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Aritoshi Iida · Akihiro Sekine · Susumu Saito
Yuri Kitamura · Takuya Kitamoto · Saori Osawa
Chihiro Mishima · Yusuke Nakamura

Catalog of 320 single nucleotide polymorphisms (SNPs) in 20 quinone oxidoreductase and sulfotransferase genes

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Abstract Single nucleotide polymorphisms (SNPs) in genes encoding drug-metabolizing enzymes, transporters, receptors, and other drug targets have been widely implicated as contributors to differences among individuals as regards the efficacy and toxicity of many medications, as well as the susceptibility to complex diseases. By combining the polymerase chain reaction (PCR) technique with direct sequencing, we screened genomic DNAs from 48 Japanese volunteers for SNPs in genes encoding three quinone oxidoreductases (*NQO1, NQO2, and PIG3*) and 17 sulfotransferases (*SULT1A1, SULT1A2, SULT1A3, SULT1C1, SULT1C2, SULT2A1, SULT2B1, ST1B2, TPST1, TPST2, SULTX3, STE, CST, HNK-1 ST, CHST2, CHST4, and CHST5*). In all, we identified 320 SNPs from these 20 loci: 22 within coding elements, 21 in 5′ flanking regions, 10 in 5′ untranslated regions, 223 in introns, 19 in 3′ untranslated regions, and 25 in 3′ flanking regions. The ratio of transitions to transversions was approximately 2.3 to 1. Of the 22 coding SNPs, 6 were nonsynonymous substitutions that resulted in amino-acid substitutions. The high-density SNP maps we constructed from this data for each of the quinone oxidoreductases and sulfotransferases examined here should provide useful information for investigations designed to detect association(s) between genetic variations and common diseases or responsiveness to drug therapy.

Key words Single nucleotide polymorphism (SNP) · Quinone oxidoreductase · Sulfotransferase · Drug-metabolizing enzymes · Nonsynonymous substitution

A. Iida · A. Sekine · S. Saito · Y. Kitamura · T. Kitamoto · S. Osawa · C. Mishima · Y. Nakamura
Laboratory for Genotyping, The SNP Research Center, The Institute of Physical and Chemical Research (RIKEN), Tokyo, 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

Introduction

Common genetic variations may, in large part, explain genetic predispositions to common diseases and individual differences in pharmacological responsiveness (Dean et al. 1996; Risch and Merikangas 1996; Kruglyak 1997). Single-nucleotide polymorphisms (SNPs) are the most frequent type of genetic variation, and are thought to be present every several hundred bases, on average, throughout the human genome (Halushka et al. 1999). SNPs can provide medically important information through: (1) their contribution to high-density maps for studies of susceptibility to common diseases; (2) the provision of genetic data for personalized medical service; and (3) the identification of genes associated with efficacy and side-effects of drugs (Kruglyak 1999). Nearly a million SNPs have already been registered in databases as a result of numerous projects to screen the entire human genome in a systematic way. However, instead of genome-wide screening, we have focused on regions that contain genes of interest, particularly genes encoding proteins involved in the metabolism of drugs, drug receptors, and transporters, and molecules that respond to oxidative stresses. Such genes are likely to have significant roles in the responsiveness to drugs, and may also influence susceptibility to common diseases such as arteriosclerosis and diabetes mellitus.

Nicotinamide adenine dinucleotide phosphate, reduced [NAD(P)H]: quinone oxidoreductase (NQO1) and dihydronicotinamide riboside (NRH): quinone oxidoreductase (NQO2) are flavoproteins that catalyze two-electron reduction and detoxification of quinones and their derivatives (for reviews, see Chen et al. 2000; Jaiswal 2000). These enzymes help to protect cells and tissues against various types of oxidative stress, as well as redox cycling caused by free radicals and reactive oxygen metabolites generated by one-electron reduction processes. NQO1 requires NADH or NADPH as a cofactor for its enzymatic activity, and is strongly inhibited by low concentrations of dicoumarol. NQO2, on the other hand, requires NRH as a cofactor. Human *NQO2* cDNA and protein are, respectively, 54%

and 49% similar to human liver cytosolic *NQO1* cDNA and protein (Jaiswal et al. 1990). PIG3 (p53 induced gene 3/ quinone oxidoreductase homolog), a molecule that shares significant homology with oxidoreductases, was recently identified as a downstream target involved in p53-mediated apoptosis (Polyak et al. 1997). Although PIG3 expression is likely to be correlated with the generation of reactive oxygen species (ROS) (Flatt et al. 2000), its biological function is unknown at present.

Sulfotransferases catalyze the sulfation of a variety of endogenous and exogenous compounds, including steroids, neurotransmitters, bile acids, and biogenic amines, as well as a large number of therapeutic drugs and environmental chemicals (for reviews, see Weinshilboum et al. 1997; Coughtrie et al. 1998; Dooley 1998). Molecules that belong to the sulfotransferase superfamily, on the basis of amino-acid sequence similarities and substrate preferences, can be divided into two major categories, SULT1 (phenol SULTs) and SULT2 (hydroxysteroid SULTs) (Weinshilboum et al. 1997; Freimuth et al. 2000). Members of the SULT1 subfamily share at least 60% identity in amino-acid sequence, but are further subdivided into four groups; namely, phenol (1A), thyroid hormone (1B), hydroxyarylamine (1C), and estrogen (1E) sulfotransferases. The enzymes are distinct, but they recognize some common substrates. From the viewpoint of pharmacogenetics, a G638A (Arg213His) substitution in the *SULT1A1* gene (conserved region in the cytosolic sulfotransferase gene family that includes *SULT1A1*, *SULT1A2*, *STM*, and *STE*) appears to be associated with reduction of enzymatic activity and thermal stability (Raftogianis et al. 1997).

By means of direct sequencing, we attempted an extensive SNP analysis of genes encoding 3 quinone oxidoreductases and 17 sulfotransferases, and report here high-density maps of these 20 genes that include a total of 320 SNPs.

Materials and methods

DNA samples

Blood samples were obtained from 48 healthy Japanese individuals. Informed consent was obtained from each participant in this study, which was approved by the SNP Research Center, RIKEN. Genomic DNA was extracted from each sample according to standard protocols.

Genes encoding drug-metabolizing enzymes

The 20 genes analyzed in this study were as follows:

NAD(P)H: quinone oxidoreductase 1 (*NQO1*, accession numbers M81596, J05348-M81600, and J05348)
NRH: quinone oxidoreductase 2 (*NQO2*, AB050248)
Quinone oxidoreductase homolog (*PIG3*, AF010309)
Sulfotransferase 1A1 (*SULT1A1*, U52852)
Sulfotransferase 1A2 (*SULT1A2*, U33886)
Sulfotransferase 1A3 (*SULT1A3*, L34160)
Sulfotransferase 1C1 (*SULT1C1*, AC019100)
Sulfotransferase 1C2 (*SULT1C2*, AF186263)
Sulfotransferase 2A1 (*SULT2A1*, AC024582)
Sulfotransferase 2B1 (*SULT2B1*, AC040922)
Thyroid hormone sulfotransferase (*ST1B2*, AC027059)
Tyrosylprotein sulfotransferase 1 (*TPST1*, AC026281)
Tyrosylprotein sulfotransferase 2 (*TPST2*, AC022814)
Sulfotransferase-related protein 3 (*SULTX3*, AC083393)
Estrogen sulfotransferase (*SULT1E1*, AC074273)
Cerebroside sulfotransferase (*CST*, AC005006)
HNK-sulfotransferase-1 (*HNK-1 ST*, AC012493)
Carbohydrate sulfotransferase 2 (*CHST2*, AC022737)
Carbohydrate sulfotransferase 4 (*CHST4*, AC010547)
Carbohydrate sulfotransferase 5 (*CHST5*, AC025287)

On the basis of the DNA sequences of these genes in the GenBank database, we designed primers to amplify each gene in its entirety and up to 2 kilobases upstream from the first exon (putative promoter region).

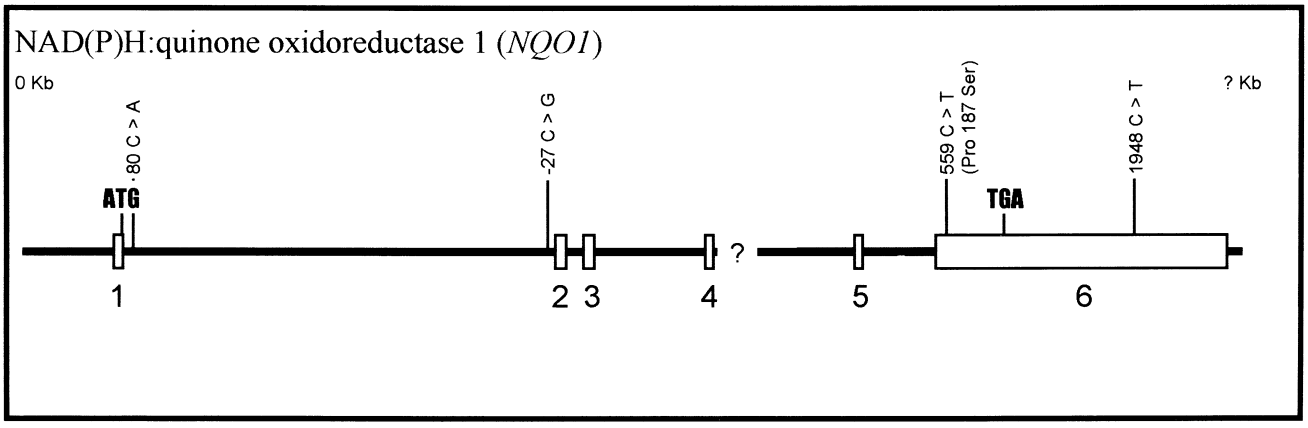
Polymerase chain reaction (PCR), direct sequencing, and detection of SNPs

PCR experiments and DNA sequencing were performed according to methods described previously (Ohnishi et al. 2000). Each PCR was carried out using 20 ng of DNA pooled from three individuals. All SNPs detected by the PolyPhred Computer Program (Nickerson et al. 1997) were confirmed by sequencing both strands of each PCR product.

Results and discussion

By direct sequencing of DNA from 48 healthy individuals, we screened SNPs in a total of 257 kilobases of genomic DNA, corresponding to 20 selected genes. Three of the genes belonged to the quinone oxidoreductase family and 17 to the sulfotransferase family. We identified 320 SNPs altogether (Fig. 1). Of these, 22 were located in coding elements, 21 in 5′ flanking regions, 10 in 5′ untranslated regions, 223 in introns, 19 in 3′ untranslated regions, and 25 in 3′ flanking regions. Of the total, 295 (92.1%) had not been deposited in the dbSNP database, and 44 were observed within regions corresponding to repetitive sequences predicted by the RepeatMasker Program (http://ftp.genome.washington.edu/cgi-bin/RepeatMasker). The ratios of transitions to transversions were approximately 7:3 in both exons and introns. Of the 22 SNPs identified within coding regions, 6 were nonsynonymous and resulted in amino-acid substitutions that might affect the structure and/or biological function of the respective gene products.

On average, we identified 16 SNPs per gene and 1 SNP in every 800 bp. However, the distribution was uneven. For example, we found 9 SNPs within one 525-bp region (1 SNP/58 bp) in intron 6 of the *SULT1A1* gene, and 11 in a

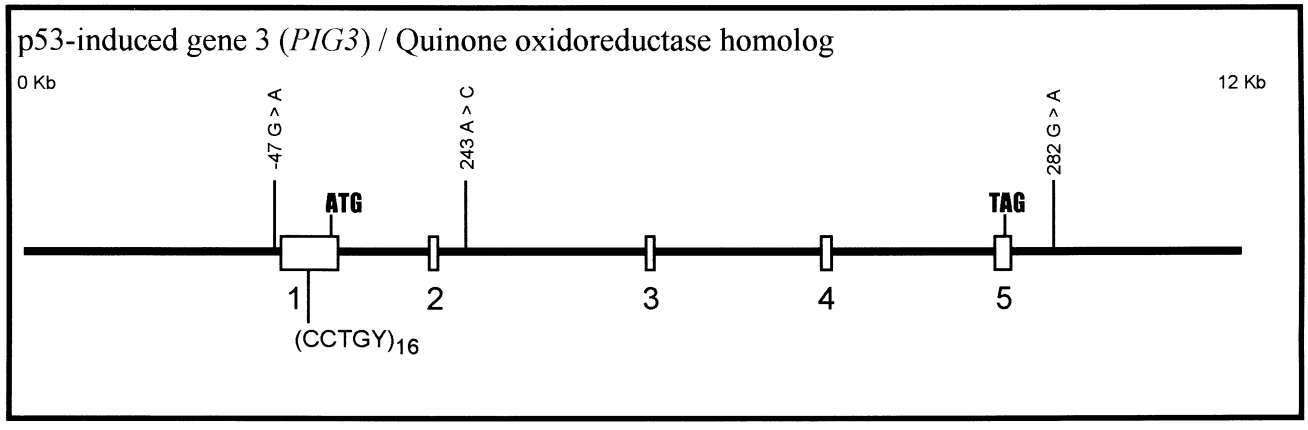


1 (intron 1 80) **aggaggttgtaggggcttgg C/A ctgaattttgttccttgact**

2 (intron 1 -27)dbSNP ID:rs689452
tggttggtaatgggttttcc C/G tgtgtgctttgtgtgtgtct

3 (exon 6 559) **gtggcttccaagtcttagaa C/T (Pro 187 Ser) ctcaactgacatatagcatt**

4 (3′ untranslated region 1948)dbSNP ID:rs10517
ttgctaaactgatgacttac C/T atgggatggggtccagtccc



1 (5′ flanking region -47)
gggaaggaggaaaggaaaga G/A ggggagggtggttctgctta

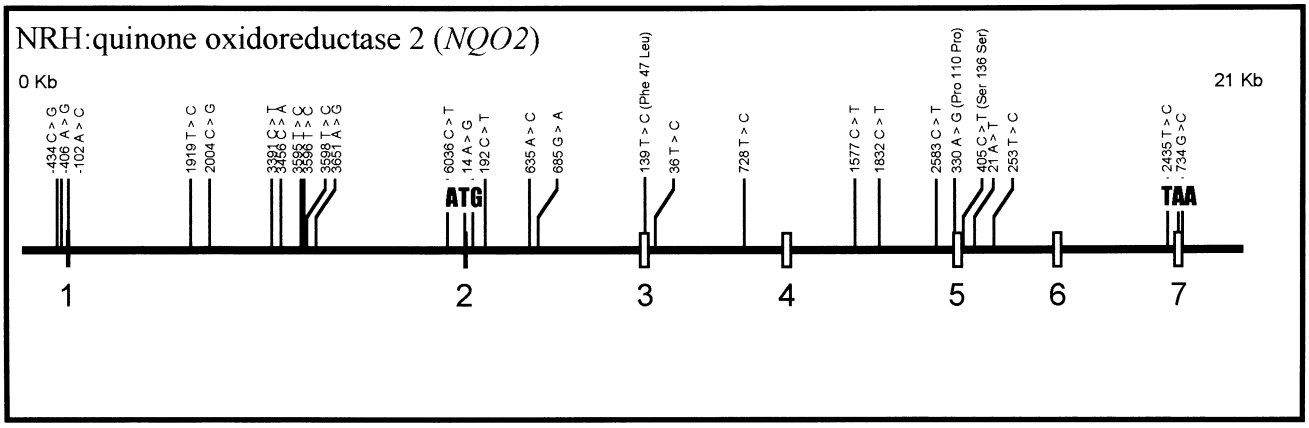
2 (intron 2 243) **taacaccggacgcccagcag A/C agtcccagcttcttagaatc**

3 (3′ flanking region 282)
agcaggccccagccctgccc G/A ctactcacctgggccccacc

VNTR polymorphism

1 (5' untranslated region -93)
tccgcgaggatacagcggcc $(CCTGY)_n$ cagacaatatgttagccgtg

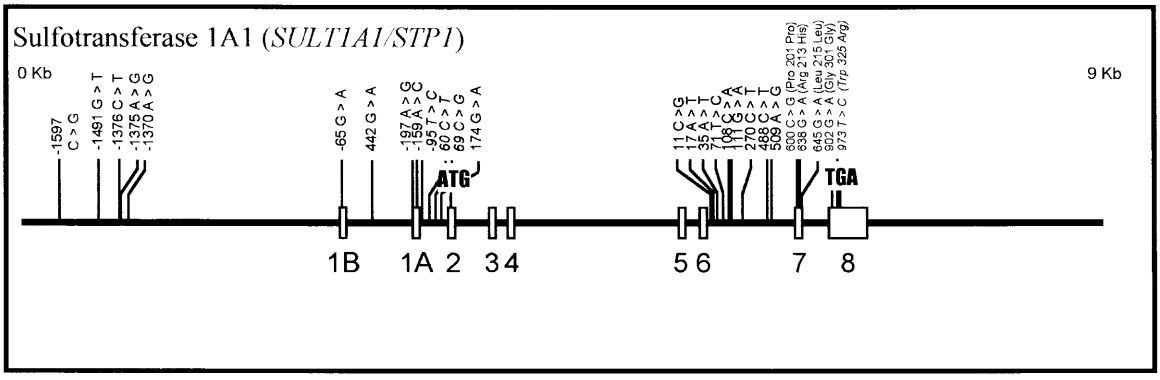
Fig. 1a–t. Genomic organization and locations of single nucleotide polymorphisms (SNPs) in three quinone oxidoreductase genes (**a–c**) and 17 sulfotransferase genes (**d–t**). Exons are represented by *open rectangles* and introns by *horizontal lines*. The identified SNPs are indicated *above each gene*, and variable number tandem repeat (*VNTR*) sequences and insertion-deletion polymorphisms are shown *below*. For cDNA and coding sequences in genomic DNA, the adenine of the initiator Met codon is denoted nucleotide +1. The first nucleotide of the 5′ untranslated region is numbered −1. Likewise, for intronic DNA, positive numbers start from the guanine of the donor-site invariant GT, and negative numbers start from the guanine of the acceptor-site invariant AG. *Italic numbers and letters* indicate SNPs located within repetitive sequences predicted by the RepeatMasker Program. The complete genomic structure of the *NQO2* gene was determined in this study, and has been submitted to the DNA Data Bank of Japan (DDBJ) under accession number AB050248



1 (5′ flanking region -434)	tttctgttgcaccacggacc	C/G tcattctgtaaccgggatac
2 (5′ flanking region -406)	gtaaccgggataccagccag	A/G gatggggagcgggaggcgca
3 (5' untranslated region -102)		
	tcctgcggctcctactgggg	A/C gtgcgctggtcggaaggtga
4 (intron 1 1919)	tcactcaaatagagctgagt	T/C agtcactcagctcttggacc
5 (intron 1 2004)	acaaactcacatgccaccag	C/G catatgatgtaaacatgtaa
6 (intron 1 3391)	aaagcagagggctgtgcagg	C/T gcccctgcccctaggctagg
7 (intron 1 3456)	caaaggcctcatcctcaggg	C/A ggccaactcttctgttttag
8 (intron 1 3595)		
9 (intron 1 3596)		
10 (intron 1 3598)	actgcccagctttaggttca	T/C T/C c T/C tgtaagtgttgctggtgtca
11 (intron 1 3651)	ccctgcgctttgaagggatg	A/G atgtgacctctcccacattc
12 (intron 1 6036)	tggtgtggcggttcactgat	C/T ccccagccttctgctcgatc
13 (intron 2 14)	atggcaggtaatgattcact	A/G ttgtggagtaagacttttt
14 (intron 2 192)	*gccacgtggaagtgtataaa*	*C/T tatctggaattatcttgttt*
15 (intron 2 635)	*caccctgtttagcacctagc*	*A/C ccatccctggcctctgccca*
16 (intron 2 685)	*agtagcacccctcccccacc*	*G/A gctgtgacaaaccaaaatgt*
17 (exon 3 139)	ctgatttgtatgccatgaac	T/C (Phe 47 Leu) ttgagccgagggccacagac
18 (intron 3 36)	aatgctctatttataaaaac	T/C atctttatgtttttacttt
19 (intron 3 728)	aacgtgggcataaaccacca	T/C ctagtgccaaaaagcaggtg
20 (intron 4 1577)	tgcctctgcacacccctcc	C/T gacaccagccctttctttac
21 (intron 4 1832)	tcggccggccacgtggagcc	C/T gctttcctcctcgcacccac
22 (intron 4 2583)	tggtgttacgcacagctcct	C/T gtcccctccctgcctgccca
23 (exon 5 330)	ctgtactggttcagcgtgcc	A/G (Pro 110 Pro) gccatcctgaagggctggat
24 (exon 5 405)	atcccaggattctacgattc	C/T (Ser 135 Ser) ggtttgctccaggtatgtgc
25 (intron 5 21)	gtatgtgctcttggataagg	A/T tcactatggatagttggagg
26 (intron 5 253)	atggcaaacaagggagtggg	T/C caggtgtcaggtgacggggg
27 (intron 6 2435)	ccccccttaaatcatttaac	T/C gaatggtatgtaacaggtgt
28 (3′ untranslated region 734)	dbSNP ID:rs6955	
	atcacgtaagcagcacacta	G/C gaggcccaggcgcaggcaaa

Fig. 1a–t. Continued

d Sulfotransferase 1A1 (*SULT1A1/STP1*)

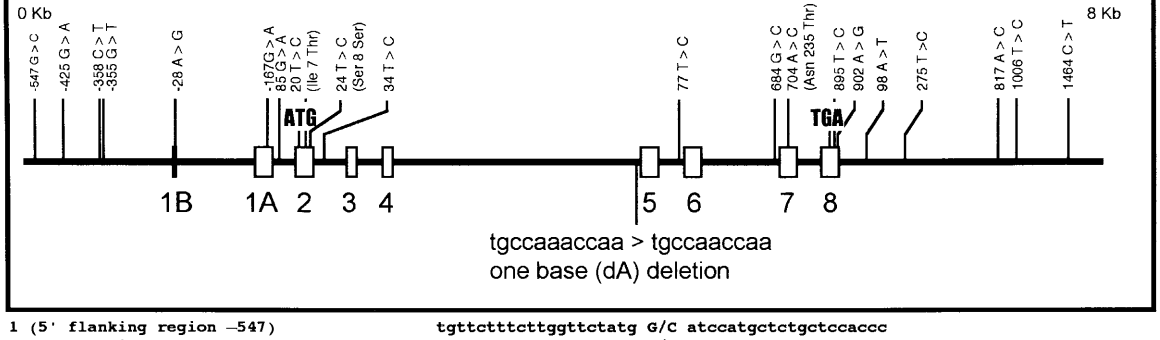


1 (5' flanking region -1597)	gcagagtaaagggactcact	C/G
2 (5' flanking region -1491)	gaggggtatattcatgaaga	G/T
3 (5' flanking region -1376)		
4 (5' flanking region -1375)		
5 (5' flanking region -1370)	cggtttcatatgttactgat	C/T A/G taca A/G
6 (exon 1B -65)	aaccctgcattccccacaca	G/A
7 (intron 1B 442)	gagccaccctgcctaggcct	G/A
8 (exon 1A -197)	gctgggggtcccagcaggaa	A/G
9 (exon 1A -159)	ctggctggcagggagacagc	A/C
10 (exon 1A -95)	gagaccttcacacaccctga	*T/C*
11 (intron 1A 60)	*ctggttttcagccccagccc*	*C/T*
12 (intron 1A 69)	*agccccagccccgccactga*	*C/G*
13 (intron 1A 174)	tgtgatggtggtaagggaac	G/A
14 (intron 6 11)		
15 (intron 6 17)		
16 (intron 6 35)		
17 (intron 6 71)		
18 (intron 6 108)		
19 (intron 6 111)		
20 (intron 6 270)		
21 (intron 6 488)		
22 (intron 6 509)		
23 (exon 7 600)		
24 (exon 7 638)		
25 (exon 7 645)		
26 (exon 8 902)		
27 (exon 8 973)		

1 (5' flanking region -1597)	gcagagtaaagggactcact	C/G
2 (5' flanking region -1491)	gaggggtatattcatgaaga	G/T
3 (5' flanking region -1376)		
4 (5' flanking region -1375)		
5 (5' flanking region -1370)	cggtttcatatgttactgat	C/T A/G taca A/G
6 (exon 1B -65)	aaccctgcattccccacaca	G/A
7 (intron 1B 442)	gagccaccctgcctaggcct	G/A
8 (exon 1A -197)	gctgggggtcccagcaggaa	A/G
9 (exon 1A -159)	ctggctggcagggagacagc	A/C
10 (exon 1A -95)	gagaccttcacacaccctga	*T/C*
11 (intron 1A 60)	*ctggttttcagccccagccc*	*C/T*
12 (intron 1A 69)	*agccccagccccgccactga*	*C/G*
13 (intron 1A 174)	tgtgatggtggtaagggaac	G/A
14 (intron 6 11)		
15 (intron 6 17)	catgaaggaggtgagaccac	C/G
16 (intron 6 35)	gaagcttccctccatgtgac	A/T
17 (intron 6 71)	ctcacagggacccaccaggg	T/C
18 (intron 6 108)		
19 (intron 6 111)	ttggcagcccccacagcagg	C/A
20 (intron 6 270)	ctccctgccaaagggtgtgc	C/T
21 (intron 6 488)	ttttacttttcctgaatcag	C/T
22 (intron 6 509)	aatccgagcctccactgagg	A/G
23 (exon 7 600)	ccctctgctgctcagaaccc	C/G (Pro 201 Pro)
24 (exon 7 638)	gatcctggagtttgtggggc	A/G (His 213 Arg)
25 (exon 7 645)	gagtttgtggggcactccct	G/A (Leu 215 Leu)
26 (exon 8 902)	gctgtgagaggggctcctgg	G/A (Gly 301 Gly)
27 (exon 8 973)	taaaatatgaattgaggg*cc*	*T/C (Trp 325 Arg)*

		gggacggtaggtcatgtctg

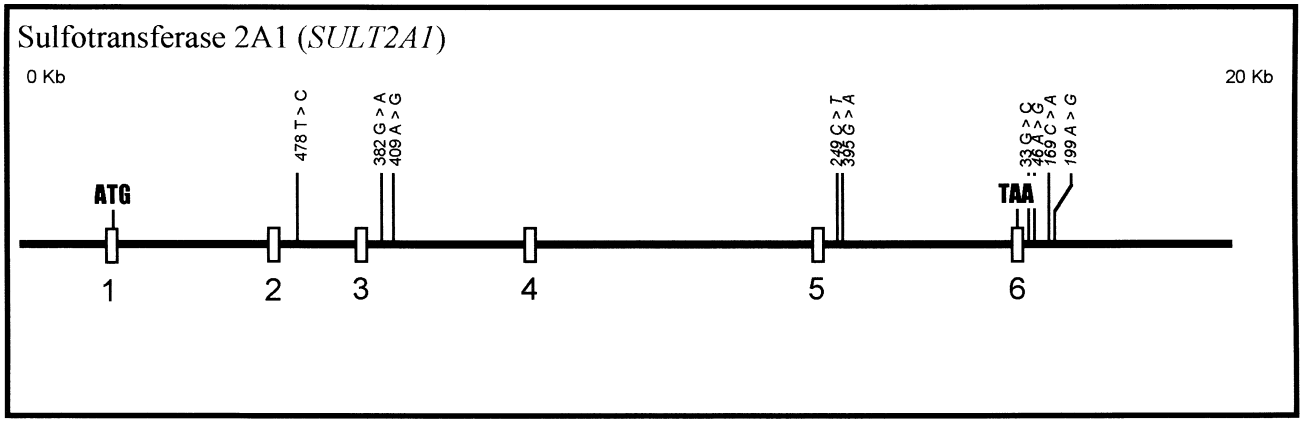
e Sulfotransferase 1A2 (*SULT1A2/STP2*)



1 (5' flanking region –547)	tgttctttcttggttctatg	G/C
2 (5' flanking region –425)	tgtgggttgcactgggccag	G/A
3 (5' flanking region –358)		
4 (5' flanking region -355)	ctttccagggcctgcctatc	C/T
5 (5' untranslated region –28)	actgcgggcgaggagggcac	A/G
6 (5' untranslated region –167)dbSNP ID:rs193675		
	aaagggcgctggctggcagg	G/A
7 (intron 1A 85)	ctgactggccttgtgagtgc	G/A
8 (exon 2 20) 9 (exon 2 24)	catggagctgatccaggaca	T/C (Ile 7 Thr) ctc T/C (Ser 8 Ser)
	cgcccgccactggagtacgt	
10 (intron 2 34)	gccacccaccctctcccagg	T/C
11 (intron 5 77)	cagcaaccctgtgtcggcac	T/C
12 (intron 6 684)	actggggtcccaggggtcga	G/C
13 (exon 7 704)	gttcaaggagatgaagaaga	A/C (Asn 235 Thr)
14 (3' untranslated region 895)	gctctgagctgtgagagggg	T/C
15 (3' untranslated region 902)dbSNP ID:rs6839		
	gctgtgagaggggttcctgg	A/G
16 (3' flanking region 98)	cctccccgctccagctcctc	A/T
17 (3' flanking region 275)dbSNP ID:rs11401		
	tccttacaagccaccacgta	T/C
18 (3' flanking region 817)	ccactgactcggggcttgcc	A/C
19 (3' flanking region 1006)	cctctcccctggaggctgct	T/C
20 (3' flanking region 1464)	tcccgtagcccaggcaagtt	C/T
One base deletion polymorphism		
1 (intron 4 1730)		cctttgccaaaccaagagatg > cctttgccaaccaagagatg

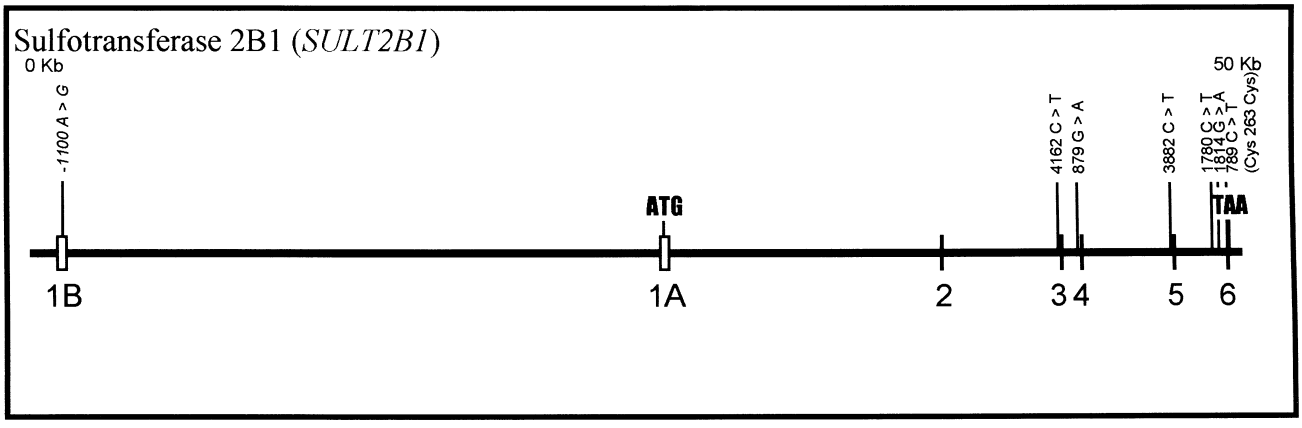
Fig. 1a–t. Continued

f Sulfotransferase 2A1 (*SULT2A1*)



1 (intron 2 478)	ggactgggctctgtacacac	T/C tcgtcttactgtgtgtaaat
2 (intron 3 382)	caaaaccctcttaatattct	G/A tttctatctgtctcagaact
3 (intron 3 409)	tctgtctcagaactgattgc	A/G tgactctaggatcgctatat
4 (intron 5 249)	*agctggaaattacaggcaca*	*C/T gccaccacacccagctaatt*
5 (intron 5 395)	*aggcatgagccacggcgccc*	*G/A gccaatttatcagctttaat*
6 (3' flanking region 33)		
7 (3' flanking region 46)		
	ttccttgttaaaagttacca	G/C ggttggccaggc A/G cggtggttcatgcctgtaat
8 (3' flanking region 169)dbSNP ID:rs296367		
	ctctactaaaaatacaaaaa	*C/A caaaaaaaattagccaggcg*
9 (3' flanking region 199)	*ttagccaggcgcattggctc*	*A/G tgtctgtaatcccagcactt*

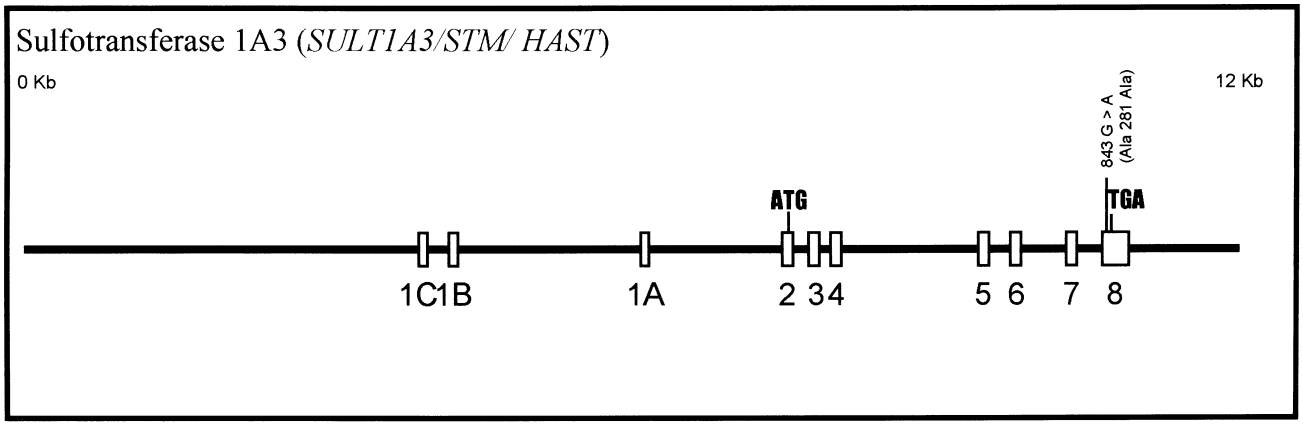
g Sulfotransferase 2B1 (*SULT2B1*)



1 (5' untranslated region -1100)dbSNP ID:rs279448		
	cctcctggtctctgtctccc	*A/G tgccctctgccctctccctt*
2 (intron 2 4162)	ttctcccctctcctcaccat	C/T cgcacacaggtgatctacat
3 (intron 3 879)	gagggcatccagctctgggg	G/A ctggacctgggggtttgtgg
4 (intron 4 3882)	ttccacgctccttccttggc	C/T gagtgccctccctccgctga
5 (intron 5 1780)	cctgcagaaggggtccctt	C/T catgtccaagcagtaatggc
6 (intron 5 1814)	taatggctgcagcatggagc	G/A ttgtgggggcattgagacag
7 (exon 6 789)	ccctcttctccaggggtctg	C/T (Cys 263 Cys) ggcgactggaagaaccactt

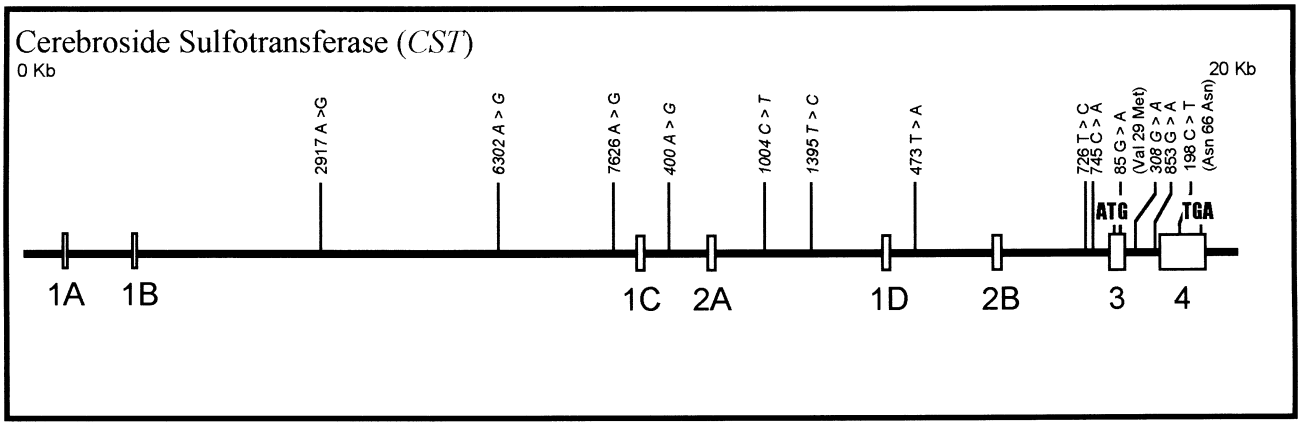
Fig. 1a–t. Continued

h Sulfotransferase 1A3 (*SULT1A3/STM/ HAST*)



1 (exon 8 843) **gcgcttcgatgcggactatgc G/A (Ala 281 Ala) gagaagatggcaggctgcag**

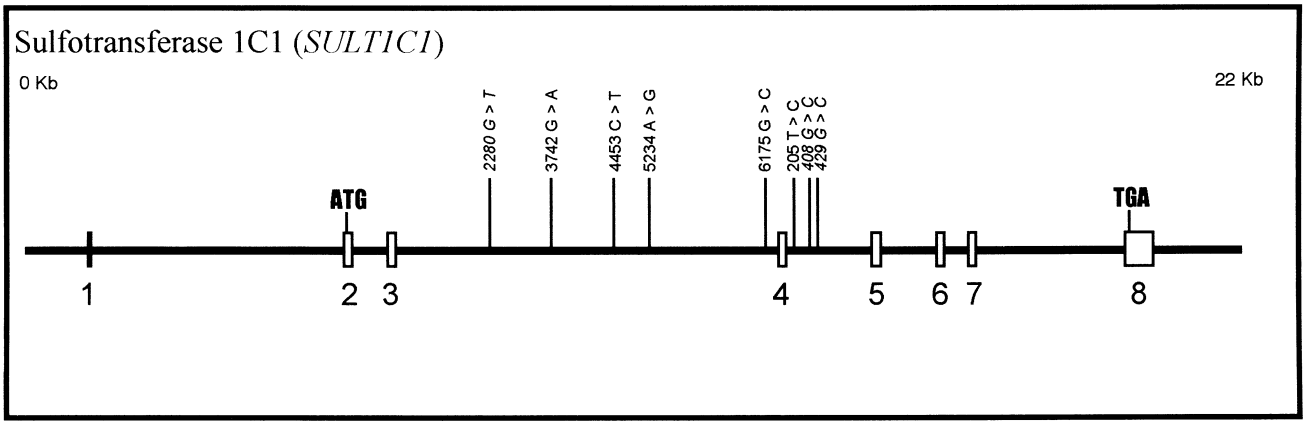
i Cerebroside Sulfotransferase (*CST*)



1 (intron 1b 2917)dbSNP ID:rs42938
gggggaatagcggtgctgca A/G actctgatacagccctagct
2 (intron 1b 6302) ***agagctccccagagaggact A/G tgaggctgcatgatgcatga***
3 (intron 1b 7626)dbSNP ID:rs42932
gagaggtgaggactggccag A/G gctgtccagtggaggcagaa
4 (intron 1c 400)dbSNP ID:rs42931
ctgctgggctgtgttacccc A/G aaggtatccttgccctctct
5 (intron 2a 1004) ***gagtgagacccccatctcta C/T aaaatttttttaaaaagta***
6 (intron 2a 1395) ***atgcctaagtttacagtagc T/C aggcaggaaaggcacaacca***
7 (intron 1d 473) **ccagagcctgaggttggtgc T/A ggggcccctccatggctgcc**
8 (intron 2b 726) **ctatctctccagtgcctctc T/C gtccctgtctggaccctgct**
9 (intron 2b 745) **ctgtccctgtctggaccctg C/A tgggggccacagagcaggc**
10 (exon 3 85) **tcactagtttcctgctgctg G/A (Val 29 Met) tgtactcctatgccgtgccc**
11 (intron 3 308) ***tcgtctgaggtcaggagttc G/A agaccagcctggccaacatg***
12 (intron 3 853) **ttttgtcctataaaatggca G/A tttcatgtggcccaagctga**
13 (exon 4 198) **gaggcagtgatccgggccaa C/T (Asn 66 Asn) ggctcggcgggggagtgcca**

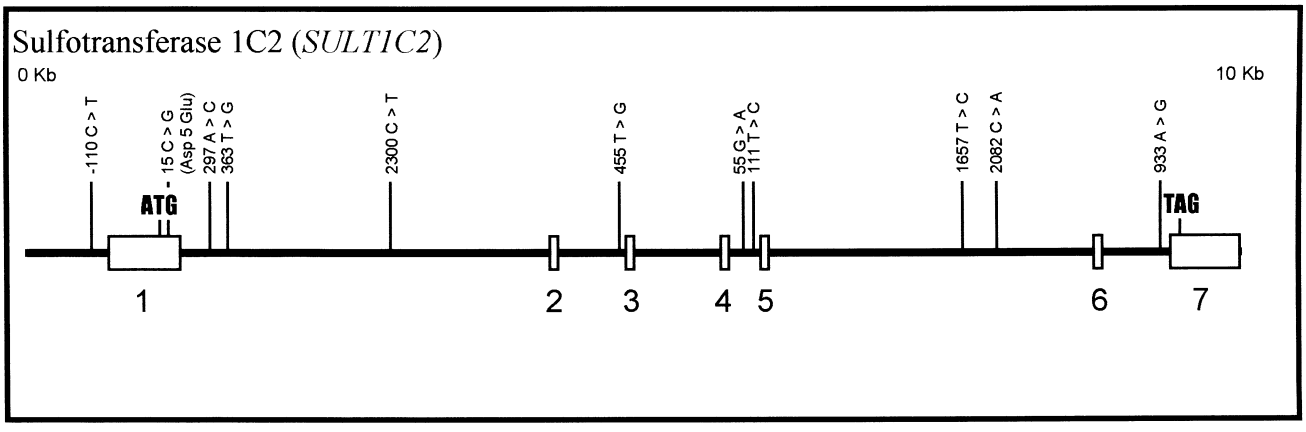
Fig. 1a–t. Continued

j Sulfotransferase 1C1 (*SULT1C1*)



1 (intron 3 2280)	*gcaaatttttggtatttta G/T tacagtcagggttttaccat*
2 (intron 3 3742)	gcagatctcactttctggca G/A attccctgaatttgctcccc
3 (intron 3 4453)	ttcatagggcttttccctca C/T ttgttttgtaattttgtata
4 (intron 3 5234)	gaaaagagactagaggcagg A/G gagctttgcagttcttctaa
5 (intron 3 6175)	tggctggcaggaaggtgagg G/C agtcctctcttctctggtcc
6 (intron 4 205)	acatgaaggcaggatccaga T/C tgaatgtttggagggaacta
7 (intron 4 408)	*ggctcacgcctgtaatccca G/C cactttgggaggccgaggcg*
8 (intron 4 429)	*cactttgggaggccgaggcg G/C gtggatcacaaagtcaggag*

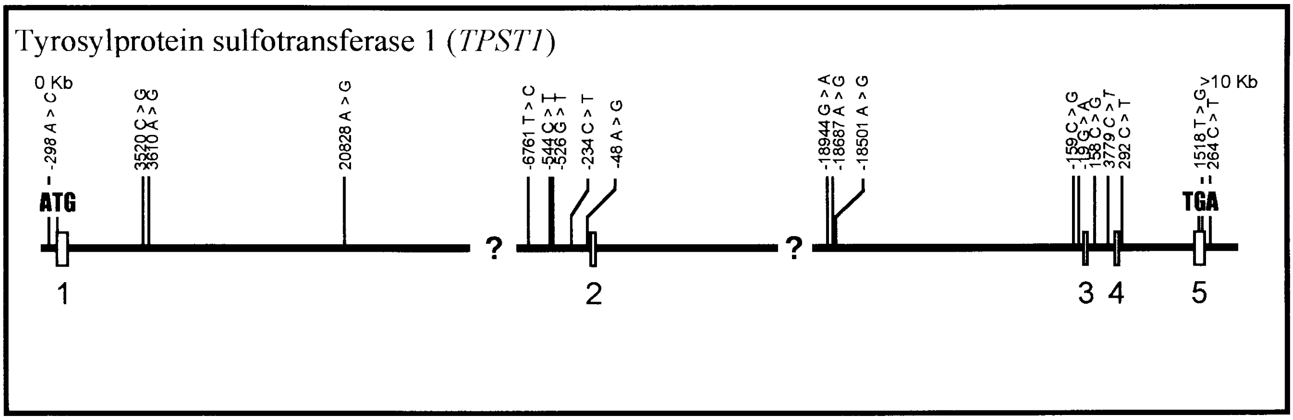
k Sulfotransferase 1C2 (*SULT1C2*)



1 (5' flanking region –110)	tcctgttaactcacagagaa C/T ggaagggctggaacgggacc
2 (exon 1 15)	acactaatggccttacacga C/G (Asp 5 Glu) atggaggattttacatttga
3 (intron 1 297)	gtagacttgtttatttattc A/C ttcccaatctaggcccttat
4 (intron 1 363)	gagtgtgtgagctagaaagg T/G gatcctgagtctgatttggg
5 (intron 1 2300)	gggctactatcagcagccac C/T acctcaggaaggatgacttc
6 (intron 2 455)	aagacttggaagcaaataga T/G aaaaaaaaaatcgtagaaat
7 (intron 4 55)	caaaatctccaaacacccta G/A aaggaaagaatcttttcttt
8 (intron 4 111)	ctgccttctttaatggaaca T/C tctcacttctcttcaggaat
9 (intron 5 1657)	ctttgtgtttactttgtttt T/C acttggtacaaaagtgttgt
10 (intron 5 2082)	tctgctcctagagatggagg C/A gtcccacagccacagtgatg
11 (intron 6 933)	agctactgaacctctcccac A/G taactgtatttcaggggcag

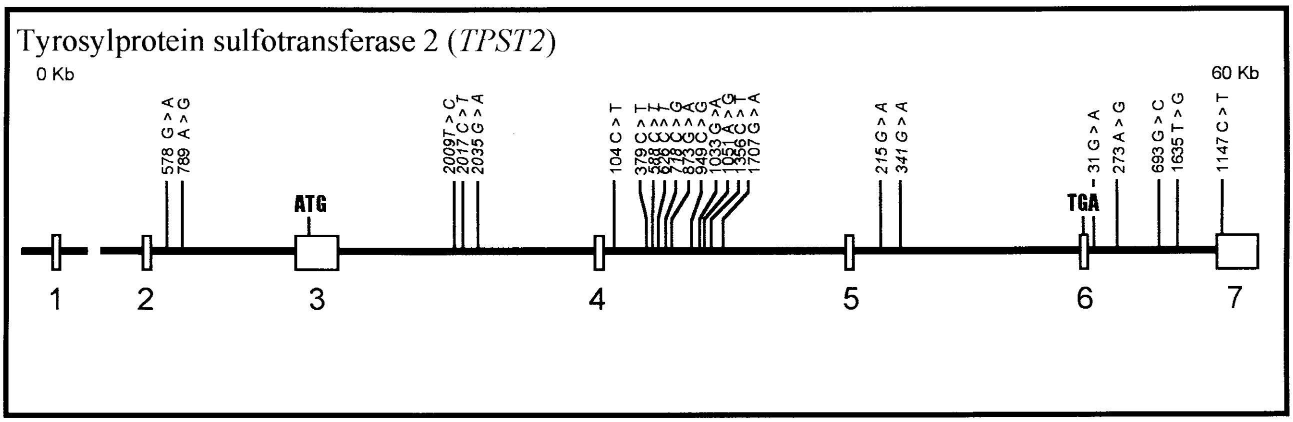
Fig. 1a–t. Continued

l



1 (5' flanking region -298) acccgccaccatgcccagct A/C atttttttgtattttttt
2 (intron 1 3520) agaaaagcagattaatgtaa C/G agtgacgcttagacaacaag
3 (intron 1 3610) ggcagaaagagaatatagca A/G ctattaaacacaaataaatt
4 (intron 1 20828) tattgctgtccacctggtca A/G tgtgtcctgctgataagtgc
5 (intron 1 -6761) aatacaatacttattctgta T/C aattctagagggcccagaga
6 (intron 1 -544) tagaacaagtgaatatttta C/T gttcttagtggtttatggtt
7 (intron 1 -526) tacgttcttagtggtttatg G/T ttggcagttttcccccaaca
8 (intron 1 -234) tcaagacatttaataatgca C/T atgtttcagctaacccttttt
9 (intron 1 -48) ttatagtgggtttaagcatg A/G tttctaaaaaatttaaataa
10 (intron 2 -18944) aaaacattagaactgggaag G/A ttaaaaaatctttagtcttt
11 (intron 2 -18687) tatgtgcaccctaataacat A/G tttccttaaaactagtacta
12 (intron 2 -18501) ttggaaggtaacttaatgta A/G gtgcctgaaaaacagggata
13 (intron 2 -159) gaatggggatttccctcagt C/G ctgcccactggctgctcttg
14 (intron 2 -19) acctgttgccttaaactcac G/A cctgctttgtttttccaggt
15 (intron 3 158) tgctggggaagaaagatcag C/G gtctgggacttgttgatttt
16 (intron 3 3779) agcagggcacgtcaccctcc C/T ggcacacccatgtgttcacc
17 (intron 4 292) ttgttattttcattatgaac C/T atgaaatatttcagctgaaa
18 (3' untranslated region 1518) gttgtctgtacatgttctaa T/G gttttgtagaacacgtgtgc
19 (3' flanking region 264) acggtgcttggcctgcatta C/T cattttgtagtgaagtttct

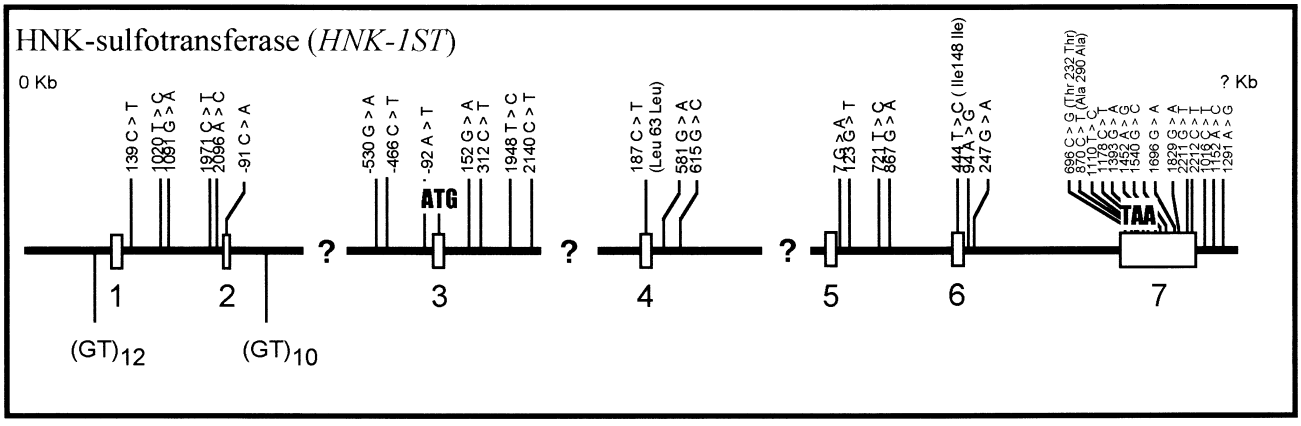
m



1 (intron 2 578) tcacctatcatcctcactgc G/A aggatgccaggatacctccc
2 (intron 2 789) cttaagccatcgtgcaggtc A/G ttgctgtcttctgctcactt
3 (intron 3 2009)
4 (intron 3 2017) cccaggctggagtgtagtgg T/C gtgatct C/T ggctcactgcaacctccgcc
5 (intron 3 2035) ctcggctcactgcaacctcc G/A cctcccgggttcaagcagtt
6 (intron 4 104) aatgttcagtctctcaattc C/T tggtcatctgatttgttcct
7 (intron 4 379) taaataaataaactattggt C/T cctttcttgtcttataaggt
8 (intron 4 588) tactgcagcctgatacttct C/T ggcttaagccatcctctcac
9 (intron 4 626) caccccaggctcctgagtag C/T taggactgcaggtgcacgcc
10 (intron 4 718) cccaggctggtctagaactc C/G tggccgtaagggatgcccct
11 (intron 4 873) gttgatggccttatttatac G/A tttccattacagcttctagt
12 (intron 4 949) caaatatttgaaaatgggac C/G caggcctgaggaagagcttt
13 (intron 4 1033) taagctcagcatttctgagc G/A tgtgctgattttaggaaata
14 (intron 4 1051) gcgtgtgctgattttaggaa A/G taaacagttatcgtattgaa
15 (intron 4 1356) gattcaacgtacataccagc C/T gacattgacaggtgaatggc
16 (intron 4 1707) gtctccttaaaaggtggctc G/T ctgcccctggcttgccccag
17 (intron 5 215) aagaccagcctgaccaaaac G/A gtgaaaccccgtctctacta
18 (intron 5 341) tgggaggcagaggtcgcagt G/A agctgagatcacgccgttgc
19 (intron 6 31) ggacttcactggggggttccc G/A ctgcttctgggtggccccgg
20 (intron 6 273) gtttgtctgacactggggac A/G gggcaggaagcaccactatg
21 (intron 6 693) aaagggattttttttgaactt G/C gtaattcaaagatttaagat
22 (intron 6 1635) tcctgggtacagagttggcc T/G tgaacaaacatgagtccttc
23 (3' untranslated region 1147) cttccccactttcagatctc C/T gcaaatgacttcattgccaa

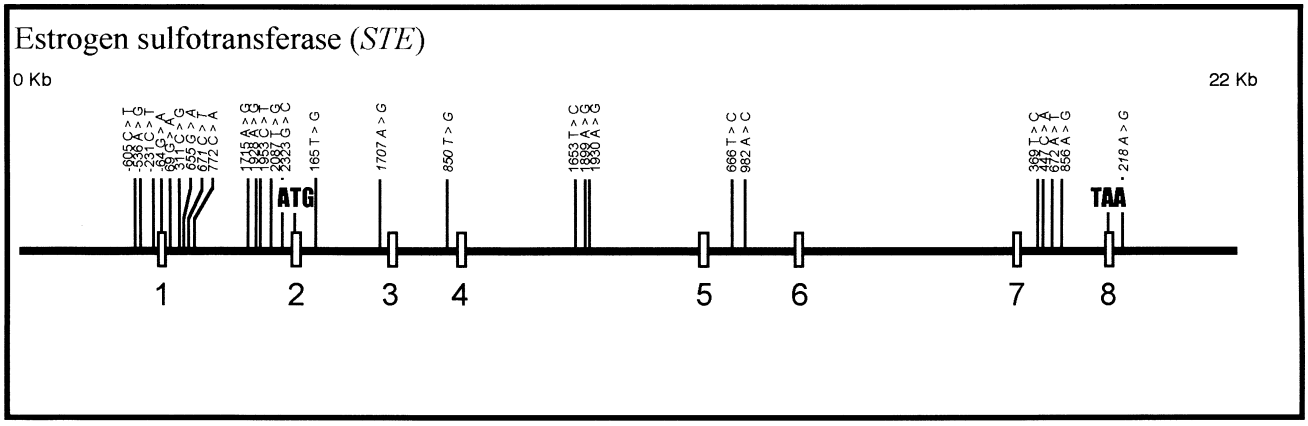
Fig. 1a–t. Continued

n HNK-sulfotransferase (*HNK-1ST*)



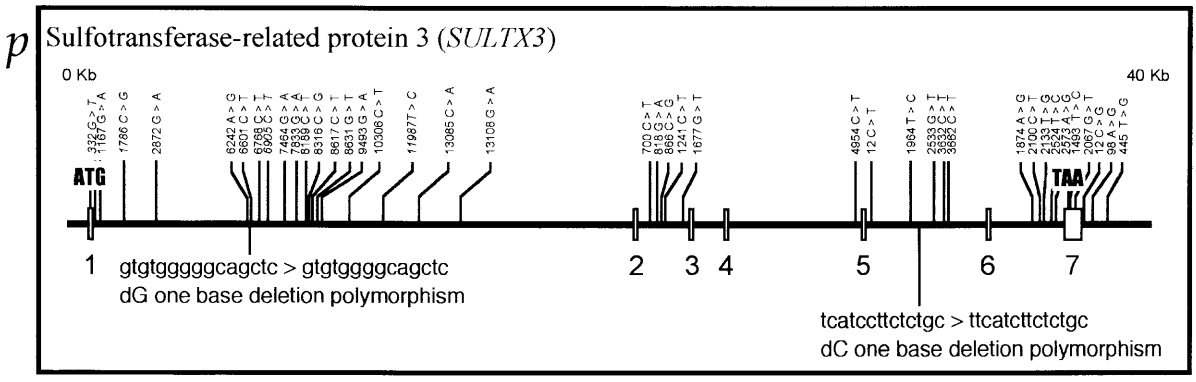
1 (intron 1 139)	gtgttttggcgacttgaaga	C/T	ctccctagttcgcgggagta
2 (intron 1 1020)	acctgagcagaaaattctct	T/C	cttcgctgaaatgaaaattg
3 (intron 1 1091)	aagaatttgtaaacatcaca	G/A	gcaacttgcagttatattcg
4 (intron 1 1971)	ctataactatttcaaacata	C/T	gaaacaggcataattggatt
5 (intron 1 2096)	atttagaatattcatttacc	A/C	agaaatccaaatataacctg
6 (5'untranslated region -91)	ctatccagtgacaagaggaa	C/A	caagaacctcagttcagggg
7 (intron 2 -530)	agtgggcggaggcgagaagc	G/A	tcagtgttcattcctttgct
8 (intron 2 -466)	gctacatcttgtcagccagt	C/T	agaattttaaacacagccag
9 (intron 2 -92)	acggaaatatttgtgctgat	A/T	cttactgactgaaatcacct
10 (intron 3 152)	catggcctccgttccttcat	G/A	ttacagaggtgtgaggggag
11 (intron 3 312)	cacagtggccttatgccttg	C/T	agcagggcgcctctcaggct
12 (intron 3 1948)	tcctttgatgtatcaagttt	T/C	gtgctgaatgttttcagtgt
13 (intron 3 2140)	ttacacctggagaggagcac	C/T	gcagcggtccttaatactgc
14 (exon 4 187)	agaagcacattcctgaggaa	C/T	(Leu 63 Leu) tgaaggtgggcacagccagg
15 (intron 4 581)	cctgatcattccctagctgg	G/A	atgaggggtgcactctggaa
16 (intron 4 615)	tctggaaggcctctcacttc	G/C	taacccccattctggatcta
17 (intron 5 7)	gattgttctaaatggtgtgt	G/A	tgggtctactgaatgtccac
18 (intron 5 123)	acctgaagggactggtggcc	G/T	tccagacaggcctgtttttg
19 (intron 5 721)	ataattatgggctctgctta	T/C	gaaatttagcttcagacagg
20 (intron 5 867)	tgctgcccacagagtcggtg	G/A	tcactcctggccactgtttg
21 (exon 6 444)	ccaggagcattttcttccat	T/C	(Ile 148 Ile) gaggagatccccgaaaacgt
22 (intron 6 94)	ctgagttctgtacttggcag	A/G	ttgatcggaggaccacagag
23 (intron 6 247)	catgaaggtgacatcatttt	G/A	ttaatagaaattagcaggca
24 (exon 7 696)	aggaggaaccggacagagac	C/G	(Thr 232 Thr) cgggggatccagtttgaaga
25 (exon 7 870)	gagaccctggaggacgatgc	C/T	(Ala 290 Ala) ccatacatcttaaaagaggc
26 (3' untranslated region 1110)	tcaaatatctttattagacc	T/C	ggggctaaccaggtgaagat
27 (3' untranslated region 1178)	ccacacccctcctttgagga	C/T	gcccggggtctcccacaggc
28 (3' untranslated region 1393)	ggaagcatcacacagcgtta	G/A	gagccgtttccttcaggtgt
29 (3' untranslated region 1452)	tgaggttctcctggctagtc	A/G	gggtggcttcacccatcact
30 (3' untranslated region 1540)	gcaagggggctgctgaaatc	G/C	cagagacttttgcagcatca
31 (3' untranslated region 1696)	gggtggtgtggtgtccaggg	G/A	tccatctttccagaatccat
32 (3' untranslated region 1829)	aggggaggctttttctacct	G/A	agaaggggagtgtctttgag
33 (3' untranslated region 2211)			
34 (3′ untranslated region 2212)	tccagcagtgcggcttcctg	G/T C/T	aacaaggtaggccctggtgc
35 (3' flanking region 1016)	cacacgaaggtgtgcactca	C/T	ggcctgcagggcacccaggt
36 (3' flanking region 1152)	gcatgctttgctcatctgga	A/C	tctccagaagcagggaacag
37 (3' flanking region 1291)	gccgagaccctcagcaggat	A/G	gtgcagttacagggctgagc

Fig. 1a–t. Continued



1 (5' flanking region -605)	caggtttctaaaataataat	C/T	gaaaggtgagtgatgtttac
2 (5' flanking region -536)	taaaattttcaggtctgctt	A/G	agagttaaaggcaaagagtt
3 (5' flanking region -231)	ccttcttccccaacccctga	C/T	ggcagacttgggaatttgaa
4 (5' untranslated region -64)	tgcagcttaagatctgcctt	G/A	gtatttgaagagatataaac
5 (intron 1 69)	aaatatagaatgaaaattat	G/A	tattacaaagctcttaaaaa
6 (intron 1 311)	caatgagaaaataaagcaag	C/G	agggtagaaggaggtagaat
7 (intron 1 655)	*tctaagaaagtagggactat*	*G/A*	*agaacccctatgtatctata*
8 (intron 1 671)	*ctatgagaaccccctatgtat*	*C/T*	*tatatccaccatagtattct*
9 (intron 1 772)	aaaaggcaggttggaagatg	C/A	aggaggggagtatgcagaaa
10 (intron 1 1715)	taaccatcttgcttaacctt	A/G	tcatttttagccaagtcatt
11 (intron 1 1928)	aaatgatacatattcaggaa	A/G	tcaaaaatctctgacttaga
12 (intron 1 1953)	aaatctctgacttagatacc	C/T	ggcaataataatcaaatgta
13 (intron 1 2087)	aattttgaaagaaattgaag	T/G	tctgtggtttttatttatca
14 (intron 1 2323)	taggtatgtaggagggtccc	G/C	ttatatacatagttgttaat
15 (intron 2 165)	tctattccatgaccacaatt	T/G	ttacctgtaacttgaatagt
16 (intron 2 1707)	*cctaggacccaacatgagac*	*A/G*	*taatataccatcagtaaaat*
17 (intron 3 850)	*ggtgtccattccctcaagaa*	*T/G*	*ttatactttgtgttacacac*
18 (intron 4 1653)	agtaacaggctagtagataa	T/C	ataaataactgaggccaacg
19 (intron 4 1899)	tacatgaacttagagaatca	A/G	gtagatcacacacaccaaca
20 (intron 4 1930)	cacaccaacaataaaattac	A/G	cagaatgataaaagaatttg
21 (intron 5 666)	ttctgatcatgtagtaacaa	T/C	tataaagaaaataataatgt
22 (intron 5 982)	aggcaaagcagaacctttg	A/C	ctcacacaacattatattat
23 (intron 7 369)	agattttattcctctctctt	T/C	ttgagttgaagaaataagtt
24 (intron 7 447)	caccttcaagggtaagtgg	C/A	aaaaaatagaaattcaaata
25 (intron 7 672)	aatcttgctctttgaaccat	A/T	ctgtcagtgagagtcaggga
26 (intron 7 856)	tgttacagaggacttaaaac	A/G	gttgtcttgcttgcaaacgg
27 (3' flanking region 218)	*cagcctcccaagtagctagg*	*A/G*	*ctacagacatgtgcaaccat*

Fig. 1a–t. Continued

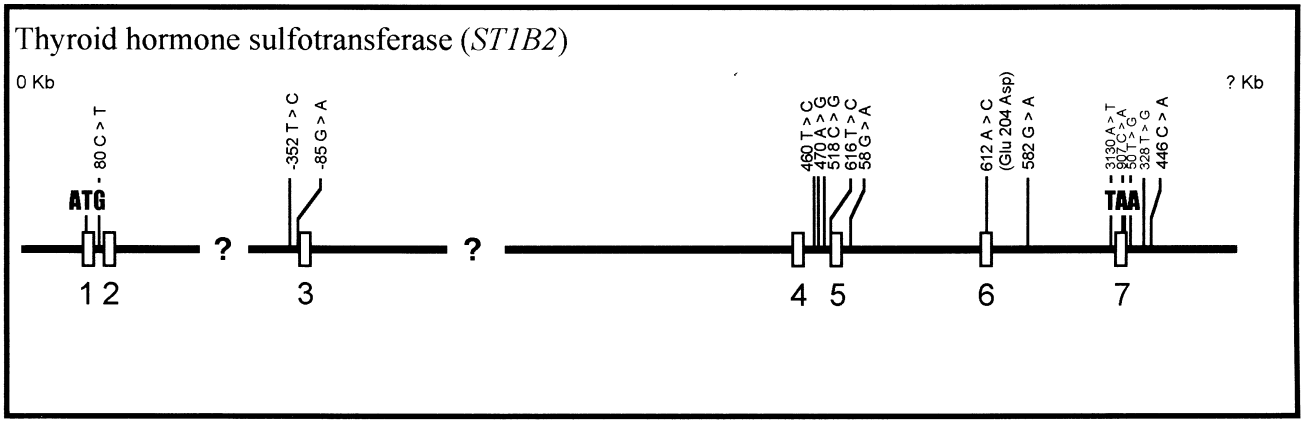


1 (intron 1 332)	*cctgcttctccctttacctg*	*G/T ctggctgtgtgaccttggac*
2 (intron 1 1167)	taggaatggctaagcgtgtc	G/A ttggcttctgtggccactca
3 (intron 1 1786)dbSNP ID:rs138017	*gggtgagaacgcttagccca*	*C/G gtccagacacacgctggaaa*
4 (intron 1 2872)	cattctcactgatgcagacg	G/A aagcttctgggcctgggcgt
5 (intron 1 6242)	caccctggctttaccagc	A/G tggaaacattttacctgaat
6 (intron 1 6601)	gcgtgggcttctggagggag	C/T gagaggagagtggagggccc
7 (intron 1 6768)	agcttgaaatgagccagact	C/T tcctgggacctgttgacccc
8 (intron 1 6905)	*agtactttgttttatcctcc*	*C/T catcctcacaactttgccat*
9 (intron 1 7464)	gccaggatcccttgagagac	G/A acatgaacacagccaggagc
10 (intron 1 7833)	tgcttcgggctgggcttggc	G/A ggggcagctgtgctccaggc
11 (intron 1 8189)	caaactggggcccttaatgc	C/T gcacaccagagcctcctttc
12 (intron 1 8316)	ctctcacacaagggcggagc	C/G tcttccccttgaggcagagc
13 (intron 1 8617)	agacagaggctggggccaag	C/T cagggttgccggagcttccc
14 (intron 1 8631)	gccaagccagggttgccgga	G/T cttcctggactggtcaggcc
15 (intron 1 9493)	ttttcctcttagagcttccc	G/A tcgtgctctgtgtcgagggc
16 (intron 1 10306)	caggcggggagcctgaatgc	C/T gcagtcgtgagggtggccag
17 (intron 1 11987)	*tcataaaataatgatatcag*	*T/C acacttttggaaatttgag*
18 (intron 1 13085)	ctctgtgcccggtgttgaga	C/A aggccatgccctagagtcct
19 (intron 1 13108)	gccatgccctagagtcctgg	G/A gagttccaccccagaacagc
20 (intron 2 700)	gaaccatctgggagtcgttc	C/T gtactgccgtgccgagggcc
21 (intron 2 818)	agccatagtagctagccagc	G/A atcagcgctgggaggggagc
22 (intron 2 866)dbSNP ID:rs138075	gggggaccagcagtctcct	C/G tggggatgtctgaggcaggt
23 (intron 2 1241)dbSNP ID:rs138074	cctccgacgccactccaagc	C/T ggggcagtagctcccaggcc
24 (intron 2 1677)	actccacttcccctgaaccc	C/T acccctccttcctcctctg
25 (intron 4 4954)	gcgtgccgaaggcgggaggg	C/T tgggatggctcaagacgtga
26 (intron 5 12)dbSNP ID:rs138070	atgcatcgggtgagtgctgc	C/T ggagcagctgtcctccgggt
27 (intron 5 1964)dbSNP ID:rs138067	ctgtctggcttctgcgcaga	T/C ggcgaggctcctccacctgc
28 (intron 5 2533)dbSNP ID:rs138065	cgtcagggtcaaggccacca	G/T ccctgcctggaactttaaga
29 (intron 5 3632)	ccagctgactcccacaccag	C/T ggtcagagaacattgtcttt
30 (intron 5 3662)	acattgtcttttaaggtttc	C/T gaagtgctgcaataaagaaa
31 (intron 6 1874)	tctgatctcagagagctgac	A/G atggaaagaattctaaacga
32 (intron 6 2100)dbSNP ID:rs138061	tttcgtttttccaaagcctt	C/T ataaaccagcgtagaccggt
33 (intron 6 2133)	agaccggtgcctgcagttta	T/G cccacagctcagccctccct
34 (intron 6 2524)	ggaagggccagggctgcctg	T/C gatgcccagagcagtgcact
35 (intron 6 2573)	agatcatactcgctcctggg	*A/G tgtttattaaaacacctgcca*
36 (3' untranslated region 1493)dbSNP ID:rs138057		
	ggtcttcagaatggacgtcc	T/C tctgccagagacttccagcg
37 (3' untranslated region 2067)dbSNP ID:rs138056		
	cccaaagtggtggtcaggag	G/T gtcgctgctgtggaaggggt
38 (3' flanking region 12)	gttcccggcgttgcgtcgag	C/G gtttctgcttgtgggggtag
39 (3′ flanking region 98)dbSNP ID:rs38055		
	gtgggccccgttgacacccc	A/G ttccctggggttgacagcag
40 (3' flanking region 445)	tccaaagcctgtcttcctga	T/G ttcctgtggaaggagagtcc

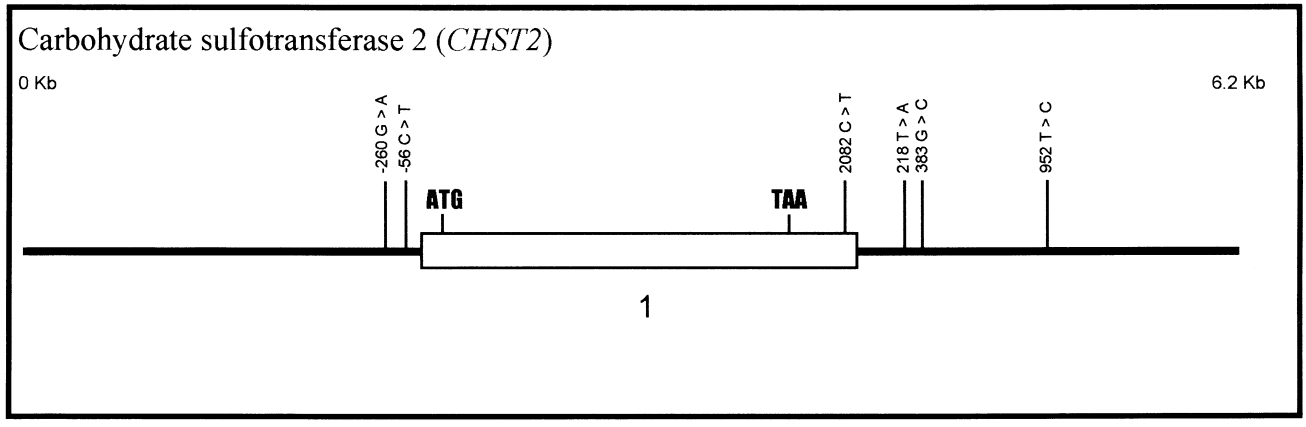
One base deletion polymorphisms

1 (intron 1 6419)	ctgttagtgtgggggcagctc > ctgttagtgtggggcagctc
2 (intron 5 2458)	ggaagttcatccttctctgcc > ggaagttcatcttctctgcc

Fig. 1a–t. Continued



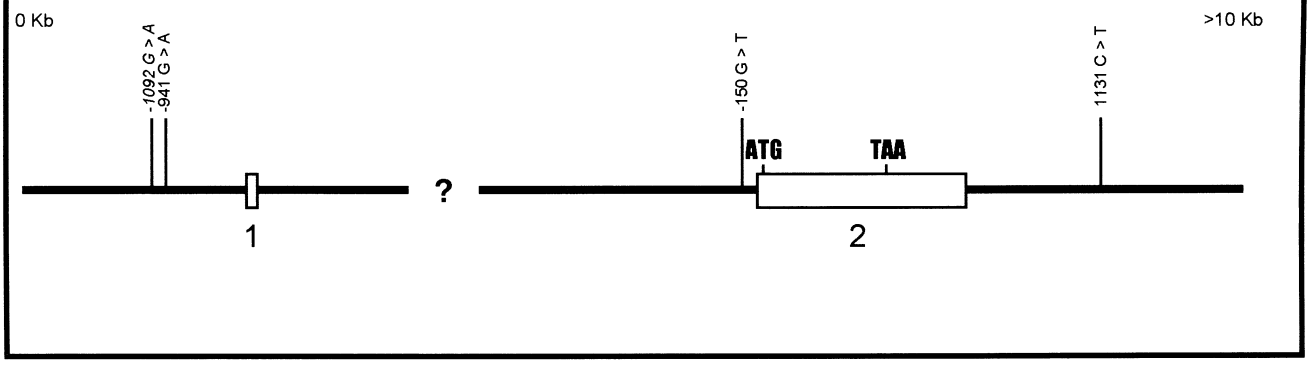
1 (intron 1 80)	acttgtccataaaatcatta	C/T	cattctaaataaagttaata
2 (intron 2 -352)	aacatttaaatagtcattta	T/C	agcaatgcacaggtataata
3 (intron 2 –85)	attacataatgctcaaaaat	G/A	tcttgaaaaactggttggca
4 (intron 4 460)			
5 (intron 4 470)	gtacttgacattaaaaaata	T/C	ctgatgttt A/G tatatccataaatagctaat
6 (intron 4 518)	tttaagattgtcctcatatt	C/G	ttacttcctttggttactaa
7 (intron 4 616)	aatgtttatgaaaatagact	T/C	ttatctggttttagtggcct
8 (intron 5 58)	ctgcatcatgctgtaaaagg	G/A	ttgatatttgctttccaact
9 (exon 6 612)	taatagaatccaaaggagga	A/C	(Glu 204 Asp) atcaagaagatcattagatt
10 (intron 6 582)	aatacattacttccatttaa	G/A	tagtctgtttattgtggctt
11 (intron 6 3130)	agatgtaaaaaattattcaa	A/T	ttttaaaagcctgaaaaatt
12 (3' untranslated region 907)			
	tttaaagtgtctaaatcaca	C/A	atctgaagaaataagagatt
13 (3' flanking region 50)	tcagatcccagttttgttcc	T/G	ttgattctgagtttccaaat
14 (3' flanking region 328)	tttgacccaggacactgtgt	T/G	ccactgctgtctaccgagtt
15 (3' flanking region 446)	gtagttcagattttggaaat	C/A	ttttttctatatcataccta



1 (5' flanking region -260)	agccggacagtccgccgggc	G/A	gtgatccgggggccgctccc
2 (5' flanking region -56)	gcgctggggaccagccgccg	C/T	gcccgcctcggagtcgcggc
3 (3' untranslated region 2082) dbSNP ID:rs6664			
	gaggaggcattcttctaaag	C/T	agacttttgtgtaaaaagca
4 (3' flanking region 218)	aggagtgaaacacatctttg	T/A	attctaaaggcagaaaccaa
5 (3' flanking region 383)	gcagagaccaatgttttggt	G/C	ctgaggctggttcagaaaaa
6 (3' flanking region 952)	tactgaaacattctgcagaa	T/C	gttatactatgagaagaaat

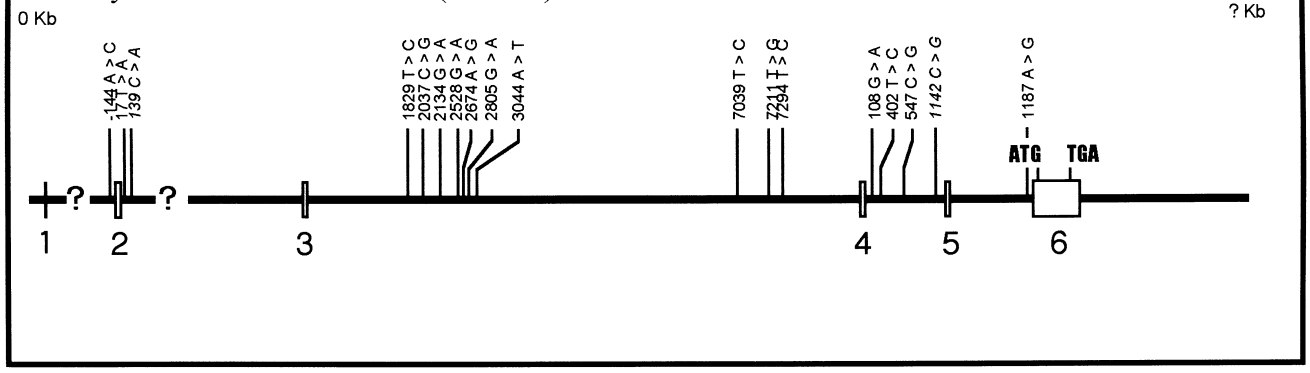
Fig. 1a–t. Continued

s Carbohydrate sulfotransferase 4 (*CHST4*)



1 (5' flanking region -1092)	*atgaagccttgtgccatctc*	*G/A*	*ctgtgtcgtgccagcacctg*
2 (5' flanking region -941)	ctgccagagagaaacaggaa	G/A	ggaggaagagccacacaatt
3 (intron 1 -150)	caggaaatgatttggagaag	G/T	actggtgccattgttggcac
4 (3' flanking region 1131)	dbSNP ID:rs310334		
	acagcagatgacagtgtgaa	C/T	agagtgaagagggccattga

t Carbohydrate sulfotransferase 5 (*CHST5*)



1 (intron 1 -144)	ggcctcttaggtttcagcca	A/C	gacaggtgactcttagcacc
2 (intron 2 17)	caacgtaagagcgcttctca	T/A	tgtccagctcctttgtttct
3 (intron 2 139)	*aatcccagcactttgggagg*	*C/A*	*ggagatgtgcggatggatca*
4 (intron 3 1829)	gactgtatgtctgctattca	T/C	ataggaacaaataattcatg
5 (intron 3 2037)	aaatgaaaccaacaccaaca	C/G	tgcagagaagcaaacaaaag
6 (intron 3 2134)	aagcagctaaattgtgttcc	G/A	tacaggtgcaattaggcagg
7 (intron 3 2528)	atggtaaagttcgcctgggt	G/A	cagtatgtcagcatcctgct
8 (intron 3 2674)	gcacttatcctagaaaggcc	A/G	tttctgaagactcagcagga
9 (intron 3 2805)	dbSNP ID:rs459211		
	cagagacaacggttctttcc	G/A	gttttgctctacacagttcc
10 (intron 3 3044)	dbSNP ID:rs364212		
	ggaacacactgtgcatttct	A/T	ccttctgttgtgagccactc
11 (intron 3 7039)	ctggctcccgccggccaccc	T/C	gggaccgcagccacgtctga
12 (intron 3 7211)	gtagccccaggacaccccca	T/G	cctcaacatcccattctggg
13 (intron 3 7294)	ggagcttccagtggcttggt	T/C	acccccgactcttcgtccat
14 (intron 4 108)	gcagggtcctgcactctgca	G/A	ggggcaatcacaggtgggag
15 (intron 4 402)	agcactggaaaaagtacagt	T/C	gcacttgtagcggaggtggg
16 (intron 4 547)	ctcctgtccccgcattgagg	C/G	gaaggagcagaggtgagatc
17 (intron 4 1142)	*gccccaggtctcatagctcc*	*C/G*	*cattggcagtgctgggattt*
18 (intron 5 1187)	cactgggcagtaattggggc	A/G	tgggatgggcatgagggccc

Fig. 1a–t. Continued

1910-bp segment (1 SNP/173 bp) of the 3′ untranslated region in *HNK-1 ST*. On the other hand, we found the only 1 SNP in a 12-kb region corresponding to the entire *SULT1A3* gene. We speculate that this uneven distribution reflects evolutionary selection and/or regional differences in mutational risk.

Quinone oxidoreductases

NQOs are flavoproteins that catalyze two-electron reduction and detoxification of quinones and quinone derivatives; NQOs play important roles in the protection of cells and tissues against various types of oxidative stress. Reactive oxygen species (ROS), such as hydrogen peroxide, superoxide, and hydroxyl radicals, can cause severe toxic damage to cells; ROS are implicated in cancer, various other diseases, and the process of aging. Hence, differences in the quality and quantity of NQO enzymes are likely to have a significant influence on the susceptibility to various common diseases, including arteriosclerosis, hypertension, and diabetes mellitus, as well as cancer. In fact, a Pro203Ser amino-acid substitution in the *NQO1* gene has been implicated as a factor influencing risk for lung cancer (Rosvold et al. 1995; Chen et al. 1999; Lin et al. 1999), cutaneous basal cell carcinoma (Clairmont et al. 1999), and urological malignancy (Schulz et al. 1997). In addition, this change appears to be associated with risk for a subtype of colon cancer characterized by mutation at codon 12 of the K-*ras* gene (Lafuente et al. 2000). Moreover, on the basis of an epidemiological study in China, Rothman et al. (1997) reported that individuals homozygous for the allele encoding the serine residue lost NQO1 activity and carried an increased risk of benzene poisoning and subsequent hematological malignancy. Because genetic variations in promoter or enhancer sequences are likely to influence the amount of enzyme production, studies of SNPs in these upstream regions may shed light on susceptibility to various diseases.

Sulfotransferases

Sulfation is catalyzed by members of the sulfotransferase family of enzymes. Sulfation has not only evolved as a key step in xenobiotic metabolism and chemical defense but it also has an important role in modulating the biological activity of numerous potent endogenous chemicals, including iodothyronines, steroids, and catecholamines. With respect to human disease, elevated activities of platelet phenol-sulfotransferases may be associated with neuropsychiatric abnormalities such as obsessive-compulsive disorder and mania (Marazziti et al. 1996). In addition, one or more of the sulfotransferases located on chromosome 16p are candidates for involvement in a pseudopheochromocytoma, in which patients have decreased serum levels of sulfo-conjugated catecholamines (Goldstein et al. 1996). Hence, variations that affect the production or structure of the gene product are likely to cause dysfunction of various signaling pathways, or to reduce the ability to detoxify various compounds.

Coughtrie et al. (1999) reported a difference in the frequencies of *SULT1A1* genotypes between two age groups (below and above 60 years) in a Caucasian population; a significantly higher frequency of the *SULT1A1*1* (Arg213Arg) homozygote was observed in the older group. Their data suggested that homozygosity at this locus might be associated with protection against damage to cells or tissues during aging. Several phenol-preferring sulfotransferases (phenol-preferring PSTs), notably SULT1A1 and SULT1A2, are thought to play essential roles in the metabolism and clearance of xenobiotic agents (e.g., simple phenols such as naphthol or *p*-nitrophenol, and drugs such as acetaminophen and minoxidil) and endogenous compounds, including catecholamines and thyroid hormones. On the other hand, monoamine neurotransmitter-preferring PST STM, a member of the PST superfamily, preferentially catalyzes the sulfation of phenolic monoamines, such as dopamine, and is relatively insensitive to inhibition by 26-dichloro-4-nitrophenol (DCNP), although both SULT1A1 and SULT1A2 are inhibited by DCNP (Dooley 1998). Hence, we suggest that the substitutions identified in this study might be immediately useful as specific markers for association studies involving common diseases and sensitivity to drugs.

We are extending our SNP discovery efforts involving genes that encode drug-metabolizing enzymes, in order to catalog common variants that may explain susceptibility to disease and/or affect drug responses, drug disposition, and toxicity.

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