the clinical condition.

In an experimental study, *UGT1A1* Gene Polymorphisms found to be common in in North Indian Neonates Presenting with Unconjugated Hyperbilirubinemia [7].

Hence the expanded TA repeat pattern observed in the *UGT1A1* promoter of this subject needs to be carefully correlated with the clinical condition.

RECOMMENDATIONS

Genetic counselling is advised.

TEST INFORMATION

UGT1A1 gene belongs to a family of genes that provide instructions for producing enzymes called UDP-glucuronosyltransferases which catalyses the glucuronidation reaction. The protein produced from the *UGT1A1* gene, called the bilirubin uridine diphosphate glucuronosyl transferase (bilirubin-UGT) enzyme, which converts the toxic form of bilirubin (unconjugated bilirubin) to its nontoxic form (conjugated bilirubin), making it able to be dissolved and removed from the body. Variations in *UGT1A1* gene can cause Crigler-Najjar syndrome, Gilbert syndrome, and transient familial neonatal hyperbilirubinemia. Gilbert syndrome is characterized by periods of mild unconjugated hyperbilirubinemia. The most common variations reported in *UGT1A1* are *UGT1A1*6* (Gly71Arg) and *UGT1A1*28*, which is characterized by the presence of $A(TA)_7TAA$ sequence in the promoter region**.**

METHODOLOGY

Promoter region and exon 1 of the *UGT1A1* gene were PCR-amplified and the products were sequenced using Sanger sequencing. The sequences were aligned to genomic reference sequence NC_000002.12 in NCBI GenBank database to detect variations using software programs.

NOTE:

- The coding DNA sequence (CDS) based allele calls (c.) for the mutations and the corresponding amino acid change is based on the *UGT1A1* mRNA reference sequence.
- The SNP numbers (rs ID) is based on the NCBI dbSNP (http://www.ncbi.nlm.nih.gov/SNP/) database. The nucleotide and SNP numbers will differ based on the reference file chosen and the database used.
- Clinical relevance, if any, is reported from previously published reports. Relevant references will be indicated for each known clinically relevant mutation.
- The sequencing results (including the chromatograms and image of sequence alignment to the reference sequence) can be provided upon request from the referring physician.

DISCLAIMER

1. This is a laboratory developed test and the development and the performance characteristics of this test was determined by MedGenome.
2. Please note that the tests are performed only after approval of referring/ ordering clinician/physician. Above recommendations /results should not be viewed as only source of information on which treatment or other clinical decisions are made. Clinical correlation is highly recommended.
3. The classification of variants of unknown significance can change over time and MedGenome cannot be held responsible for this. Please contact MedGenome later to inquire about any changes.
4. This sanger custom test is not a clinically validated assay for each and every primer set. No form of test can guarantee 100% accuracy. This assay is no such exception, and it has some Inherent pitfalls.
5. The PCR based assay will not amplify genic regions outside primer binding site, may not detect the exact size for the deletion or duplication which is more than 50bp.
6. Pseudogenes can present challenges during sequencing and analysis, which may impact the accuracy and interpretation of the results.
7. Though PCR is a highly sensitive and specific technique, performance may vary based on several factors including allelic dropout & preferential amplification (Chance phenomenon) causing a potential source of misdiagnosis for both

dominant and recessive diseases. About 0.44% of total cases are susceptible to allele dropout phenomenon, which can lead to misdiagnosis.

8. Testing of affected/carrier index/proband samples parallelly with test samples is highly recommended to rule out false negative/positive results.
9. The accuracy of the results is based on the assumption that samples received were correctly identified, family relationships are true and clinical diagnosis of relatives is correct.
10. In a very few cases genetic tests may not show the correct results leading to false positives and negatives; e.g. because of the quality of the sample provided to MedGenome. In case where any test provided by MedGenome fails for unforeseeable or unknown reason that cannot be influenced by MedGenome in advance, MedGenome shall not be responsible for the incomplete, potentially misleading, or even wrong result of testing if such could not be recognized by MedGenome in advance.
11. Negative results do not negate the absence of mutations that are not covered by the test.
12. The report shall be generated within turnaround time (TAT), however, such TAT may vary depending upon the complexity of test(s) requested. MedGenome under no circumstances will be liable for any delay beyond afore mentioned TAT.
13. If results obtained do not match the clinical findings, additional testing should be considered as per the referring clinician's recommendations.
14. MedGenome Labs hereby recommends the patients and/ or guardians of the patients, as the cause may be, to take assistance of the clinician or a certified physician or doctor, to interpret the report(s) thus generated. MedGenome hereby disclaims all liability arising in connection with the report (s).

Ms. Rashmi Rasalkar	Mr. Manjunath V	Dr. Ram Murthy Anjanappa	Dr. Pragya Gupta
Associate Scientist – Lab Operations	Senior Manager – Lab Operations	PhD Senior Scientist	MBBS. MD Path, PDF Molecular Genetics (TMCK) Senior Molecular Pathologist & Clinical Head

REFERENCES

1. Bosma, P.J., 2003. Inherited disorders of bilirubin metabolism. Journal of hepatology, 38(1), pp.107-117.
2. Beutler E, Gelbart T, Demina A. Racial variability in the UDP-glucuronosyltransferase 1 (UGT1A1) promoter: a balanced polymorphism for regulation of bilirubin metabolism? Proc Natl Acad Sci U S A. 1998;95: 8170–4.
3. Wolkoff, A.W., Chowdhury, J.R. and Arias, I.M., 1983. Hereditary jaundice and disorders of bilirubin metabolism. Metabolic basis of inherited disease/[edited by] John B. Stanbury...[et al.].
4. Koiwai, O., Nishizawa, M., Hasada, K., Aono, S., Adachi, Y., Mamlya, N. and Sato, H., 1995. Gilbert's syndrome is caused by a heterozygous missense mutation in the gene for bilirubin UDP-glucuronosyltransferase. Human molecular genetics, 4(7), pp.1183-1186.
5. Hsieh, S.Y., Wu, Y.H., Lin, D.Y., Chu, C.M., Wu, M. and Liaw, Y.F., 2001. Correlation of mutational analysis to clinical features in Taiwanese patients with Gilbert's syndrome. The American journal of gastroenterology, 96(4), p.1188.
6. Schmid, R., 1995. Gilbert's syndrome—a legitimate genetic anomaly?
7. Agrawal, S., Kumar, P., Rathi, R. et al. UGT1A1 Gene Polymorphisms in North Indian Neonates Presenting with Unconjugated Hyperbilirubinemia. Pediatr Res 65, 675–680 (2009).

END OF REPORT