



## ***In silico* Analysis of UGT Gene as A Preliminary Data: (A-Review)**

**USHA ADIGA**

Department of Biochemistry, K. S. Hegde Medical Academy, Nitte (Deemed to be University),  
Mangalore, India.

\*Corresponding author E-mail: ushachidu@yahoo.com

<http://dx.doi.org/10.13005/ojc/390402>

(Received: February 13, 2023; Accepted: July 01, 2023)

### **ABSTRACT**

Recurrent unprovoked seizures are a hallmark of epilepsy, a chronic neurological condition caused by momentary changes in the way cortical neurons conduct electricity. Epilepsy patients have been treated with more than 20 anti-epileptic medicines (AEDs) to control their seizures, but one-third of them are resistant to the drugs. The pharmacological treatment of epilepsy frequently involves therapeutic drug monitoring (TDM), although the plasma levels of various AEDs do not always correspond well with the doses and/or the therapeutic or harmful effects of the medications. The genetic polymorphisms of numerous enzymes involved in the metabolism of these medications may be to blame for this. The study's goal was to examine UGT1A6 and UGT2B7 gene polymorphisms using bioinformatics methods.

**Keywords:** UGT gene, SIFT, Polyphen, Bioinformatics.

### **INTRODUCTION**

#### **Single Nucleotide Polymorphisms**

SNPs, also known as single nucleotide polymorphisms, are variations in the DNA sequence brought on by changes to one single nucleotide (A, T, C or G). Around 90% of the genetic diversity in humans is made up of SNPs. SNPs are distributed differently throughout areas of the 3-billion-base human genome, occurring every 100–300 bases<sup>1</sup>. SNPs can exist in both coding and noncoding areas of the genome. SNPs can have a variety of effects on how cells behave, from no effect to a disease state or a changed reaction to a treatment. Since they account for almost half of all known genetic differences, nonsynonymous SNPs (nsSNPs) that

cause an amino acid residue substitution in the protein product are of particular interest related to human inherited disease<sup>2</sup>. Coding synonymous SNPs (sSNPs) and SNPs outside of the gene promoter or coding regions may nonetheless have an impact on transcription factor binding, splicing, or gene expression<sup>3,4</sup>.

Identification of the SNPs is crucial since they cause particular symptoms. This is a difficult operation, though, as it necessitates repeatedly evaluating thousands of SNPs in candidate genes<sup>5</sup>. The selection of a collection of SNPs is a challenging undertaking whenever a study is being prepared to determine the role of an SNP in disease. To distinguish between neutral and functional SNPs in such



circumstances, bioinformatics prediction techniques may be of tremendous use. They might also show the structural underpinnings of the mutations.

The sole purpose of these bioinformatics tools is to rank SNPs according to their functional importance<sup>6,7</sup>.

By employing bioinformatics methods for *in silico* gene analysis, it is possible to detect a link between a gene and a disease at a level of statistical significance without screening a sizable number of people. In other words, these techniques aid in the selection of SNPs prior to analysis<sup>5</sup>.

If disease-associated SNPs can be distinguished from neutral SNPs before using wet lab-based techniques, it would be very helpful. When the illness connections could not be verified by further independent investigations, *in silico* analyses are helpful<sup>6,8</sup>. Consequently, independent confirmation of SNP functioning gained through the use of prediction tools could potentially be used as additional resources to discriminate true associations from false positives.

### **Epilepsy AND valproate metabolism**

Because of its several modes of action and favourable safety profile, sodium valproate (VPA) is frequently used to treat paediatric epilepsy. VPA is metabolised primarily by three pathways: glucuronidation, mitochondrial oxidation, and cytochrome P450 (CYP)-mediated oxidation. The first two are the main pathways, respectively metabolising 50% and 40% of the injected dose, while the third is regarded as a minor route, metabolising 10%. Uridine-5'-diphosphate glucuronosyl transferases (UGTs), a superfamily of enzymes that catalyses the binding of glucuronic acid to a wide range of endobiotics and xenobiotics, catalyse the glucuronidation reaction. VPA metabolism may change as a result of polymorphisms in the genes that code for UGT enzymes. Drug toxicity or inadequate treatment may result from differences in the blood level of VPA due to changes in its rate of glucuronidation. Additionally, a decrease in these enzymes' ability to glucuronidate VPA may result in a switch in metabolic pathways in favour of two additional pathways that have been linked to the hepatotoxic effects of VPA. UGT genetic variants may affect VPA metabolism, which could change the drug's steady-state plasma levels. To maintain the therapeutic levels, this may necessitate giving

epileptics a higher or lower dose of VPA. Monitoring VPA concentrations is important for clinic use in order to prevent adverse responses, decrease adverse reactions, and manage seizures.

The high inter-individual variability may be caused by genetic variations in the genes encoding drug-metabolizing enzymes and their functional effects. The idea of "individualised medicine" is developing, and the idea of "one drug fits all" has given way to the idea of "right drug for the right patient at the right dose and time." Therefore, it is crucial to look into any potential involvement that genetic polymorphisms may have in the metabolism of VPA. To the best of our knowledge, there aren't many studies on the impact of UGT1A6 and UGT2B7 gene polymorphism on VPA metabolism, particularly in Indian contexts. Although there are already a number of studies documenting the relationship between SNPs in the UGT gene and various disorders, computational investigation of the functional effects of SNPs in this gene has not yet been done. To detect potentially harmful SNPs, a variety of publically accessible computational techniques, including Sorting Intolerant From Tolerant (SIFT)<sup>9</sup> and Polymorphism Phenotyping (PolyPhen)<sup>10</sup>, were used<sup>11</sup>.

The SIFT method makes predictions about how changing amino acids would impact protein function. Sequence homology between related genes and domains and the physical-chemical characteristics of the amino acid residues are the foundations for its operation<sup>12-14</sup>.

PolyPhen also considers the nature of the relevant amino acid residues and the preservation of the sequence, but it also gives importance to the substitution's location within the protein's structural properties that are listed in the SwissProt annotated database<sup>5,15</sup>. It has been estimated that the "false negative" and "false positive" error rates of SIFT are 31% and 20%, and 31% and 9% for PolyPhen, respectively, in benchmarking studies using amino acid substitutions assumed to have a significant negative impact on the residual activity of the variant protein as the test set<sup>10,13,15-17</sup>.

Objective of the study was to evaluate the single nucleotide polymorphisms of UGT 1A6 and UGT2B7 gene using bioinformatics tools.

**Methodology****Evaluation of the functional impact of missense SNPs using SIFT**

The total number of non-intronic missense mutations in the UGT1A6 FASTA amino acid sequence with protein accession ID NP\_001063.2 was 231; rs numbers and the locations of the SNPs on the chromosomes were noted in a format suitable for analysis using the online tool Sort the Intolerant from Tolerant (SIFT). Polyphen tool was used to the selected SNPs of UGT gene.

**RESULTS AND DISCUSSION**

Following the analysis, we found the following things;

Coding variants had a 100% success rate, but anticipated ones had a 98% success rate

(227 out of 231), were tolerated at 46% (106/227), and were harmful at 54% (121/227). Only 1% (2 of 231) were synonymous, while 91% (229 of 231) were non-synonymous. 192 out of 231 of them, or 83 percent, were new. The SIFT scale runs from 0 to 1. SNPs with a SIFT score of less than or equal to 0.05 are deemed harmful, whereas those with a value higher than that are deemed tolerable. The optimal range for the median information is between 2.75 and 3.5. This is used to gauge the diversity of the prediction sequences. An indicator indicating the prediction was based on closely similar sequences is a number larger than 3.25. The number of sequences at a certain place is known as the number of sequences at prediction. SIFT automatically selects sequences, however if the alteration is at the start or end of the protein, there might only be a few sequences represented there, as this column demonstrates.

**Table 1: SIFT analysis results of 231 SNPs of UGT1A6**

Coordinates	Substitution	dbSNP ID	SNP Type	Prediction	Score	Median Info	#Seqs at position
2,234602202,1,A/C	R184S	rs1105879:C	Nonsynonymous	TOLERATED	0.39	2.77	125
2,234602191,1,A/G	T181A	rs2070959:G	Nonsynonymous	TOLERATED	0.63	2.77	125
2,234601669,1,T/A	S7T	Novel(P19224)	Nonsynonymous	TOLERATED	0.69	3	38
2,234676979,1,A/C	N132H	novel	Nonsynonymous	DAMAGING	0	2.83	341
2,234681059,1,T/A	Y218N	rs34993780:A	Nonsynonymous	DAMAGING	0.01	2.86	319
2,234677012,1,G/A	V143M	novel	Nonsynonymous	DAMAGING	0.01	2.83	341
2,234676880,1,C/G	R99G	rs55750087:G	Nonsynonymous	DAMAGING	0	2.83	341
2,234675738,1,G/A	G40E	rs62625011:A	Nonsynonymous	DAMAGING	0	2.83	341
2,234675807,1,A/G	Q63R	rs72551348:G	Nonsynonymous	DAMAGING	0	2.84	340
2,234676519,1,C/G	R73G	novel	Nonsynonymous	DAMAGING	0.02	2.83	341
2,234676568,1,A/C	Q89P	novel	Nonsynonymous	DAMAGING	0	2.83	341
2,234676905,1,C/T	S107F	rs72551353:T	Nonsynonymous	DAMAGING	0.04	2.83	341
2,234680955,1,C/T	P183L	rs114982090:T	Nonsynonymous	DAMAGING	0.02	2.85	322
2,234676504,1,C/T	R68W	rs139607673:T	Nonsynonymous	DAMAGING	0	2.83	341
2,234676989,1,G/A	R135H	rs140613392:A	Nonsynonymous	TOLERATED	0.38	2.83	341
2,234680927,1,C/T	R174C	rs143033456:T	Nonsynonymous	DAMAGING	0	2.85	321
2,234676937,1,G/A	V118I	rs143573365:A	Nonsynonymous	TOLERATED	0.24	2.83	341
2,234676526,1,C/A	S75*	novel	Damaging due to stop	N/A	N/A	N/A	N/A
2,234681098,1,G/A	V231M	novel	Nonsynonymous	DAMAGING	0.02	2.86	319
2,234680952,1,G/A	R182H	novel	Nonsynonymous	DAMAGING	0	2.85	321
2,234675779,1,A/G	I54V	novel	Nonsynonymous	TOLERATED	0.08	2.84	340
2,234680951,1,C/T	R182C	novel	Nonsynonymous	DAMAGING	0	2.85	321
2,234680925,1,T/A	M173K	novel	Nonsynonymous	TOLERATED	0.23	2.85	321
2,234681062,1,C/T	H219Y	novel	Nonsynonymous	TOLERATED	0.26	2.86	319
2,234676881,1,G/A	R99H	novel	Nonsynonymous	DAMAGING	0	2.83	341
2,234681161,1,A/C	K252Q	novel	Nonsynonymous	TOLERATED	0.07	2.87	256
2,234680957,1,G/A	V184M	novel	Nonsynonymous	TOLERATED	0.88	2.85	322
2,234681167,1,G/A	G254R	novel	Nonsynonymous	TOLERATED	0.43	2.89	256
2,234676889,1,A/G	I102V	novel	Nonsynonymous	TOLERATED	0.57	2.83	341
2,234602207,1,C/T	P186L	novel	Nonsynonymous	TOLERATED	0.32	2.77	125
2,234676866,1,G/A	G94D	novel	Nonsynonymous	DAMAGING	0	2.83	341
2,234676582,1,G/A	G94S	novel	Nonsynonymous	DAMAGING	0	2.83	341
2,234676499,1,T/A	L66Q	novel	Nonsynonymous	DAMAGING	0	2.83	341
2,234601998,1,G/C	M116I	novel	Nonsynonymous	TOLERATED	0.2	2.77	123

2,234681032,1,G/A	A209T	novel	Nonsynonymous	TOLERATED	0.06	2.85	322
2,234601796,1,T/G	L49R	novel	Nonsynonymous	DAMAGING	0	2.77	123
2,234675722,1,G/A	V35M	novel	Nonsynonymous	DAMAGING	0	2.83	341
2,234681151,1,A/T	K248N	novel	Nonsynonymous	DAMAGING	0.03	2.87	252
2,234681014,1,G/A	A203T	novel	Nonsynonymous	DAMAGING	0	2.85	322
2,234681147,1,G/A	R247Q	novel	Nonsynonymous	TOLERATED	0.24	2.87	285
2,234676988,1,C/A	R135S	novel	Nonsynonymous	DAMAGING	0	2.83	341
2,234676979,1,A/C	N132H	novel	Nonsynonymous	DAMAGING	0	2.83	341
2,234601859,1,C/A	S70Y	rs1042708:A	Nonsynonymous	DAMAGING	0.01	2.77	124
2,234681134,1,G/C	A243P	rs1042709:C	Nonsynonymous	TOLERATED	0.2	2.86	303
2,234675780,1,T/C	I54T	rs17851756:C	Nonsynonymous	DAMAGING	0	2.84	340
2,234601714,1,G/T	G22C	rs45547342:T	Nonsynonymous	DAMAGING	0.04	2.8	106
2,234675696,1,T/C	I26T	rs72551347:C	Nonsynonymous	DAMAGING	0	2.83	341
2,234676883,1,G/A	A100T	rs72551352:A	Nonsynonymous	DAMAGING	0.02	2.83	341
2,234676924,1,C/G	S113R	rs72551354:G	Nonsynonymous	DAMAGING	0	2.83	341
2,234676982,1,G/C	A133P	rs72551355:C	Nonsynonymous	DAMAGING	0.01	2.83	341
2,234677063,1,A/G	K160E	rs72551356:G	Nonsynonymous	TOLERATED	0.15	2.83	340
2,234680991,1,A/C	E195A	rs72551358:C	Nonsynonymous	DAMAGING	0	2.85	322
2,234681066,1,C/G	S220C	rs72551360:G	Nonsynonymous	TOLERATED	0.16	2.86	319
2,234602180,1,C/G	S177C	rs74429718:G	Nonsynonymous	TOLERATED	0.16	2.77	124
2,234602423,1,A/G	D258G	rs112793692:G	Nonsynonymous	TOLERATED	0.21	2.77	125
2,234675764,1,A/G	K49E	rs114000345:G	Nonsynonymous	TOLERATED	1	2.84	340
2,234601762,1,C/G	H38D	rs114430142:G	Nonsynonymous	DAMAGING	0	2.77	122
2,234601667,1,G/A	R6H	rs115279280:A	Nonsynonymous	TOLERATED	0.38	3.34	24
2,234680981,1,T/C	F192L	rs115410088:C	Nonsynonymous	DAMAGING	0	2.85	322
2,234602030,1,A/G	Q127R	rs115940468:G	Nonsynonymous	TOLERATED	0.49	2.77	125
2,234680992,1,G/A	E195E	novel	Synonymous	N/A	N/A	N/A	322
2,234602174,1,C/T	P175L	rs116011063:T	Nonsynonymous	TOLERATED	0.16	2.77	125
2,234601739,1,T/G	L30R	rs116067611:G	Nonsynonymous	DAMAGING	0	2.77	122
2,234602111,1,C/G	P154R	novel	Nonsynonymous	DAMAGING	0	2.77	125
2,234602012,1,T/A	L121Q	rs141940106:A	Nonsynonymous	TOLERATED	0.15	2.77	125
2,234602449,1,G/T	V267F	rs148089971:T	Nonsynonymous	TOLERATED	0.23	2.77	125
2,234601774,1,A/G	M42V	rs148594741:G	Nonsynonymous	TOLERATED	0.12	2.77	122
2,234601941,1,T/A	N97K	rs149122547:A	Nonsynonymous	TOLERATED	0.93	2.77	125
2,234676530,1,T/A	N76K	rs149750520:A	Nonsynonymous	DAMAGING	0.04	2.83	341
2,234681027,1,G/A	R207H	rs150687296:A	Nonsynonymous	DAMAGING	0	2.85	322
2,234602311,1,C/A	L221I	novel	Nonsynonymous	TOLERATED	0.36	2.77	125
2,234602353,1,G/T	A235S	novel	Nonsynonymous	DAMAGING	0.01	2.77	125
2,234676535,1,C/T	A78V	novel	Nonsynonymous	DAMAGING	0	2.83	341
2,234602309,1,A/G	Y220C	novel	Nonsynonymous	DAMAGING	0.01	2.77	125
2,234602029,1,C/G	Q127E	novel	Nonsynonymous	TOLERATED	0.96	2.77	125
2,234602105,1,C/A	A152D	novel	Nonsynonymous	DAMAGING	0.01	2.77	125
2,234675801,1,T/C	I61T	novel	Nonsynonymous	DAMAGING	0	2.84	340
2,234601928,1,C/T	S93L	novel	Nonsynonymous	TOLERATED	0.35	2.77	125
2,234676573,1,G/A	D91N	novel	Nonsynonymous	DAMAGING	0	2.83	341
2,234676874,1,A/C	M97L	novel	Nonsynonymous	DAMAGING	0.01	2.83	341
2,234676965,1,G/A	G127D	novel	Nonsynonymous	DAMAGING	0.02	2.83	341
2,234602279,1,C/G	A210G	novel	Nonsynonymous	TOLERATED	0.15	2.77	125
2,234681040,1,C/A	H211Q	novel	Nonsynonymous	DAMAGING	0.01	2.85	321
2,234602438,1,A/G	Y263C	novel	Nonsynonymous	DAMAGING	0	2.77	125
2,234602359,1,C/T	L237F	novel	Nonsynonymous	TOLERATED	0.08	2.77	125
2,234602087,1,C/G	A146G	novel	Nonsynonymous	DAMAGING	0.03	2.77	125
2,234676875,1,T/C	M97T	novel	Nonsynonymous	DAMAGING	0.01	2.83	341
2,234602495,1,G/C	R15T	novel	Nonsynonymous	DAMAGING	0.03	2.83	335
2,234675792,1,T/A	L58*	novel	Damaging due to stop	N/A	N/A	N/A	N/A
2,234602021,1,T/A	I124N	novel	Nonsynonymous	TOLERATED	0.47	2.77	125
2,234680976,1,C/T	A190V	novel	Nonsynonymous	DAMAGING	0	2.85	322
2,234601891,1,C/T	P81S	novel	Nonsynonymous	TOLERATED	0.98	2.77	124
2,234602381,1,T/A	I244N	novel	Nonsynonymous	TOLERATED	0.31	2.77	125
2,234601679,1,G/A	R10K	novel	Nonsynonymous	TOLERATED	0.95	2.93	56

---

2,234676944,1,T/C	M120T	novel	Nonsynonymous	DAMAGING	0	2.83	341
2,234680973,1,T/A	L189Q	novel	Nonsynonymous	TOLERATED	0.17	2.84	320
2,234602390,1,A/G	Y247C	novel	Nonsynonymous	DAMAGING	0	2.77	125
2,234601678,1,A/G	R10G	novel	Nonsynonymous	TOLERATED	0.57	2.93	56
2,234601666,1,C/A	R6S	novel	Nonsynonymous	TOLERATED	0.82	3.34	24
2,234676992,1,T/C	M136T	novel	Nonsynonymous	DAMAGING	0	2.83	341
2,234676549,1,C/G	L83V	novel	Nonsynonymous	TOLERATED	0.08	2.83	341
2,234601723,1,G/A	V25I	novel	Nonsynonymous	TOLERATED	0.09	2.78	115
2,234602107,1,T/A	L153I	novel	Nonsynonymous	TOLERATED	0.41	2.77	125
2,234602183,1,T/C	L178P	novel	Nonsynonymous	DAMAGING	0.02	2.77	124
2,234675770,1,G/C	A51P	novel	Nonsynonymous	DAMAGING	0.01	2.84	340
2,234602167,1,G/A	G173S	novel	Nonsynonymous	TOLERATED	0.48	2.77	125
2,234681026,1,C/A	R207S	novel	Nonsynonymous	DAMAGING	0	2.85	322
2,234680939,1,C/T	L178F	novel	Nonsynonymous	DAMAGING	0.01	2.85	321
2,234601732,1,A/G	K28E	novel	Nonsynonymous	DAMAGING	0	2.77	121
2,234681171,1,G/A	R255Q	novel	Nonsynonymous	DAMAGING	0.03	2.87	252
2,234602132,1,A/G	E161G	novel	Nonsynonymous	DAMAGING	0.02	2.77	125
2,234681003,1,G/A	R199K	novel	Nonsynonymous	TOLERATED	0.21	2.85	322
2,234601757,1,G/A	G36E	novel	Nonsynonymous	DAMAGING	0.01	2.77	122
2,234602134,1,T/C	Y162H	novel	Nonsynonymous	TOLERATED	0.32	2.77	125
2,234675720,1,T/C	I34T	novel	Nonsynonymous	DAMAGING	0	2.83	341
2,234681074,1,G/A	V223M	novel	Nonsynonymous	DAMAGING	0	2.86	319
2,234601988,1,G/A	R113K	novel	Nonsynonymous	TOLERATED	0.85	2.77	124
2,234680928,1,G/A	R174H	novel	Nonsynonymous	TOLERATED	0.06	2.85	321
2,234676510,1,A/G	T70A	novel	Nonsynonymous	TOLERATED	0.37	2.83	341
2,234602231,1,G/A	R194K	novel	Nonsynonymous	TOLERATED	0.47	2.78	124
2,234675773,1,A/G	M52V	novel	Nonsynonymous	TOLERATED	0.07	2.84	340
2,234602363,1,A/G	K238R	novel	Nonsynonymous	TOLERATED	0.2	2.77	125
2,234677057,1,G/T	A158S	novel	Nonsynonymous	DAMAGING	0.03	2.83	340
2,234601871,1,C/A	T74K	novel	Nonsynonymous	TOLERATED	0.41	2.77	124
2,234676505,1,G/A	R68Q	novel	Nonsynonymous	DAMAGING	0	2.83	341
2,234601724,1,T/C	V25A	novel	Nonsynonymous	TOLERATED	0.42	2.78	115
2,234676954,1,G/A	M123I	novel	Nonsynonymous	TOLERATED	0.69	2.83	341
2,234681041,1,G/A	D212N	novel	Nonsynonymous	TOLERATED	0.25	2.85	321
2,234601856,1,A/G	E69G	novel	Nonsynonymous	TOLERATED	0.2	2.77	124
2,234681108,1,T/C	V234A	novel	Nonsynonymous	TOLERATED	0.28	2.86	318
2,234602197,1,A/T	S183C	novel	Nonsynonymous	DAMAGING	0.01	2.77	125
2,234601828,1,G/A	V60M	novel	Nonsynonymous	TOLERATED	0.19	2.77	124
2,234601715,1,G/A	G22D	novel	Nonsynonymous	TOLERATED	0.13	2.8	106
2,234602471,1,T/C	I7T	novel	Nonsynonymous	DAMAGING	0.04	2.84	336
2,234681038,1,C/T	H211Y	novel	Nonsynonymous	TOLERATED	0.4	2.85	321
2,234680987,1,G/A	V194M	novel	Nonsynonymous	DAMAGING	0.02	2.85	322
2,234602224,1,A/G	I192V	novel	Nonsynonymous	TOLERATED	1	2.77	125
2,234677080,1,C/A	D165E	novel	Nonsynonymous	TOLERATED	0.15	2.83	340
2,234676981,1,T/A	N132K	novel	Nonsynonymous	DAMAGING	0	2.83	341
2,234602110,1,C/A	P154T	novel	Nonsynonymous	DAMAGING	0.05	2.77	125
2,234601977,1,G/C	Q109H	novel	Nonsynonymous	TOLERATED	0.54	2.76	122
2,234602228,1,C/G	P193R	novel	Nonsynonymous	DAMAGING	0	2.77	125
2,234676974,1,T/C	M130T	novel	Nonsynonymous	TOLERATED	0.36	2.83	341
2,234677058,1,C/T	A158V	novel	Nonsynonymous	DAMAGING	0.01	2.83	340
2,234601876,1,A/C	K76Q	novel	Nonsynonymous	TOLERATED	0.08	2.77	124
2,234602141,1,G/T	G164V	novel	Nonsynonymous	DAMAGING	0.04	2.77	125
2,234602510,1,A/C	Q20P	novel	Nonsynonymous	DAMAGING	0.02	2.83	338
2,234680931,1,T/C	L175P	novel	Nonsynonymous	DAMAGING	0	2.85	321
2,234680990,1,G/A	E195K	novel	Nonsynonymous	DAMAGING	0.02	2.85	322
2,234601719,1,G/T	M23I	novel	Nonsynonymous	TOLERATED	0.39	2.79	110
2,234602480,1,T/C	I10T	novel	Nonsynonymous	DAMAGING	0.03	2.84	336
2,234675690,1,C/A	A24D	novel	Nonsynonymous	TOLERATED	0.46	2.83	341
2,234602362,1,A/G	K238E	novel	Nonsynonymous	TOLERATED	0.22	2.77	125
2,234676932,1,A/G	N116S	novel	Nonsynonymous	DAMAGING	0	2.83	341

---

2,234601913,1,A/G	K88R	novel	Nonsynonymous	TOLERATED	0.07	2.77	124
2,234601817,1,T/C	I56T	novel	Nonsynonymous	DAMAGING	0.03	2.77	123
2,234681095,1,G/A	V230I	novel	Nonsynonymous	TOLERATED	0.82	2.85	318
2,234602458,1,A/C	N3H	novel	Nonsynonymous	TOLERATED	0.06	2.84	335
2,234675783,1,C/T	A55V	novel	Nonsynonymous	DAMAGING	0.03	2.84	340
2,234601804,1,C/T	R52W	novel	Nonsynonymous	DAMAGING	0	2.77	123
2,234681113,1,T/C	F236L	novel	Nonsynonymous	TOLERATED	0.35	2.85	315
2,234601708,1,C/G	L20V	novel	Nonsynonymous	TOLERATED	0.48	2.78	92
2,234601944,1,C/G	H98Q	novel	Nonsynonymous	TOLERATED	0.33	2.77	124
2,234680964,1,C/T	P186L	novel	Nonsynonymous	DAMAGING	0	2.85	322
2,234602298,1,G/C	L216F	novel	Nonsynonymous	TOLERATED	0.12	2.77	125
2,234677023,1,T/A	N146K	novel	Nonsynonymous	DAMAGING	0.01	2.83	341
2,234601934,1,G/A	G95E	rs147637194:A	Nonsynonymous	TOLERATED	0.32	2.77	124
2,234681102,1,T/C	L232P	novel	Nonsynonymous	DAMAGING	0.05	2.86	319
2,234602206,1,C/T	P186S	novel	Nonsynonymous	DAMAGING	0.03	2.77	125
2,234602302,1,G/A	E218K	novel	Nonsynonymous	TOLERATED	0.31	2.77	125
2,234601851,1,G/C	L67F	novel	Nonsynonymous	TOLERATED	0.18	2.77	124
2,234681107,1,G/A	V234M	novel	Nonsynonymous	DAMAGING	0.02	2.86	318
2,234602481,1,C/A	I10I	novel	Synonymous	N/A	N/A	N/A	336
2,234601703,1,T/C	L18S	novel	Nonsynonymous	TOLERATED	0.27	2.78	71
2,234601820,1,T/C	V57A	novel	Nonsynonymous	DAMAGING	0	2.77	123
2,234602464,1,G/A	V5I	novel	Nonsynonymous	TOLERATED	0.37	2.84	336
2,234680910,1,A/G	Y168C	novel	Nonsynonymous	DAMAGING	0.01	2.85	321
2,234680972,1,C/A	L189M	novel	Nonsynonymous	DAMAGING	0.02	2.84	320
2,234601780,1,G/A	D44N	novel	Nonsynonymous	TOLERATED	0.46	2.77	122
2,234681114,1,T/A	F236Y	novel	Nonsynonymous	TOLERATED	0.27	2.85	315
2,234602096,1,C/G	T149R	novel	Nonsynonymous	DAMAGING	0.01	2.77	125
2,234676564,1,C/A	P88T	novel	Nonsynonymous	DAMAGING	0	2.83	341
2,234601949,1,C/T	A100V	novel	Nonsynonymous	TOLERATED	0.28	2.77	123
2,234681200,1,C/T	H265Y	novel	Nonsynonymous	DAMAGIN	0	3.36	59
				G *Warning!			
2,234602069,1,A/G	K140R	novel	Nonsynonymous	TOLERATED	0.46	2.77	125
2,234681173,1,G/C	V256L	novel	Nonsynonymous	TOLERATED	0.28	2.89	236
2,234675758,1,C/A	P47T	novel	Nonsynonymous	TOLERATED	0.47	2.84	340
2,234601918,1,C/T	R90C	novel	Nonsynonymous	TOLERATED	0.18	2.77	124
2,234677004,1,G/A	G140E	novel	Nonsynonymous	DAMAGING	0.01	2.83	341
2,234681053,1,T/C	Y216H	novel	Nonsynonymous	DAMAGING	0.02	2.86	319
2,234602186,1,A/G	E179G	novel	Nonsynonymous	DAMAGING	0.04	2.77	125
2,234602259,1,G/C	M203I	novel	Nonsynonymous	DAMAGING	0	2.77	125
2,234601805,1,G/A	R52Q	novel	Nonsynonymous	DAMAGING	0.03	2.77	123
2,234676922,1,A/T	S113C	novel	Nonsynonymous	DAMAGING	0	2.83	341
2,234681078,1,T/C	I224T	novel	Nonsynonymous	DAMAGING	0.04	2.86	319
2,234676534,1,G/A	A78T	novel	Nonsynonymous	DAMAGING	0	2.83	341
2,234602450,1,T/G	V267G	novel	Nonsynonymous	DAMAGING	0.02	2.77	125
2,234676522,1,C/A	P74T	novel	Nonsynonymous	DAMAGING	0.02	2.83	341
2,234601784,1,T/C	I45T	novel	Nonsynonymous	DAMAGING	0.03	2.77	122
2,234602101,1,C/G	P151A	novel	Nonsynonymous	TOLERATED	0.33	2.77	125
2,234676910,1,G/A	G109S	novel	Nonsynonymous	TOLERATED	0.12	2.83	341
2,234681020,1,C/T	H205Y	novel	Nonsynonymous	DAMAGING	0.01	2.85	320
2,234680971,1,C/G	D188E	novel	Nonsynonymous	TOLERATED	0.21	2.85	322
2,234601800,1,T/A	S50R	novel	Nonsynonymous	TOLERATED	0.62	2.77	123
2,234602447,1,C/T	P266L	novel	Nonsynonymous	DAMAGING	0	2.77	125
2,234675782,1,G/T	A55S	novel	Nonsynonymous	DAMAGING	0.01	2.84	340
2,234602084,1,A/G	D145G	novel	Nonsynonymous	DAMAGING	0	2.77	125
2,234677036,1,A/G	T151A	novel	Nonsynonymous	DAMAGING	0	2.83	341
2,234601942,1,C/T	H98Y	novel	Nonsynonymous	TOLERATED	1	2.77	124
2,234602173,1,C/G	P175A	novel	Nonsynonymous	DAMAGING	0.05	2.77	125
2,234602290,1,G/T	V214F	novel	Nonsynonymous	TOLERATED	0.41	2.77	125
2,234675771,1,C/T	A51V	novel	Nonsynonymous	DAMAGING	0.05	2.84	340
2,234676544,1,C/A	T81K	novel	Nonsynonymous	DAMAGING	0	2.83	341

2,234602188,1,C/T	H180Y	novel	Nonsynonymous	TOLERATED	0.69	2.77	125
2,234601906,1,G/A	E86K	novel	Nonsynonymous	TOLERATED	0.11	2.77	124
2,234601808,1,G/T	G53V	novel	Nonsynonymous	DAMAGING	0	2.77	123
2,234676991,1,A/C	M136L	novel	Nonsynonymous	TOLERATED	0.39	2.83	341
2,234676931,1,A/G	N116D	novel	Nonsynonymous	DAMAGING	0	2.83	341
2,234602247,1,T/A	F199L	novel	Nonsynonymous	TOLERATED	0.76	2.77	125
2,234680938,1,C/A	S177R	novel	Nonsynonymous	TOLERATED	1	2.85	321
2,234601985,1,A/G	Y112C	novel	Nonsynonymous	TOLERATED	0.18	2.77	124
2,234601773,1,T/A	S41R	novel	Nonsynonymous	DAMAGING	0.01	2.77	122
2,234602230,1,A/G	R194G	novel	Nonsynonymous	TOLERATED	0.36	2.78	124
2,234676977,1,A/G	D131G	novel	Nonsynonymous	TOLERATED	0.15	2.83	341
2,234601878,1,A/C	K76N	novel	Nonsynonymous	DAMAGING	0.02	2.77	124
2,234676520,1,G/A	R73Q	novel	Nonsynonymous	TOLERATED	0.06	2.83	341
2,234681128,1,T/G	C241G	novel	Nonsynonymous	TOLERATED	0.07	2.86	307
2,234601756,1,G/A	G36R	novel	Nonsynonymous	DAMAGING	0	2.77	122
2,234602384,1,C/T	T245I	novel	Nonsynonymous	DAMAGING	0	2.77	125
2,234675726,1,T/C	V36A	novel	Nonsynonymous	DAMAGING	0	2.83	341
2,234681001,1,G/A	M198I	novel	Nonsynonymous	TOLERATED	0.28	2.85	322

Three SNPs were chosen from 231 missense mutations: rs1105879 (A552C), rs6759892 (T19G), and rs2070959 (A541G). A detrimental variant, rs1105879 (A552C), was identified with a SIFT score of 0.026. The PolyPhen tool also looked at these SNPs. Scores between 0.0-0.15 indicate benign mutation, 0.15 and 1.0

may be harmful, and scores between 0.85 and 1.0 are harmful, as firmly expected. To forecast the effects of single point protein mutations of the first three SNPs of UGT1A6, I mutant suite 3.0 was utilised. All three SNPs of UGT1A6 had DDG values for binary classification that were 0, indicating decreased stability.

**Table 2: Polyphen as well as I mutant 3.0 Analysis of three selected SNPs of UGT1A6**

SNP	Nucleotide Change	Amino acid Change	Polyphen Score	Sensitivity	Specificity	Tolerated/ Deleterious	DDG(Kcal/ mol/stability)
rs1105879 (A552C)	A/C	Arg184Ser	0.038	0.94	0.82	Tolerated	-1.19/decr stability
rs6759892 (T19G)	T/G	Ser7Ala	0.0	1	0	Tolerated	-0.68/decr stability
rs2070959 (A541G)	A/G	Thr181Ala	0.0	1	0	Tolerated	-1.17/decr stability

Following the discovery of SNPs associated with the protein accession ID NP\_001065.2 in NCBI, the UGT2B7 gene was also examined using the same methods. A total of 240 SNPs were found after missense mutations were removed. The majority (100%) of the

changes were coding variations, of which 91% (220 of 240) were anticipated, 38% (85 of 220) were tolerated, 62% (135 of 220) were damaged, 93% (225 of 240) were non-synonymous, and 7% (15 of 240) were synonymous. 206 out of 240 SNPs, or 85%, were new.

**Table 3: SIFT analysis results for UGT2B7**

Coordinates	Substitution	dbSNP ID	SNP Type	Prediction	Score	Median Info	# Seqs at position
4,69968621,1,G/A	V323I	Novel	Nonsynonymous	TOLERATED	0.31	2.76	130
4,69964273,1,T/C	L246S	Novel	Nonsynonymous	DAMAGING	0.04	2.76	138
4,69962623,1,G/T	D129Y	Novel	Nonsynonymous	DAMAGING	0.02	2.75	140
4,69973910,1,C/T	P394S	Novel	Nonsynonymous	DAMAGING	0.03	2.75	217
4,69978302,1,G/C	A480P	Novel	Nonsynonymous	DAMAGING	0	2.75	214
4,69962662,1,G/A	E142K	Novel	Nonsynonymous	TOLERATED	0.3	2.75	140
4,69978365,1,G/T	V501L	Novel	Nonsynonymous	TOLERATED	0.19	2.75	213
4,69962736,1,A/G	I166M	Novel	Nonsynonymous	DAMAGING	0	2.75	140
4,69978287,1,C/T	H475Y	Novel	Nonsynonymous	DAMAGING	0.02	2.75	214
4,69962426,1,T/C	L63P	Novel	Nonsynonymous	DAMAGING	0.03	2.75	140
4,69972953,1,A/G	K355E	Novel	Nonsynonymous	TOLERATED	0.33	2.77	129

4,69962669,1,G/C	R144T	Novel	Nonsynonymous	DAMAGING	0.02	2.75	140
4,69964331,1,G/A	Q265Q	Novel	Synonymous	N/A	N/A	N/A	138
4,69978219,1,A/C	Q452P	Novel	Nonsynonymous	DAMAGING	0	2.75	214
4,69968616,1,C/G	A321G	Novel	Nonsynonymous	DAMAGING	0.04	2.76	130
4,69962313,1,G/A	K25K	Novel	Synonymous	N/A	N/A	N/A	137
4,69962831,1,T/C	M198T	Novel	Nonsynonymous	TOLERATED	0.22	2.76	139
4,69962389,1,C/G	H51D	Novel	Nonsynonymous	DAMAGING	0	2.75	140
4,69973922,1,G/A	D398N	rs145725367:A	Nonsynonymous	DAMAGING	0.03	2.75	217
4,69972963,1,C/T	P358L	Novel	Nonsynonymous	DAMAGING	0.02	2.77	129
4,69962770,1,T/C	Y178H	Novel	Nonsynonymous	TOLERATED	0.53	2.75	140
4,69962682,1,T/G	I148M	Novel	Nonsynonymous	TOLERATED	0.29	2.75	140
4,69978230,1,C/T	P456S	Novel	Nonsynonymous	DAMAGING	0	2.75	215
4,69964395,1,C/T	P287S	Novel	Nonsynonymous	DAMAGING	0.02	2.76	138
4,69968530,1,G/A	M292I	Novel	Nonsynonymous	TOLERATED	0.17	2.76	131
4,69964287,1,G/C	G251R	Novel	Nonsynonymous	TOLERATED	0.12	2.76	138
4,69968538,1,T/C	F295S	Novel	Nonsynonymous	DAMAGING	0	2.75	130
4,69968640,1,C/T	A329V	Novel	Nonsynonymous	DAMAGING	0	2.76	130
4,69973997,1,A/G	T423A	Novel	Nonsynonymous	TOLERATED	0.69	2.75	216
4,69962551,1,T/C	F105L	Novel	Nonsynonymous	TOLERATED	0.59	2.78	138
4,69972903,1,G/T	R338I	Novel	Nonsynonymous	DAMAGING	0	2.77	131
4,69964374,1,C/T	L280F	Novel	Nonsynonymous	TOLERATED	0.15	2.76	138
4,69978218,1,C/G	Q452E	Novel	Nonsynonymous	DAMAGING	0	2.75	214
4,69962586,1,G/A	M116I	Novel	Nonsynonymous	TOLERATED	0.4	2.77	139
4,69962906,1,G/A	W223*	Novel	Damaging due to stop	N/A	N/A	N/A	N/A
4,69973866,1,G/A	G379D	Novel	Nonsynonymous	DAMAGING	0	2.75	217
4,69972920,1,C/G	P344A	Novel	Nonsynonymous	DAMAGING	0	2.77	131
4,69962744,1,T/C	V169A	Novel	Nonsynonymous	DAMAGING	0	2.75	140
4,69962387,1,G/A	G50D	Novel	Nonsynonymous	DAMAGING	0.01	2.75	140
4,69973877,1,G/A	A383T	Novel	Nonsynonymous	DAMAGING	0	2.75	217
4,69962680,1,A/G	I148V	Novel	Nonsynonymous	TOLERATED	1	2.75	140
4,69962365,1,C/G	L43V	Novel	Nonsynonymous	TOLERATED	0.07	2.75	140
4,69962762,1,C/A	S175Y	Novel	Nonsynonymous	DAMAGING	0.02	2.75	140
4,69962540,1,C/A	P101Q	Novel	Nonsynonymous	TOLERATED	0.23	2.79	135
4,69964279,1,A/G	E248G	Novel	Nonsynonymous	DAMAGING	0	2.76	138
4,69973857,1,G/A	G376E	Novel	Nonsynonymous	DAMAGING	0	2.75	217
4,69962887,1,G/A	V217M	Novel	Nonsynonymous	TOLERATED	0.26	2.76	138
4,69973995,1,G/A	S422N	Novel	Nonsynonymous	DAMAGING	0.01	2.75	217
4,69964366,1,T/C	V277A	Novel	Nonsynonymous	DAMAGING	0.03	2.76	138
4,69978346,1,T/G	I494M	Novel	Nonsynonymous	DAMAGING	0.01	2.75	213
4,69962704,1,T/C	C156R	Novel	Nonsynonymous	DAMAGING	0.04	2.74	139
4,69968588,1,A/G	M312V	Novel	Nonsynonymous	TOLERATED	0.16	2.76	131
4,69962473,1,A/T	T79S	Novel	Nonsynonymous	DAMAGING	0.05	2.76	139
4,69973958,1,G/A	G410R	Novel	Nonsynonymous	DAMAGING	0	2.75	217
4,69962587,1,T/C	S117P	Novel	Nonsynonymous	TOLERATED	0.3	2.77	138
4,69978186,1,A/C	M368L	Novel	Nonsynonymous	DAMAGING	0	2.75	120
4,69964314,1,A/G	N260D	Novel	Nonsynonymous	DAMAGING	0	2.76	138
4,69973971,1,G/C	R414T	Novel	Nonsynonymous	TOLERATED	0.75	2.75	217
4,69973884,1,A/G	Y385C	Novel	Nonsynonymous	TOLERATED	0.48	2.75	217
4,69962935,1,G/A	D233N	Novel	Nonsynonymous	TOLERATED	0.19	2.75	139
4,69978413,1,T/C	W517R	Novel	Nonsynonymous	TOLERATED	1	2.76	202
4,69962494,1,T/A	L86M	Novel	Nonsynonymous	TOLERATED	0.63	2.78	137
4,69972926,1,A/G	T346A	Novel	Nonsynonymous	TOLERATED	0.12	2.77	131
4,69962290,1,T/G	F18V	Novel	Nonsynonymous	TOLERATED	0.26	2.8	117
4,69968535,1,A/G	D294G	Novel	Nonsynonymous	DAMAGING	0	2.75	130
4,69978307,1,C/A	H481Q	Novel	Nonsynonymous	DAMAGING	0	2.75	214
4,69972933,1,G/T	G348V	Novel	Nonsynonymous	DAMAGING	0	2.76	130
4,69962692,1,G/A	A152T	Novel	Nonsynonymous	DAMAGING	0.02	2.75	140
4,69978177,1,A/G	I365V	Novel	Nonsynonymous	DAMAGING	0	2.76	130
4,69968559,1,A/G	N302S	Novel	Nonsynonymous	TOLERATED	0.12	2.75	130
4,69962471,1,C/A	P78H	Novel	Nonsynonymous	TOLERATED	0.12	2.76	139



4,69962956,1,C/A	L240I	Novel	Nonsynonymous	DAMAGING	0.01	2.76	136
4,69964288,1,G/A	G251E	Novel	Nonsynonymous	DAMAGING	0.01	2.76	138
4,69973902,1,T/C	V391A	Novel	Nonsynonymous	DAMAGING	0	2.75	217
4,69973946,1,A/C	M406L	Novel	Nonsynonymous	TOLERATED	0.14	2.75	217
4,69972967,1,G/C	Q359H	Novel	Nonsynonymous	DAMAGING	0	2.77	129
4,69972930,1,T/C	L347S	Novel	Nonsynonymous	DAMAGING	0.03	2.76	130
4,69978176,1,T/A	D364E	Novel	Nonsynonymous	DAMAGING	0	2.76	130
4,69978253,1,G/A	W463*	Novel	Damaging due to stop	N/A	N/A	N/A	N/A
4,69968552,1,G/A	G300R	Novel	Nonsynonymous	DAMAGING	0	2.75	129
4,69973894,1,C/G	I388M	Novel	Nonsynonymous	DAMAGING	0	2.75	217
4,69962466,1,T/G	I76M	Novel	Nonsynonymous	TOLERATED	0.06	2.76	138
4,69962798,1,T/A	F187Y	Novel	Nonsynonymous	DAMAGING	0	2.75	140
4,69962695,1,A/C	I153L	Novel	Nonsynonymous	TOLERATED	0.55	2.75	140
4,69962555,1,G/A	W106*	Novel	Damaging due to stop	N/A	N/A	N/A	N/A
4,69973998,1,C/T	T423I	Novel	Nonsynonymous	TOLERATED	0.11	2.75	216
4,69962807,1,C/T	P190L	Novel	Nonsynonymous	DAMAGING	0	2.75	140
4,69978267,1,T/C	M468T	Novel	Nonsynonymous	DAMAGING	0	2.75	215
4,69962569,1,C/A	Q111K	Novel	Nonsynonymous	TOLERATED	1	2.76	138
4,69962677,1,G/A	V147I	Novel	Nonsynonymous	TOLERATED	0.21	2.75	140
4,69974025,1,T/C	V432A	Novel	Nonsynonymous	DAMAGING	0	2.75	216
4,69964385,1,A/C	K283N	Novel	Nonsynonymous	DAMAGING	0.01	2.76	138
4,69962934,1,G/C	W232C	Novel	Nonsynonymous	DAMAGING	0	2.75	139
4,69962390,1,A/C	H51P	Novel	Nonsynonymous	DAMAGING	0	2.75	140
4,69964404,1,A/C	K290Q	Novel	Nonsynonymous	TOLERATED	0.09	2.76	132
4,69962267,1,T/A	L10*	novel	Damaging due to stop	N/A	N/A	N/A	N/A
4,69978417,1,A/G	K518R	Novel	Nonsynonymous	TOLERATED	0.21	2.74	177
4,69962306,1,G/A	C23Y	Novel	Nonsynonymous	DAMAGING	0.01	2.75	135
4,69964336,1,C/T	P267L	Novel	Nonsynonymous	DAMAGING	0	2.76	138
4,69962824,1,G/A	V196I	Novel	Nonsynonymous	TOLERATED	0.36	2.76	139
4,69973823,1,C/T	H365Y	Novel	Nonsynonymous	DAMAGING	0	2.75	217
4,69972944,1,C/A	R352R	Novel	Synonymous	N/A	N/A	N/A	129
4,69962614,1,T/A	F126I	Novel	Nonsynonymous	TOLERATED	0.88	2.75	139
4,69973845,1,T/C	I372T	Novel	Nonsynonymous	DAMAGING	0	2.75	217
4,69962843,1,C/G	T202S	Novel	Nonsynonymous	TOLERATED	0.6	2.75	140
4,69972948,1,T/C	L353P	Novel	Nonsynonymous	DAMAGING	0	2.76	130
4,69962719,1,G/A	A161T	Novel	Nonsynonymous	DAMAGING	0.01	2.75	140
4,69962493,1,G/A	E85E	Novel	Synonymous	N/A	N/A	N/A	137
4,69973964,1,G/A	A412T	Novel	Nonsynonymous	DAMAGING	0	2.75	217
4,69968597,1,A/T	N315Y	Novel	Nonsynonymous	DAMAGING	0.04	2.76	130
4,69973973,1,G/A	V415M	Novel	Nonsynonymous	DAMAGING	0.01	2.75	217
4,69964329,1,C/A	Q265K	Novel	Nonsynonymous	DAMAGING	0.05	2.76	138
4,69964258,1,G/A	G241E	Novel	Nonsynonymous	DAMAGING	0	2.76	138
4,69962734,1,A/G	I166V	Novel	Nonsynonymous	TOLERATED	0.4	2.75	140
4,69968592,1,T/G	V313G	Novel	Nonsynonymous	DAMAGING	0	2.76	130
4,69962822,1,C/T	P195L	Novel	Nonsynonymous	DAMAGING	0	2.76	139
4,69973890,1,G/A	G387E	Novel	Nonsynonymous	DAMAGING	0	2.75	217
4,69968603,1,A/G	T317A	Novel	Nonsynonymous	DAMAGING	0.02	2.76	130
4,69972927,1,C/A	T346N	Novel	Nonsynonymous	DAMAGING	0.03	2.77	131
4,69964335,1,C/A	P267T	Novel	Nonsynonymous	DAMAGING	0	2.76	138
4,69962395,1,G/A	V53M	Novel	Nonsynonymous	DAMAGING	0	2.75	140
4,69972941,1,A/G	T351A	Novel	Nonsynonymous	DAMAGING	0	2.76	130
4,69962693,1,C/A	A152D	Novel	Nonsynonymous	DAMAGING	0	2.75	140
4,69968570,1,G/A	V306M	Novel	Nonsynonymous	DAMAGING	0.03	2.75	130
4,69962317,1,C/A	L27M	Novel	Nonsynonymous	DAMAGING	0.01	2.76	137
4,69973904,1,G/A	G392R	Novel	Nonsynonymous	DAMAGING	0.03	2.75	217
4,69973839,1,C/A	A370D	Novel	Nonsynonymous	DAMAGING	0	2.75	217
4,69972945,1,G/A	R352Q	Novel	Nonsynonymous	TOLERATED	0.2	2.75	129
4,69978182,1,G/A	K366K	Novel	Synonymous	N/A	N/A	N/A	129
4,69962425,1,C/A	L63I	Novel	Nonsynonymous	TOLERATED	0.21	2.75	140
4,69973913,1,T/A	L395M	Novel	Nonsynonymous	TOLERATED	0.24	2.75	217

4,69964312,1,G/A	R259Q	Novel	Nonsynonymous	DAMAGING	0.05	2.76	136
4,69962666,1,C/A	S143*	novel	Damaging due to stop	N/A	N/A	N/A	N/A
4,69973994,1,A/G	S422G	Novel	Nonsynonymous	DAMAGING	0	2.75	217
4,69962356,1,A/G	K40E	Novel	Nonsynonymous	DAMAGING	0	2.75	140
4,69964351,1,C/A	P272Q	Novel	Nonsynonymous	DAMAGING	0	2.76	138
4,69962899,1,G/T	D221Y	Novel	Nonsynonymous	DAMAGING	0	2.75	139
4,69972893,1,G/A	V335I	Novel	Nonsynonymous	DAMAGING	0.01	2.76	134
4,69978214,1,T/C	H450H	Novel	Synonymous	N/A	N/A	N/A	214
4,69962437,1,A/C	N67H	Novel	Nonsynonymous	DAMAGING	0.04	2.75	140
4,69973865,1,G/A	G379S	Novel	Nonsynonymous	DAMAGING	0.03	2.75	217
4,69964270,1,C/A	T245K	Novel	Nonsynonymous	TOLERATED	0.12	2.76	137
4,69962673,1,T/G	F145L	Novel	Nonsynonymous	DAMAGING	0	2.75	140
4,69962737,1,C/A	P167T	Novel	Nonsynonymous	DAMAGING	0.01	2.75	140
4,69968620,1,C/G	N322K	Novel	Nonsynonymous	DAMAGING	0.02	2.76	130
4,69962504,1,T/G	F89C	Novel	Nonsynonymous	TOLERATED	0.1	2.76	139
4,69973982,1,A/C	N418H	Novel	Nonsynonymous	TOLERATED	0.59	2.75	217
4,69962640,1,G/A	K134K	Novel	Synonymous	N/A	N/A	N/A	140
4,69962833,1,T/G	S199A	Novel	Nonsynonymous	TOLERATED	0.13	2.76	139
4,69973992,1,C/G	S421W	Novel	Nonsynonymous	DAMAGING	0	2.75	217
4,69968625,1,T/C	I324T	Novel	Nonsynonymous	DAMAGING	0	2.76	130
4,69964344,1,C/T	L270F	Novel	Nonsynonymous	TOLERATED	0.82	2.77	137
4,69972955,1,G/A	K355K	Novel	Synonymous	N/A	N/A	N/A	129
4,69972908,1,G/C	D340H	Novel	Nonsynonymous	TOLERATED	0.06	2.77	131
4,69962362,1,A/G	I42V	Novel	Nonsynonymous	TOLERATED	0.22	2.75	140
4,69978294,1,G/A	R477Q	Novel	Nonsynonymous	DAMAGING	0.03	2.75	214
4,69968644,1,G/C	Q330H	Novel	Nonsynonymous	DAMAGING	0	2.76	130
4,69973920,1,C/A	A397D	Novel	Nonsynonymous	DAMAGING	0	2.75	217
4,69962910,1,C/A	F224L	Novel	Nonsynonymous	TOLERATED	0.1	2.75	139
4,69964296,1,G/A	D254N	Novel	Nonsynonymous	DAMAGING	0	2.76	138
4,69978352,1,C/G	F496L	Novel	Nonsynonymous	DAMAGING	0.03	2.75	213
4,69973986,1,C/A	T419K	Novel	Nonsynonymous	TOLERATED	0.22	2.75	217
4,69973927,1,A/G	Q399Q	Novel	Synonymous	N/A	N/A	N/A	217
4,69962659,1,C/A	Q141K	Novel	Nonsynonymous	TOLERATED	0.26	2.75	140
4,69964350,1,C/G	P272A	Novel	Nonsynonymous	DAMAGING	0	2.76	138
4,69973919,1,G/T	A397S	Novel	Nonsynonymous	TOLERATED	0.07	2.75	217
4,69968536,1,C/G	D294E	Novel	Nonsynonymous	TOLERATED	1	2.75	130
4,69978255,1,T/A	I464N	Novel	Nonsynonymous	DAMAGING	0	2.75	215
4,69972956,1,T/C	W356R	Novel	Nonsynonymous	DAMAGING	0	2.77	129
4,69962936,1,A/T	D233V	Novel	Nonsynonymous	DAMAGING	0	2.75	139
4,69962954,1,T/A	V239D	Novel	Nonsynonymous	DAMAGING	0	2.76	138
4,69962800,1,A/G	I188V	Novel	Nonsynonymous	TOLERATED	0.12	2.75	140
4,69964337,1,A/T	P267P	rs7438284:T	Synonymous	N/A	N/A	N/A	138
4,69962458,1,A/G	I74V	Novel	Nonsynonymous	TOLERATED	0.19	2.75	140
4,69962924,1,T/C	M229T	Novel	Nonsynonymous	TOLERATED	0.5	2.76	138
4,69962398,1,A/T	T54S	Novel	Nonsynonymous	DAMAGING	0.05	2.75	140
4,69968628,1,C/T	A325V	Novel	Nonsynonymous	DAMAGING	0	2.76	130
4,69962735,1,T/C	I166T	Novel	Nonsynonymous	DAMAGING	0.03	2.75	140
4,69962572,1,G/A	V112I	Novel	Nonsynonymous	TOLERATED	0.33	2.77	139
4,69962519,1,T/G	I94S	Novel	Nonsynonymous	TOLERATED	0.06	2.76	138
4,69964369,1,G/A	G278E	Novel	Nonsynonymous	DAMAGING	0	2.76	138
4,69962447,1,C/T	S70F	Novel	Nonsynonymous	TOLERATED	0.3	2.75	139
4,69962477,1,C/A	S80Y	Novel	Nonsynonymous	TOLERATED	0.55	2.76	139
4,69962373,1,G/A	E45E	Novel	Synonymous	N/A	N/A	N/A	140
4,69962691,1,T/A	D151E	Novel	Nonsynonymous	DAMAGING	0	2.75	140
4,69962959,1,G/A	G241R	Novel	Nonsynonymous	DAMAGING	0.03	2.76	138
4,69978201,1,C/T	S446L	Novel	Nonsynonymous	DAMAGING	0	2.75	214
4,69978240,1,G/A	R459Q	Novel	Nonsynonymous	TOLERATED	0.29	2.76	212
4,69962459,1,T/C	I74T	Novel	Nonsynonymous	DAMAGING	0	2.75	140
4,69962511,1,G/A	M91I	Novel	Nonsynonymous	TOLERATED	0.23	2.76	139
4,69962939,1,A/G	Q234R	Novel	Nonsynonymous	TOLERATED	0.21	2.75	138

4,69962476,1,T/A	S80T	Novel	Nonsynonymous	TOLERATED	0.27	2.76	139
4,69962648,1,T/A	M137K	Novel	Nonsynonymous	DAMAGING	0	2.75	140
4,69962546,1,A/G	D103G	Novel	Nonsynonymous	TOLERATED	0.41	2.8	136
4,69962649,1,G/A	M137I	Novel	Nonsynonymous	TOLERATED	0.12	2.75	140
4,69978266,1,A/G	M468V	Novel	Nonsynonymous	DAMAGING	0	2.75	215
4,69973940,1,G/A	A404T	Novel	Nonsynonymous	TOLERATED	0.09	2.75	217
4,69962401,1,G/A	V55I	Novel	Nonsynonymous	TOLERATED	0.06	2.75	140
4,69978269,1,C/A	R469S	Novel	Nonsynonymous	DAMAGING	0	2.75	215
4,69962312,1,A/G	K25R	Novel	Nonsynonymous	TOLERATED	0.08	2.76	137
4,69973947,1,T/C	M406T	Novel	Nonsynonymous	DAMAGING	0	2.75	217
4,69964294,1,C/A	A253D	Novel	Nonsynonymous	DAMAGING	0	2.76	138
4,69964299,1,G/A	V255I	rs182011163:A	Nonsynonymous	TOLERATED	1	2.75	137
4,69973832,1,A/T	T368S	rs151128457:T	Nonsynonymous	DAMAGING	0.01	2.75	217
4,69978300,1,G/A	L395L	Novel	Synonymous	N/A	N/A	N/A	217
4,69978409,1,T/C	C515C	rs149223174:C	Synonymous	N/A	N/A	N/A	206
4,69962383,1,A/G	R49G	rs148671766:G	Nonsynonymous	DAMAGING	0	2.75	140
4,69973988,1,A/G	M420V	rs148274136:G	Nonsynonymous	DAMAGING	0.04	2.75	217
4,69972925,1,T/A	D345E	rs147582860:A	Nonsynonymous	TOLERATED	0.85	2.77	131
4,69962408,1,C/A	A57E	rs147538491:A	Nonsynonymous	TOLERATED	0.06	2.75	140
4,69978300,1,C/T	A479V	rs147176472:T	Nonsynonymous	DAMAGING	0	2.75	214
4,69962676,1,C/A	D146E	Novel	Nonsynonymous	DAMAGING	0.05	2.75	140
4,69962911,1,G/A	E225K	rs146308452:A	Nonsynonymous	TOLERATED	0.26	2.75	139
4,69978184,1,G/T	R367I	rs145217059:T	Nonsynonymous	DAMAGING	0	2.77	125
4,69962420,1,C/T	S61F	rs144693330:T	Nonsynonymous	DAMAGING	0.05	2.75	140
4,69973974,1,T/A	V415E	rs144232904:A	Nonsynonymous	DAMAGING	0	2.75	217
4,69962818,1,G/A	V194I	rs143338928:A	Nonsynonymous	TOLERATED	0.07	2.75	140
4,69973932,1,A/T	D401V	rs142806461:T	Nonsynonymous	DAMAGING	0	2.75	217
4,69962404,1,C/G	L56V	rs142158304:G	Nonsynonymous	TOLERATED	0.12	2.75	140
4,69962882,1,T/A	I215N	rs142000539:A	Nonsynonymous	DAMAGING	0	2.76	137
4,69974004,1,T/C	L425S	rs141309270:C	Nonsynonymous	DAMAGING	0	2.75	216
4,69978329,1,C/T	H489Y	rs140395996:T	Nonsynonymous	DAMAGING	0.04	2.75	213
4,69962559,1,A/G	L107L	Novel	Synonymous	N/A	N/A	N/A	139
4,69974040,1,C/T	S437L	rs139693571:T	Nonsynonymous	TOLERATED	0.13	2.75	215
4,69964269,1,A/G	T245A	rs139488772:G	Nonsynonymous	DAMAGING	0.02	2.76	137
4,69978188,1,G/A	M368I	rs138450721:A	Nonsynonymous	DAMAGING	0	2.75	120
4,69973931,1,G/C	D401H	rs138302870:C	Nonsynonymous	DAMAGING	0.02	2.75	217
4,69964359,1,G/T	D275Y	rs112352348:T	Nonsynonymous	DAMAGING	0.05	2.75	137
4,69978386,1,G/A	V508I	rs112292219:A	Nonsynonymous	TOLERATED	0.86	2.75	212
4,69962758,1,T/C	F174L	rs111720546:C	Nonsynonymous	TOLERATED	0.08	2.75	140
4,69962375,1,T/C	L46P	rs61361928:C	Nonsynonymous	DAMAGING	0	2.75	140
4,69962452,1,C/G	L72V	Novel	Nonsynonymous	TOLERATED	0.31	2.75	138
4,69962774,1,C/A	T179N	Novel	Nonsynonymous	TOLERATED	0.41	2.75	140
4,69962360,1,C/T	T41I	rs58632287:T	Nonsynonymous	TOLERATED	0.54	2.75	140
4,69973863,1,A/C	N378T	Novel	Nonsynonymous	DAMAGING	0	2.75	217
4,69974018,1,A/C	K430Q	rs34851008:C	Nonsynonymous	DAMAGING	0.01	2.75	216
4,69968550,1,C/T	S299F	rs34620993:T	Nonsynonymous	DAMAGING	0	2.75	130
4,69973956,1,G/A	R409K	rs34308305:A	Nonsynonymous	TOLERATED	1	2.75	217
4,69962610,1,A/G	R124R	rs28365063:G	Synonymous	N/A	N/A	N/A	140
4,69964338,1,T/C							

**Table 4: Polyphen Analysis of three selected SNPs of UGT2B7**

SNP	Nucleotide Change	Amino acid Change	Polyphen Score	Sensitivity	Specificity	Tolerated/Deleterious	DDG(Kcal/mol/stability)
rs7662029	A268G	A71T	0.013	0.96	0.78	Tolerated	-0.8/decr stability

**CONCLUSION**

Utilising computational prediction techniques, the functional effects of the UGT gene's SNPs (UGT1A6 and UGT2B7) were examined. The results were helpful for

the pre-selection of SNPs. For the wet lab investigation, three SNPs can be chosen: rs6759892, rs2070959, rs1105879 of UGT1A6 and rs7662029 (UGT2B7). Studies have revealed that even though the chosen variations were deemed to be tolerable, they play a substantial effect in certain groups. Consequently, bioinformatics methods may be helpful in determining the negative impact of SNPs.

#### ACKNOWLEDGMENT

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

#### Conflict of interest

The author declare that we have no conflict of interest.

#### REFERENCES

1. J.-E. Lee.; J. H. Choi.; J. H. Lee and M. G. Lee, "Gene SNPs and mutations in clinical genetic testing: haplotype-based testing and analysis," *Mutation Research.*, **2005**, 573 (1-2), 195–204.
2. M. Krawczak.; E. V. Ball.; I. Fenton "Human gene mutation database-a biomedical information and research resource," *Human Mutation.*, **2000**, 15(1), 45–51.
3. L. Prokunina and M. E. Alarcón-Riquelme, "Regulatory SNPs in complex diseases: their identification and functional validation," *Expert Reviews in Molecular Medicine.*, **2004**, 6, 10.
4. P. D. Stenson.; M. Mort.; E. V. Ball., "The human gene mutation database: 2008 update," *Genome Medicine.*, **2009**, 1(1), 13.
5. V. Ramensky.; P. Bork and S. Sunyaev, "Human non-synonymous SNPs: server and survey," *Nucleic Acids Research.*, **2002**, 30(17), 3894–3900.
6. T. Emahazion.; L. Feuk.; M. Jobs "SNP association studies in Alzheimer's disease highlight problems for complex disease analysis," *Trends in Genetics.*, **2001**, 17(7), 407–413.
7. N. J. Schork.; D. Fallin and J. S. Lanchbury "Single nucleotide polymorphisms and the future of genetic epidemiology," *Clinical Genetics.*, **2000**, (58)4, 250–264.
8. N. J. Risch "Searching for genetic determinants in the new millennium," *Nature.*, **2000**, 405 (6788), 847–856.
9. P. C. Ng and S. Henikoff, "SIFT: predicting amino acid changes that affect protein function," *Nucleic Acids Research.*, **2003**, 31(13), 3812–3814.
10. S. Sunyaev, V. Ramensky, and P. Bork, "Towards a structural basis of human non-synonymous single nucleotide polymorphisms," *Trends in Genetics*, vol. 16, no. 5, pp. 198–200, 2000.
11. H.-Y. Yuan.; J.-J. Chiou.; W.-H. Tseng "FASTSNP: an always up-to-date and extendable service for SNP function analysis and prioritization," *Nucleic Acids Research.*, **2006**, 34, W635–W641, .
12. P. C. Ng and S. Henikoff "Predicting deleterious amino acid substitutions," *Genome Research.*, **2001**, 11(5), 863–874.
13. P. C. Ng and S. Henikoff "Accounting for human polymorphisms predicted to affect protein function," *Genome Research.*, **2002**, 12(3), 436–446.
14. P. C. Ng and S. Henikoff, "Predicting the effects of amino acid substitutions on protein function," *Annual Review of Genomics and Human Genetics.*, **2006**, 7, 61–80.
15. S. Sunyaev.; W. Lathe III and P. Bork, "Integration of genome data and protein structures: prediction of protein folds, protein interactions and "molecular phenotypes" of single nucleotide polymorphisms," *Current Opinion in Structural Biology.*, **2001**, 11(1), 125–130.
16. T. Xi, I. M. Jones and H. W. Mohrenweiser, "Many amino acid substitution variants identified in DNA repair genes during human population screenings are predicted to impact protein function," *Genomics.*, **2004**, 83(6), 970–979.
17. D. Chasman and R. M. Adams, "Predicting the functional consequences of non-synonymous single nucleotide polymorphisms: structure-based assessment of amino acid variation," *Journal of Molecular Biology.*, **2001**, 307(2), 683–706.