J Hum Genet (2002) 47:505–510

ORIGINAL ARTICLE

Aritoshi Iida · Susumu Saito · Akihiro Sekine
Chihiro Mishima · Yuri Kitamura · Kimie Kondo
Satoko Harigae · Saori Osawa · Yusuke Nakamura

Catalog of 86 single-nucleotide polymorphisms (SNPs) in three uridine diphosphate glycosyltransferase genes: *UGT2A1*, *UGT2B15*, and *UGT8*

Received: June 12, 2002 / Accepted: June 13, 2002

Abstract We report here three high-density maps of variations found among 48 Japanese individuals in three uridine diphosphate glycosyltransferase (UGT) genes, *UGT2A1*, *UGT2B15*, and *UGT8.* A total of 86 single-nucleotide polymorphisms (SNPs) were identified through systematic screening of genomic regions containing these genes: 8 in 5′ flanking regions, 7 in coding regions, 67 in introns, 3 in 3′ untranslated regions, and 1 in a 3′ flanking region. We also discovered 14 variations of other types. Of the 86 SNPs, 63 (73%) were considered to be novel on the basis of comparison of our data with the Database of SNPs (dbSNP) of the National Center for Biotechnology Information. Among the seven SNPs identified in exonic sequences, five were non-synonymous changes that would result in amino-acid substitutions. The collection of SNPs derived from this study will serve as an additional resource for studies of complex genetic diseases and responsiveness to drug therapy.

Key words Uridine diphosphate glycosyltransferase (UGT) · Single-nucleotide polymorphism (SNP) · High-density SNP map · Nonsynonymous substitution · Japanese population

Introduction

Uridine diphosphate glycosyltransferases (UDP glycosyltransferases; UGTs) represent a superfamily of enzymes that catalyze the transfer of nucleotide sugars to a large number of exogenous and endogenous compounds to facilitate their elimination from target cells (see reviews by Mackenzie et al. 1997; King et al. 2000). Structurally, members of the UGT superfamily are defined by the presence of a "signature sequence" in their carboxy-terminal halves, which is thought to be involved in the binding of the UDP moiety of the nucleotide sugar (Mackenzie et al. 1997). Endoplasmic reticulum-bound UGTs, which catalyze glucuronidation of numerous endogenous substrates, including bilirubin, bile acids, and steroids, have been well studied in pharmacogenetics and clinical research because they have central roles in the metabolism and detoxification of foreign chemicals such as carcinogens and hydrophobic drugs.

So far, at least 47 mammalian cDNAs/genes have been identified and assigned to one of three distinct subfamilies based on sequence identities, namely, *UGT1*, *UGT2*, and *UGT8* (Mackenzie et al. 1997). In humans the *UGT1A* gene family is located on chromosome 2q37, where each *UGT1* gene is composed of a unique first exon that is subsequently spliced to four common exons (2 to 5). Members of the UGT1A family conjugate mainly bilirubin, bile acids, phenols, and steroid hormones (Mackenzie et al. 1997). The *UGT2* family is different in that its mRNAs are transcribed from individual genes. On the basis of tissue-specific expression patterns, *UGT2* genes are subdivided into the *UGT2A* subfamily, encoding olfactory-specific isoforms, and the *UGT2B* subfamily, encoding steroid-metabolizing isoforms in the liver (King et al. 2000). UGT2A1 catalyzes glucuronidation of many odorant compounds including monoterpenoids, as well as aliphatic alcohols, phenols, and coumarins (Jedlitschky et al. 1999). UGT2B15 catalyzes glucuronidation of a wide range of substrates, including simple phenolic compounds, aliphatic alcohols, and endogenous steroids such as testosterone, catechol estrogens, 5 alpha-androstane-3 alpha, 17 beta-diol, and dihydrotestosterone (Chen et al. 1993; Green et al. 1994). On the other hand, the UGT8 family contains only a single member to date, which encodes a key enzyme in the biosynthesis of glycosphingolipids, cerebrosides, and sulfatides, essential

A. Iida · S. Saito · A. Sekine · C. Mishima · Y. Kitamura · K. Kondo · S. Harigae · S. Osawa · Y. Nakamura
Laboratory for Genotyping, RIKEN SNP Research Center, c/o RIKEN Yokohama Institute, Kanagawa, Japan

Y. Nakamura (✉)
Laboratory of Molecular Medicine, Human Genome Center, Institute of Medical Science, The University of Tokyo, 4-6-1 Shirokanedai, Minato-ku, Tokyo 108-8639, Japan
Tel. +81-3-5449-5372; Fax +81-3-5449-5433
e-mail: yusuke@ims.u-tokyo.ac.jp

Table 1. Characterization of 100 variations in the *UGT2A1, UGT2B15*, and *UGT8* loci

ID	Accession no.	Region	Exon	Position[a]	Flanking sequence[b]	Variation[c]	Flanking sequence[b]	Substitution	Repetitive sequence	Identity to dbSNP
UDP-glycosyltransferase 2A1 (*UGT2A1*)										
i-UGT2A1-1	AC011254.3	5′ Flanking region		−1,602	ataacatcttctgcagagaa	A/C	cttcaatggaaatacactca			
i-UGT2A1-2	AC011254.3	5′ Flanking region		−1,480	tacagattatctttggtgat	G/C	ggagagcttagaagagacat			
i-UGT2A1-3	AC011254.3	5′ Flanking region		−1,406	atttcagaagatttattaac	A/T	tgaaaaggatcactctgC/Ttt			
i-UGT2A1-4	AC011254.3	5′ Flanking region		−1,388	acA/Ttgaaaaggatcactctg	C/T	ttattcacagacatatgcat			
i-UGT2A1-5	AC011254.3	5′ Flanking region		−935	aaattattcaatctctttgg	G/A	cagtggtttctttttctttg		+	
i-UGT2A1-6	AC011254.3	5′ Flanking region		−287	cctgaatgtagagttgagat	G/A	tacagaagctttatccaatt			rs1432329
i-UGT2A1-7	AC011254.3	5′ Flanking region		−128	gagaagtaagacacattacc	C/T	ataaatctgtaaatatccta			rs1432330
i-UGT2A1-8	AC011254.3	Intron 1		535	cattgatcagggtgatttat	C/T	catgctaagcttatttaatt			
i-UGT2A1-9	AC011254.3	Intron 1		642	tatattgatcatgttgatac	A/C	tttatacacatatttgtcta			
i-UGT2A1-10	AC011254.3	Intron 1		1,221	ttttaatctaataagcaatt	C/G	aggaccatctaaagggaaat			rs1560605
i-UGT2A1-11	AC011254.3	Intron 1		1,448	aggtgcttacaggcaacatc	C/T	acatagcagtctgtggctgg			
i-UGT2A1-12	AC011254.3	Intron 1		2,000	gacacattagcttcttttct	A/G	cagatctctgttctaaaaca			
i-UGT2A1-13	AC011254.3	Intron 1		3,118	cttaaaattctttaatgaaa	T/G	cattgcaacaaatttatatc			
i-UGT2A1-14	AC011254.3	Intron 1		3,191	ataaatagaacaactcccta	A/T	gtttacttctctgcagtgga			
i-UGT2A1-15	AC011254.3	Intron 1		3,770	atcaccagataatttactat	C/T	cattaaggagtaggtcatca			
i-UGT2A1-16	AC011254.3	Intron 1		4,584	tgattggttagaatctttga	A/C	aaatcttctagtatcattcc			
i-UGT2A1-17	AC011254.3	Intron 1		4,854	tactctgtgcattgttaata	G/A	cctatcacttgtggtctgcc			rs2331685
i-UGT2A1-18	AC011254.3	Intron 1		−19,146	ctgtttaaattctcattcaa	C/T	ggccacatggttaaaataaa			
i-UGT2A1-19	AC011254.3	Intron 1		−19,085	tagacaaagacccttt caat	A/C	aacaaagttagaaatgtgtt			
i-UGT2A1-20	AC011254.3	Intron 1		−18,346	atggcaatatttttagaaat	G/A	ttaactcccaataatgaata			
i-UGT2A1-21	AC011254.3	Intron 1		−18,218	tatatcattattttaactta	T/G	agatagcactagccctaatt			
i-UGT2A1-22	AC011254.3	Intron 1		−17,937	ctcctaataatttggactca	C/T	catacttattcagcactatc			
i-UGT2A1-23	AC011254.3	Intron 1		−12,585	ttccacacagggacaagtca	A/G	cagaggaaatttttcttgct			
i-UGT2A1-24	AC011254.3	Intron 1		−11,430	aacaaaggtttatttttctta	C/G	agttctgatggctagacgtc		+	
i-UGT2A1-25	AC011254.3	Intron 1		−10,761	tttaaaatatgcatgtattt	T/G	ccacttttaaaaactatatc			
i-UGT2A1-26	AC011254.3	Intron 1		−381	aaatcctccctccttccttc	C/T	tttcccaggccccactctac		+	
i-UGT2A1-27	AC011254.3	Intron 1		−329	ttccctttctccttttctcc	A/G	tctctctctcttcctctctc		+	
i-UGT2A1-28	AC011254.3	Intron 1		−41	ttttctcctcagcaaacata	T/A	aagctaatttcctccatcca			
i-UGT2A1-29	AC011254.3	Intron 2		263	caccttgatactggacttgg	T/C	gggacagaaaaccagatcat			
i-UGT2A1-30	AC011254.3	Intron 2		454	agaaagcccattgaaataag	G/C	cagggtttttaggttttaat			
i-UGT2A1-31	AC011254.3	Intron 2		554	aaaaactttttgagttgac	A/T	atggtgagtttagtttctga			
i-UGT2A1-32	AC011254.3	Intron 2		1,113	ctgcaggcaagctctagtga	A/T	tgtttattataggaaataat			
i-UGT2A1-33	AC011254.3	Intron 2		1,304	gacaaatcagccatgtttta	C/T	A/Gatagcagacattatgccat			rs1432314
i-UGT2A1-34	AC011254.3	Intron 2		1,305	acaaatcagccatgttttaC/T	A/G	atagcagacattatgccatt			rs1432315
i-UGT2A1-35	AC011254.3	Intron 2		1,367	atcgatataggctttgggaa	A/C	tatgaataccaaccatgggt			rs1432316
i-UGT2A1-36	AC011254.3	Intron 2		2,074	aaatttttcttagacctat	G/T	aatcaaaggaggcatacagt			rs1319811
i-UGT2A1-37	AC011254.3	Intron 2		2,164	attttattagatataactgg	A/C	atgctaacaattttaaaagc			rs2010207
i-UGT2A1-38	AC011254.3	Intron 2		2,298	taacaatttcagttagcatg	A/C	gaagagttgtcccttattta			rs1821185
i-UGT2A1-39	AC011254.3	Intron 2		2,346	tttctgtaatggttttgctt	T/C	catgcttggacttgtaatca			rs1158439
i-UGT2A1-40	AC011254.3	Coding region	3	922	gtgttgtggtgttttctctg	G/A	gatcaatggtcaaaaacctt	Gly308Arg		
i-UGT2A1-41	AC011254.3	Intron 3		−217	aagcttagaagtgataaata	T/C	caaaacaataatactatact			
i-UGT2A1-42	AC011254.3	Intron 3		−194	aaacaataatactatactgg	G/A	tagactattagtacaagact			
i-UGT2A1-43	AC011254.3	Coding region	5	1,171	acggagtccctatggtggga	G/A	ttcccatgtttgctgatcag	Val391Ile		
i-UGT2A1-44	AC011254.3	Intron 5		1,546	ttttttaaaattcagaaactc	A/G	G/Attatggtgtattcttacaa			
i-UGT2A1-45	AC011254.3	Intron 5		1,547	ttttaaaattcagaaactcA/G	G/A	ttatggtgtattcttacaaa			
i-UGT2A1-46	AC011254.3	Intron 5		2,013	atcatattcattaccctccc	G/T	ctattattgtattttgaatc			rs1432324
i-UGT2A1-47	AC011254.3	Intron 5		2,318	aatttagtgctttttcttaa	C/T	ggaagtaacctgcttaaaaa			rs1432327
i-UGT2A1-48	AC011254.3	Intron 5		2,505	taattgacttttattaatac	G/A	tacatgttgtataagtcata			rs2163658
i-UGT2A1-49	AC011254.3	Intron 5		2,639	tagactattacaaagttgtt	A/G	gttgctgacaattttgttca			
i-UGT2A1-50	AC011254.3	Intron 5		4,009	gaatccaggctggaacttttt	C/A	ttccagacacaaaccaaaat			
i-UGT2A1-51	AC011254.3	Intron 5		4,311	atacagacactgtccttttc	G/A	tcacaaacatacagatgtgt			
i-UGT2A1-52	AC011254.3	Intron 5		4,545	agctcacacagtatcaaaat	T/C	atttttggaaaaattatgct			rs1438537
i-UGT2A1-53	AC011254.3	Intron 5		4,616	actttttatgtctacattt	G/C	atcatactgtgttaagcata			

Table 1. Continued

ID	Accession no.	Region	Exon	Position[a]	Flanking sequence[b]	Variation[c]	Flanking sequence[b]	Substitution	Repetitive sequence	Identity to dbSNP
i-UGT2A1-54	AC011254.3	Intron 5		4,717	tgcaagaattatattttctc	C/A	acgtaactatggccttaaac			
i-UGT2A1-55	AC011254.3	Coding region	6	1,524	gctatatttttggtcataca	A/G	tgttgtttgttttcctgtca	Gln508Gln		
i-UGT2A1-56	AC011254.3	3′ Untranslated region	6	1,683	aaggagtttaacaaaaaacac	G/A	tctcccatcctgtttccaaa			
i-UGT2A1-57	AC011254.3	3′ Flanking region		685	aatctagaaaataattatca	T/C	ttttataaaatttttagtca			
i-UGT2A1-58	AC011254.3	Intron 1		(−18,967)–(−18,965)	ctcccaattagattgattag	TAT/del	gagttcctgggttactggt			
i-UGT2A1-59	AC011254.3	Intron 1		(−18,862)–(−18,803)	aatacattcttccccttca	$(AC)_{14–17}$	atgcttactggcctatttat			
i-UGT2A1-60	AC011254.3	Intron 1		(−17,463)–(−17,447)	aaacttagaaacctctattc	$(A)_{16–27}$	gtaaagaaaatggcagagaa			
i-UGT2A1-61	AC011254.3	Intron 1		−10,860	attcaatgcaacttttttt	T/del	gtaatggcagaattagaaca			
i-UGT2A1-62	AC011254.3	Intron 2		528–538	ctgttaggaaacaattggtt	$(A)_{8–10}$	ctttttgagttgacA/Tatgg			
i-UGT2A1-63	AC011254.3	Intron 2		1,514–1,533	ttgtgtgtatgtgtatgttt	$(GT)_{9–11}$	tattttaatgaattaatatc			
i-UGT2A1-64	AC011254.3	Intron 5		916–917	gcttagtatattatatatat	AA/del	gtctatatatatagcttagt			
i-UGT2A1-65	AC011254.3	Intron 5		1,163	caatatttatgtcatttttt	T/del	ctcacatttactctgtttcc			
i-UGT2A1-66	AC011254.3	Intron 5		3,819–3,838	agacagacagacacacaaac	$(AC)_{8–12}$	tcaacacatgtaaactactc			
i-UGT2A1-67	AC011254.3	Intron 5		4,785	tatcttcaatgaaaataaaa	A/del	caaaaattgtctaatttctg			
UDP-glycosyltransferase 2B15 (*UGT2B15*)										
i-UGT2B15-1	AC019173.4	5′ Flanking region		−277	ccgaacaggcaggagcctct	C/A	acttgccactgttcttaaca			
i-UGT2B15-2	AC019173.4	Coding region	1	253	ctacatctttaactaaaaat	G/T	atttggaagattctcttctg	Asp85Tyr[d]		rs1902023
i-UGT2B15-3	AC019173.4	Intron 1		670	catcaaagaaaatagggcc	A/T	aattaagggagagcacatat			
i-UGT2B15-4	AC019173.4	Intron 1		775	ctaattatattaagatctta	A/C	gatgaaccaagacagtagta			
i-UGT2B15-5	AC019173.4	Intron 2		56	ttttcagaaggaatggctgg	A/T	tatgtttctttcagagtgtt			rs2045100
i-UGT2B15-6	AC019173.4	Intron 2		1,629	tgttgatattatgattattt	T/C	agtcattatttttaatactt			rs1531022
i-UGT2B15-7	AC019173.4	Intron 2		2,183	cagagtttcaccatgttggc	C/T	aggctggtcttgaactcctg		+	
i-UGT2B15-8	AC019173.4	Intron 2		2,430	tatttcaaaagaataagact	C/G	ttgccaaaaagtatcaagtg			
i-UGT2B15-9	AC019173.4	Intron 2		4,806	aaaaaattactccaatagct	C/T	ctgaC/Gtttctcatcttagat			
i-UGT2B15-10	AC019173.4	Intron 2		4,811	attactccaatagctC/Tctga	C/G	tttctcatcttagatgtttg			rs1947435
i-UGT2B15-11	AC019173.4	Intron 3		129	ctaattatctcagacatctg	T/C	tcaaaG/Acaaaaacatatatg			
i-UGT2B15-12	AC019173.4	Intron 3		135	atctcagacatctgT/Ctcaaa	G/A	caaaaacatatatggaagat			rs1454255
i-UGT2B15-13	AC019173.4	Intron 3		424	caataacaataagcaggtat	T/C	gaaaaaactttgaaatgcat			
i-UGT2B15-14	AC019173.4	Intron 3		476	gtcttaccaagcaatctggc	T/A	gtttttacttcccatgC/Tatt			rs1026337
i-UGT2B15-15	AC019173.4	Intron 3		493	ggcT/Agtttttacttcccatg	C/T	attggaataggtctatttag			
i-UGT2B15-16	AC019173.4	Intron 3		514	attggaataggtctatttag	C/T	gttctgttcagggtgccatt			rs1026338
i-UGT2B15-17	AC019173.4	Intron 3		570	ctagtctgactagccactgc	T/G	ctggaggtacccacctagcc			rs1026339
i-UGT2B15-18	AC019173.4	Intron 3		906	gccctctctgaatgatctat	G/A	caagtttttgctgaaaacac			
i-UGT2B15-19	AC019173.4	Intron 3		1,036	tcagtaccttagtttggtac	T/C	agacatggtaatgactggct			
i-UGT2B15-20	AC019173.4	Intron 3		1,544	aataaatatataggttatta	C/G	taatttgctacttttttatt			
i-UGT2B15-21	AC019173.4	Intron 3		5,550	gtgtggtgaatcaatgtgtg	C/T	tgcttgtgggcagtactcca			
i-UGT2B15-22	AC019173.4	Intron 3		5,720	ttttttaaaagttaattttt	C/A	ttggggatttccctgcaggg			
i-UGT2B15-23	AC019173.4	Intron 4		134	atcaaatttaactactttat	A/G	tttattttccagtcttagta			
i-UGT2B15-24	AC019173.4	Intron 5		6,627	ttttaatgttgatatcttta	T/C	atttatccttcagctataaa			
i-UGT2B15-25	AC019173.4	Coding region	6	1,568	tttccgaaagcttgccaaaa	A/C	aggaaagaagaagaaaagag	Lys523Thr		
i-UGT2B15-26	AC019173.4	3′ Untranslated region	6	1,761	ggatttaatacgtactttag	C/T	tggaattattctatgtcA/Tat			
i-UGT2B15-27	AC019173.4	3′ Untranslated region	6	1,779	agC/Ttggaattattctatgtc	A/T	atgatttttaagctatgaaa			
i-UGT2B15-28	AC019173.4	Intron 2		1,980–1,981	aagagagtagcagaataagg	AGG/ins	acaagggataaatgactagt			
i-UGT2B15-29	AC019173.4	Intron 3		605–618	ctagccaagtagatttagag	$(A)_{11–15}$	cttgtctgctctgctgactt			
i-UGT2B15-30	AC019173.4	3′ Untranslated region	6	1,957–1,968	aagtataatttaaaaaaagc	$(A)_{11–14}$	tacaactctttttttaaac			
UDP-glycosyltransferase 8 (*UGT8*)										
i-UGT8-1	U31353.1	Coding region	1	677	gcagaagtacaacctgctgc	C/T	ggagaagtccatgtatgatt	Pro226Leu		
i-UGT8-2	U31353.1	Coding region	1	741	atgctgtgtactgacgtagc	A/G	ctggaattcccaagacccac	Ala247Ala		
i-UGT8-3	U31461.1	Intron 2		53–54	ttgacaatcaatatctcctt	GT/del	ttagtgcacaggtcccagta			

dbSNP, Database of Single-Nucleotide Polymorphisms; ins, insertion polymorphism; del, deletion polymorphism

[a] Nucleotide numbering is according to the mutation nomenclature (den Dunnen and Antonarakis 2000)

[b] Both 5′ and 3′ flanking sequences to each variation are denoted by small letters

[c] Variation is shown by capital letters

[d] SNP identified previously by Lévesque et al. (1997)

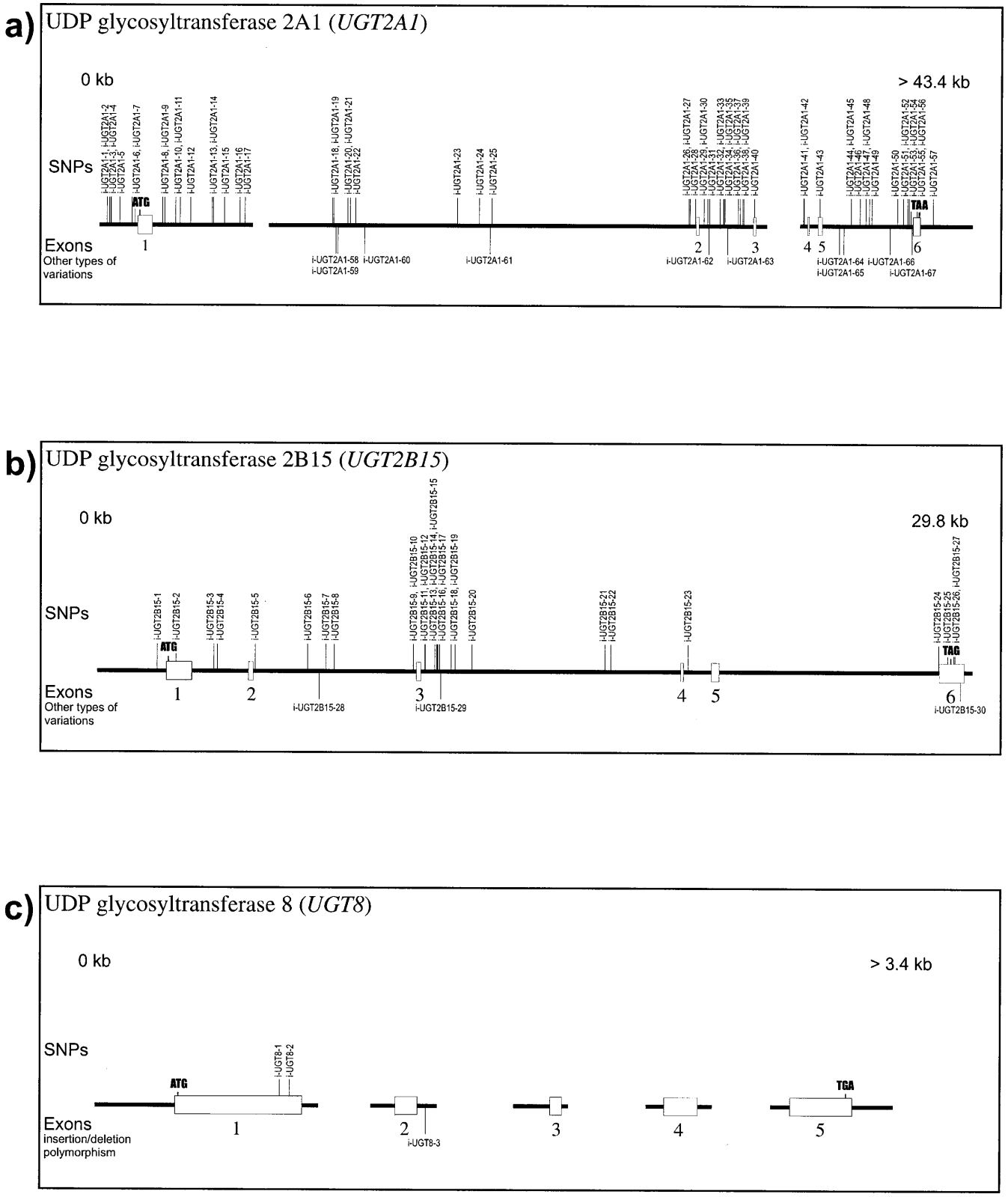

Fig. 1a–c. Fine-scale single-nucleotide polymorphism (*SNP*) maps of three loci containing uridine diphosphate glycosyltransferase (*UDP glycosyltransferase*) genes. Exons and introns are represented by *rectangles* and *horizontal lines*, respectively. SNPs are indicated *above the genes* (designations correspond to the left-most column in Table 1). Other types of variation, where present, are indicated *below the genes*

constituents of myelin membranes of the central and peripheral nervous systems (Bosio et al. 1996; Kapitonov and Yu 1997).

In this report we provide high-resolution single-nucleotide polymorphism (SNP) maps of three *UGT* gene loci, in which we detected a total of 86 SNPs and 14 variations of other types among 96 chromosomes from a representative Japanese population sample.

Subjects and methods

Blood samples were obtained with written informed consent from 48 healthy Japanese volunteers for this study, which was approved by the ethical committee of the RIKEN SNP Research Center. The detailed methods used to screen for SNPs are available in an earlier report (Ohnishi et al. 2000) and from our website (http://snp.ims.u-tokyo.ac.jp). In brief, on the basis of genomic sequences from the Genbank database in the United States National Center for Biotechnology Information (NCBI; accession numbers *UGT2A1*, AC011254.3; *UGT2B15*, AC019173.4; *UGT8*, U31353.1, U31461.1, U31658.1, U31861.1 and U32370.1), we designed primers to amplify all three genes in their entirety as well as 2-kb regions upstream of their first exons and downstream of their polyA sites (Iida et al. 2002). However, we excluded from the screening process most regions that corresponded to repetitive sequences predicted by the RepeatMasker program (http://repeatmasker.genome.washington.edu/cgi-bin/RepeatMasker).

Each polymerase chain reaction (PCR) was performed with 20 ng of mixed genomic DNA derived from three individuals. All 16 mixed samples were amplified in the GeneAmp PCR System 9700 (PE Applied Biosystems, Foster City, CA, USA) under the following conditions: initial denaturation at 94°C for 2 min, followed by 35 cycles of denaturation at 94°C for 30 s, annealing at 60°C for 30 s, and extension at 72°C for 2 min. Products obtained from the PCR experiments were used as templates for direct sequencing and detection of SNPs using the fluorescent dye-terminator cycle sequencing method. All SNPs detected by the Polyphred computer program (Nickerson et al. 1997) were confirmed by sequencing both strands of each PCR product. The nomenclature we have used for these genes is according to Online Mendelian Inheritance in Man of NCBI and a review published previously by Mackenzie et al. (1997).

Results and discussion

Sequencing of approximately 36 kb of genomic DNA corresponding to three loci containing the *UGT2A1*, *UGT2B15*, and *UGT8* genes identified a total of 100 variations among 48 Japanese individuals, including 86 SNPs and 14 variations of other types. The extent of each screened genomic sequence was 22.4 kb at the *UGT2A1* locus, 10.8 kb at the *UGT2B15* locus, and 2.8kb at the *UGT8* locus, except for most of the regions corresponding to repetitive sequences. Fine-scale SNP maps of each locus were constructed (Fig. 1). We found 57 SNPs at the *UGT2A1* locus (1 in 393 bp on average), 27 at the *UGT2B15* locus (1 in 401 bp), and 2 at the *UGT8* locus (1 in 1385 bp). Detailed information about each SNP is given in Table 1. Regional distributions of the SNPs identified herein were as follows: 8 in 5′ flanking regions, 7 within coding regions, 67 in introns, 3 within 3′ untranslated regions, and 1 in a 3′ flanking region. Of the 86 SNPs detected in our experiments, 63 (73%) were not previously archived in the Database of SNPs (dbSNP) of NCBI.

Of the seven SNPs we detected within coding regions, five were non-synonymous: 922G>A (Gly308Arg) in exon 3 and 1171G>A (Val391Ile) in exon 5 of the *UGT2A1* gene; 253G>T (Asp85Tyr) in exon 1 and 1568A>C (Lys523Thr) in exon 6 of the *UGT2B15* gene; and 677C>T (Pro226Leu) in exon 1 of *UGT8*. Four of these nonsynonymous substitutions were considered to be novel, the exception being the 253G>T SNP of *UGT2B15* (Lévesque et al. 1997). All five could affect structures and/or biological functions of the respective gene products.

The overall frequencies of nucleotide substitutions in our test population (96 chromosomes) were counted as 31.4% for C/T, 25.6% for G/A, 15.1% for A/C, 10.5% for T/A, 9.3% for C/G, and 8.1% for G/T. As expected, the most common substitution was C/T (G/A) (57%); transitions occurred 1.3 times more frequently than transversions.

The 86 SNPs identified here provide genetic data that should be helpful for personalized medical care and also for identifying genes associated with drug efficacy and/or adverse drug reactions.

References

Bosio A, Binczek E, Le Beau MM, Fernald AA, Stoffel W (1996) The human gene CGT encoding the UDP-galactose ceramide galactosyl transferase (cerebroside synthase): cloning, characterization, and assignment to human chromosome 4, band q26. Genomics 34:69–75

Chen F, Ritter JK, Wang MG, McBride OW, Lubet RA, Owens IS (1993) Characterization of a cloned human dihydrotestosterone/androstanediol UDP-glucuronosyltransferase and its comparison to other steroid isoforms. Biochemistry 32:10648–10657

den Dunnen JT, Antonarakis SE (2000) Mutation nomenclature extensions and suggestions to describe complex mutations: a discussion. Hum Mutat 15:7–12

Green MD, Oturu EM, Tephly TR (1994) Stable expression of a human liver UDP-glucuronosyltransferase (UGT2B15) with activity toward steroid and xenobiotic substrates. Drug Metab Dispos 22:799–805

Iida A, Saito S, Sekine A, Kondo K, Mishima C, Kitamura Y, Harigae S, Osawa S, Nakamura Y (2002) Thirteen single-nucleotide polymorphisms (SNPs) in the alcohol dehydrogenase 4 (*ADH4*) gene locus. J Hum Genet 47:74–76

Jedlitschky G, Cassidy AJ, Sales M, Pratt N, Burchell B (1999) Cloning and characterization of a novel human olfactory UDP-glucuronosyltransferase. Biochem J 340:837–843

Kapitonov D, Yu RK (1997) Cloning, characterization, and expression of human ceramide galactosyltransferase cDNA. Biochem Biophys Res Commun 232:449–453

King CD, Rios GR, Green MD, Tephly TR (2000) UDP-glucuronosyltransferases. Curr Drug Metab 1:143–161

Lévesque E, Beaulieu M, Green MD, Tephly TR, Bélanger A, Hum DW (1997) Isolation and characterization of UGT2B15(Y85): a UDP-glucuronosyltransferase encoded by a polymorphic gene. Pharmacogenetics 7:317–325

Mackenzie PI, Owens IS, Burchell B, Bock KW, Bairoch A, Belanger A, Fournel-Gigleux S, Green M, Hum DW, Iyanagi T, Lancet D, Louisot P, Magdalou J, Chowdhury JR, Ritter JK, Schachter H, Tephly TR, Tipton KF, Nebert DW (1997) The UDP glycosyltransferase gene superfamily: recommended nomenclature update based on evolutionary divergence. Pharmacogenetics 7:255–269

Nickerson DA, Tobe VO, Taylor SL (1997) PolyPhred: automating the detection and genotyping of single nucleotide substitutions using fluorescence-based resequencing. Nucleic Acids Res 25:2745–2751

Ohnishi Y, Tanaka T, Yamada R, Suematsu K, Minami M, Fujii K, Hoki N, Kodama K, Nagata S, Hayashi T, Kinoshita N, Sato H, Sato H, Kuzuya T, Takeda H, Hori M, Nakamura Y (2000) Identification of 187 single nucleotide polymorphisms (SNPs) among 41 candidate genes for ischemic heart disease in the Japanese population. Hum Genet 106:288–292