J Hum Genet (2002) 47:576–584

ORIGINAL ARTICLE

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Catalog of 238 variations among six human genes encoding solute carriers (*hSLCs*) in the Japanese population

Received: July 24, 2002 / Accepted: July 25, 2002

Abstract We screened DNAs of 48 Japanese individuals for single-nucleotide polymorphisms (SNPs) in six genes encoding proteins of the solute carrier (SLC) family by direct sequencing of their entire genomic regions except for repetitive-sequence elements. This approach identified 213 SNPs and 25 insertion/deletion polymorphisms among the six genes. On average, we identified 1 SNP in every 509 nucleotides. Of the 213 SNPs, 14 were identified in the *SLC10A1* gene, 51 in *SLC15A1*, 29 in *SLC22A1*, 27 in *SLC22A2*, 54 in *SLC22A4*, and 38 in *SLC22A5*. Eight were located in 5′ flanking regions, 172 in introns, 25 in exons, and 8 in 3′ flanking regions. These variants should contribute to investigations of possible correlations between genotypes and phenotypes as regards disease susceptibilities or responsiveness to drug therapy.

Key words SNP · SLC10A1 · SLC15A1 · SLC22A1 · SLC22A2 · SLC22A4 · SLC22A5

Introduction

Member 1 of human solute carrier (SLC) family 10 (sodium/bile acid cotransporters), SLC10A1 (NTCP1), is the major transport protein responsible for sodium-dependent uptake of bile salts by hepatocytes from the portal circulation (Meier 1995). This protein is localized specifically to liver sinusoidal membranes (Craddock et al. 1998; Muller and Jansen 1997). The promoter region of the gene encoding *SLC10A1* contains potential DNA-binding sites for transcription factors C/EBP and HNF3/HNF6, and in some experiments mutations of these C/EBP sites have resulted in loss of 77% of transcriptional activity (Shiao et al. 2000). Expression of this gene is markedly reduced in several experimental rodent models exhibiting cholestasis (Gartung et al. 1996; Green et al. 1997).

Member 1 (SLC15A1, PEPT1) of human solute carrier family 15 (oligopeptide transporters) is located in the intestinal brush border membrane (Leibach and Ganapathy 1996). SLC15A1 mediates absorption of dipeptides and tripeptides that arise from the digestion of dietary proteins or beta-lactam antibiotics and other peptide-like drugs (Adibi 1997). This protein contains 12 predicted transmembrane domains (TMDs), and a large extracellular loop carries potential *N*-glycosylation sites (Liang et al. 1995; Covitz et al. 1998).

A newly described transporter family (solute carrier family 22; SLC22) consists of organic cation transporters (OCTs). OCTs function primarily to eliminate cationic drugs and other xenobiotics from tissues such as kidney, small intestine, and liver (Koepsell 1998; Zhang et al. 1998). Member 1 of family 22 (*SLC22A1*, *OCT1*) is transcribed primarily in the liver (Gorboulev et al. 1997; Zhang et al. 1997). However, member 2 (*SLC22A2*, *OCT2*) is expressed mainly in the kidney (Gorboulev et al. 1997). Member 4 (SLC22A4, OCTN1) is a renal proton/organic cation antiporter functioning at the epithelial apical membrane (Tamai et al. 1997; Yabuuchi et al. 1999); it is strongly expressed in kidney, trachea, bone marrow, and fetal liver, but not in adult liver. Member 5 (*SLC22A5*, *OCTN2*) is strongly expressed in kidney, skeletal muscle, heart, and placenta in adult humans (Tamai et al. 1998); mutations in the *SLC22A5* gene cause carnitine deficiency (Lamhonwah and Tein 1998; Burwinkel et al. 1999; Nezu et al. 1999; Tang et al. 1999; Vaz et al. 1999; Wang et al. 1999, 2000, 2001). All

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these transporters have 11 (SLC22A4) or 12 (SLC22A1, SLC22A2, and SLC22A5) TMDs, and each has a large extracellular loop carrying potential *N*-glycosylation sites (Tamai et al. 1997; Burckhardt and Wolff 2000). Conserved amino acid motifs reveal a relationship to the sugar transport-facilitator family of molecules (Burckhardt and Wolff 2000).

To investigate in more detail the nature of apparent genotype/phenotype correlations for some SLCs, we began by searching for additional single-nucleotide polymorphisms (SNPs) in the six genes encoding the transporters described above, including their promoter regions and introns except for repetitive elements, and report here a total of 238 genetic variations, of which 129 have not been reported before.

Subjects and methods

Total genomic DNAs were isolated from peripheral leukocytes of 48 unrelated Japanese individuals by the standard phenol/chloroform extraction method, after informed consent was obtained from each participant. On the basis of sequence information from GenBank we designed polymerase chain reaction (PCR) primers to amplify DNA fragments from all six *SLC* genes, excluding repetitive elements, by invoking the REPEAT MASKER computer program (http://ftp.genome.washington.edu/cgi-bin/RepeatMasker). PCR experiments and DNA sequencing were performed according to methods described previously (Iida et al. 2001; Saito et al. 2001; Sekine et al. 2001). All SNPs detected by the PolyPhred computer program (Nickerson et al. 1997) were confirmed by sequencing both strands of each PCR product.

Results

Exon–intron boundaries were defined by comparison of genomic sequences with cDNA sequences; all accession numbers are listed in Table 1. We screened 96 Japanese chromosomes for SNPs in these *SLC* genes by means of direct DNA sequencing.

Subsequent resequencing of a total of about 109 kb of genomic DNA (13.2 kb for the *SLC10A1* gene, 23 kb for *SLC15A1*, 17 kb for *SLC22A1*, 13.4 kb for *SLC22A2*, 22.9 kb for *SLC22A4*, and 19 kb for *SLC22A5*) identified 213 SNPs and 25 insertion/deletion polymorphisms (Table 2). Figure 1a–f illustrates the location of each variation we found; detailed information on nucleotide positions and substitutions is summarized in Table 3a–f. On average, we identified 1 SNP in every 509 nucleotides. Of the 238 genetic variations identified in our screening (including insertion/deletion polymorphisms), 129 (54%) were not reported previously.

Among the 213 SNPs mapped in our experiments, 8 were located in 5′ flanking regions, 172 in introns, 25 in exons, and 8 in 3′ flanking regions (Table 4). Among the 25 SNPs detected in exons, 1 was located in a 5′UTR, 18 were in coding regions, and 6 were in 3′UTRs. Ten of the 18 SNPs detected in the coding regions would cause substitution of amino acids and 4 of those had not been reported before (Gly419Ala in *SLC15A1*, Pro283Leu and Arg287Gly in *SLC22A1*, and Gly462Glu in *SLC22A4*) (Table 5).

Table 1. Accession numbers for the genomic and cDNA sequences used in this study

Gene name	Chromosomal localization	Accession number		
		Genomic sequence		cDNA sequence
SLC10A1	14q24.1	AL157789.6		XM_007466.3
SLC15A1	13q33–q34	AL353574.8	AL391670.6	NM_005073.1
SLC22A1	6q26	AL353625.5		X98332.1
SLC22A2	6q26	AL162582.18		NM_003058.1
SLC22A4	5q31.1	AC008599.6		Y09881.1
SLC22A5	5q31	AC023861.3	AB016625.1	XM_003701.3

Table 2. Summary of genetic variations in six *SLC* genes

Gene	All genetic variations	SNPs	Insertion/deletion polymorphisms	Novel	Total base pairs sequenced (kb)	Frequency (bp/1SNP)
SLC10A1	18	14	4	15	13.2	943
SLC15A1	57	51	6	38	23.0	451
SLC22A1	33	29	4	22	17.0	586
SLC22A2	32	27	5	12	13.4	496
SLC22A4	58	54	4	30	22.9	424
SLC22A5	40	38	2	12	19.0	500
Total	238	213	25	129	108.5	(average) 509

SNP, Single-nucleotide polymorphism; SLC, solute carrier

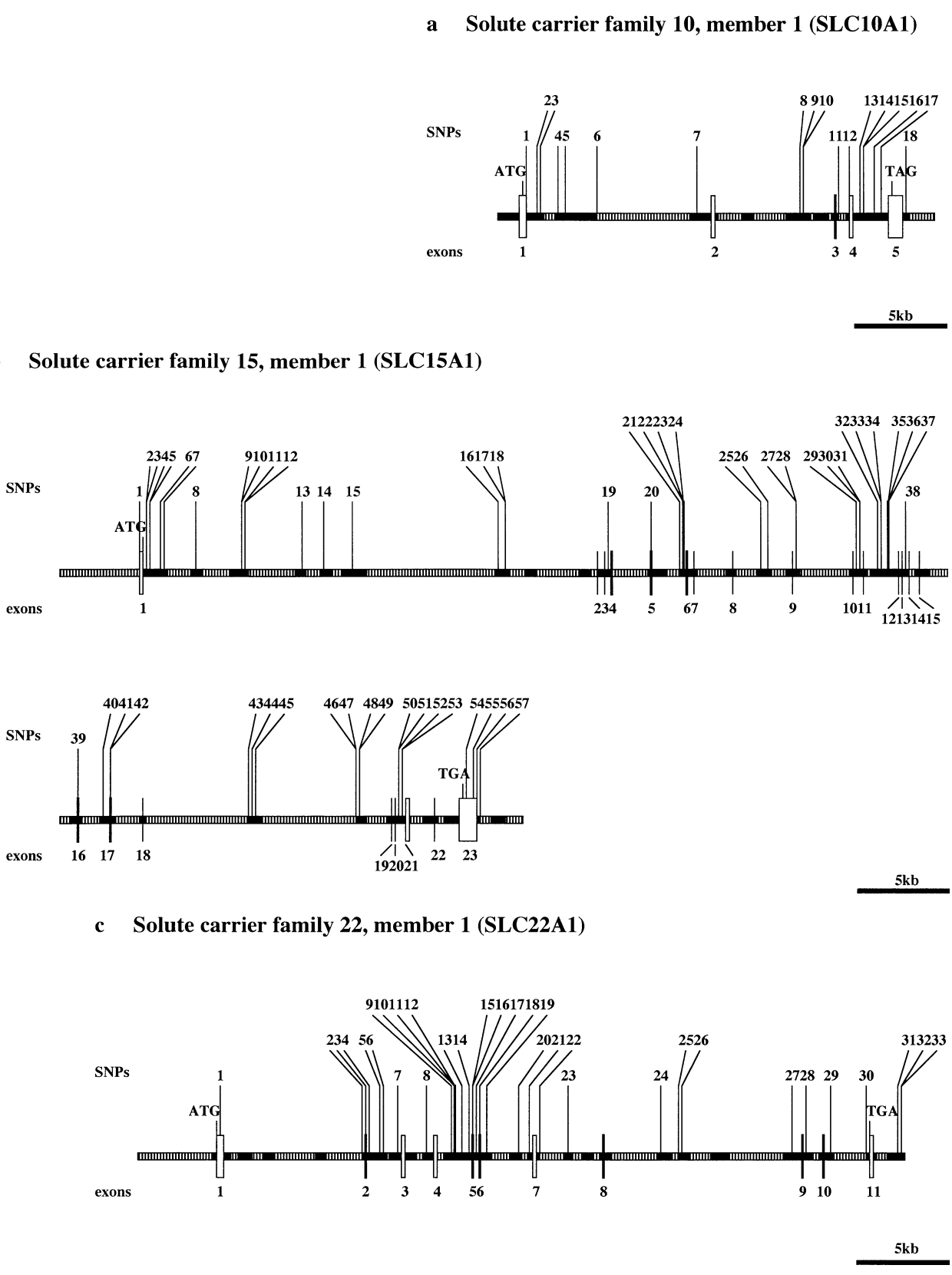
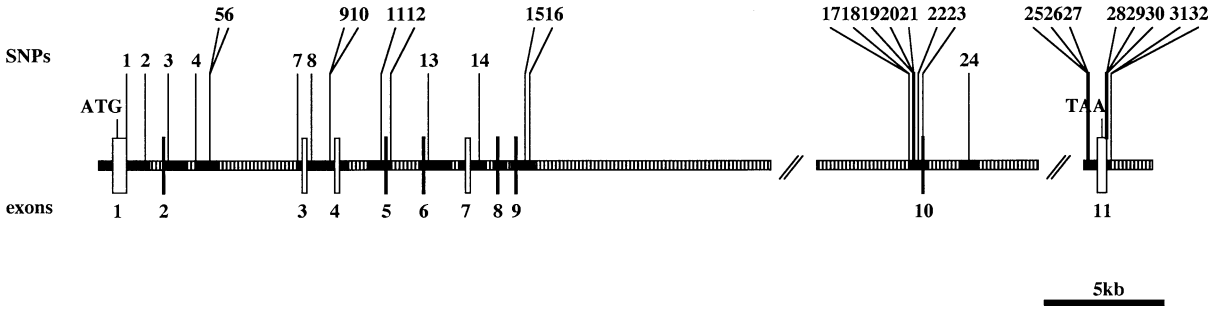
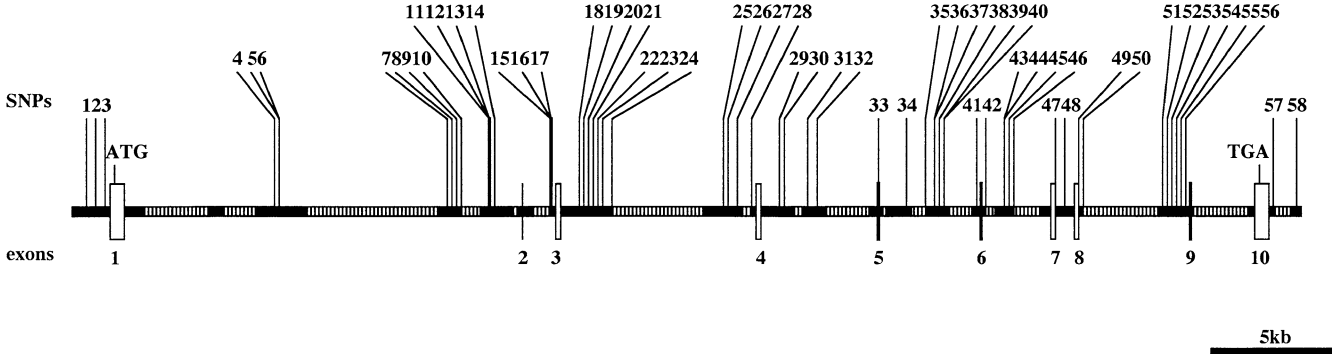


Fig. 1. Locations of single-nucleotide polymorphisms (SNPs) in the *SLC10A1* (**a**), *SLC15A1* (**b**), *SLC22A1* (**c**), *SLC22A2* (**d**), *SLC22A4* (**e**), and *SLC22A5* (**f**) genes, indicated by *vertical lines*. *Open boxes* represent exons; *hatching* on the chromosomes indicates unsequenced repetitive elements. *ATG*, initiation codon; *TGA*, *TAG*, or *TAA*, stop codons

d Solute carrier family 22, member 2 (SLC22A2)



e Solute carrier family 22, member 4 (SLC22A4)



f Solute carrier family 22, member 5 (SLC22A5)

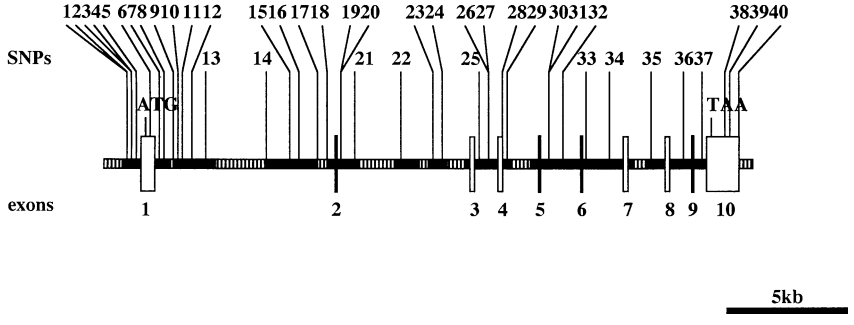


Fig. 1a–f. Continued

Table 3a. Summary of genetic variations detected in the *SLC10A1* gene

No.	Location	Position[a]	Genetic variation	NCBI SNP ID	No.	Location	Position[a]	Genetic variation	NCBI SNP ID
1	Exon 1	307	G/A(Thr75Thr)		10	Intron 2	5046	A/T	
2	Intron 1	607	G/C		11	Intron 3	(8–21)	$(T)_{12–15}$	
3	Intron 1	702	G/A		12	Exon 4	54	C/T(Ser267Phe)	rs2296651
4	Intron 1	2192	C/T	rs943277	13	Intron 4	(484–495)	$(A)_{10–13}$	
5	Intron 1	2587	C/T	rs943276	14	Intron 4	(728–754)	$(A)_{25–27}$	
6	Intron 1	(3950–3966)	$(T)_{14–17}$		15	Intron 4	747	A/C	
7	Intron 1	9597	C/G		16	Intron 4	1339	C/A	
8	Intron 2	4808	C/T		17	Intron 4	1545	G/C	
9	Intron 2	5032	G/C		18	3′ Flanking	559	G/A	

SLC10A1, Solute carrier family 10, member 1; NCBI, National Center for Biotechnology Information; UTR, untranslated region; del, deletion; ins, insertion

[a] For SNPs in the 5′ flanking region, intron, or 3′ flanking region, nucleotide positions are counted from the first intronic nucleotide at the exon/intron junction (for SNPs in the exon, nucleotide positions are counted from the first exonic nucleotide at the exon/intron junction)

Table 3b. Summary of genetic variations detected in the *SLC15A1* gene

No.	Location	Position[a]	Genetic variation	NCBI SNP ID	No.	Location	Position[a]	Genetic variation	NCBI SNP ID
1	Exon 1	25	C/T(5′UTR)		30	Intron 10	388	C/T	
2	Intron 1	88	G/A		31	Intron 10	457	A/G	rs1289393
3	Intron 1	106	A/T		32	Intron 11	720	G/A	rs1289392
4	Intron 1	248	G/A		33	Intron 11	985	C/T	
5	Intron 1	326	C/A		34	Intron 11	(1022–1045)	$(T)_{20–24}$	
6	Intron 1	1147	C/A	rs914300	35	Intron 11	1234	C/T	rs1892503
7	Intron 1	1238	C/T		36	Intron 11	1285	T/C	rs1289391
8	Intron 1	3001	C/T		37	Intron 11	1320	C/T	
9	Intron 1	5673	G/C		38	Intron 13	37	C/T	rs2297319
10	Intron 1	5679	C/G		39	Exon 16	107	G/C(Gly419Ala)	
11	Intron 1	5917	C/T		40	Intron 16	1414	T/C	rs1756988
12	Intron 1	5966	C/T		41	Exon 17	78	T/C(Ala449Ala)	rs1339067
13	Intron 1	9255	A/G		42	Exon 17	79	G/A(Val459Ile)	rs2274828
14	Intron 1	10278	A/G		43	Intron 18	6048	T/del	
15	Intron 1	11945	T/C	rs1331251	44	Intron 18	(6141–6142)	T/ins	
16	Intron 1	20251	C/T		45	Intron 18	(6241–6242)	G/ins	
17	Intron 1	20509	C/A		46	Intron 18	12102	C/T	
18	Intron 1	20532	T/C		47	Intron 18	12104	G/A	rs2802393
19	Intron 3	55	C/del		48	Intron 18	12203	C/A	
20	Exon 5	105	G/A(Ser117Asn)	rs2297322	49	Intron 18	12307	A/G	
21	Intron 5	1720	C/A		50	Intron 20	12	G/A	rs2297318
22	Intron 5	1790	G/A		51	Intron 20	79	A/G	
23	Intron 5	1860	G/A		52	Intron 20	417	C/T	rs950906
24	Intron 5	1943	G/A		53	Intron 20	465	A/G	rs950905
25	Intron 8	1478	A/G		54	Exon 23	(348–370)	$(T)_{18–23}$(3′UTR)	
26	Intron 8	1898	A/G		55	Exon 23	790	A/G(3′UTR)	
27	Intron 9	149	C/G	rs2297321	56	Exon 23	880	G/A(3′UTR)	rs1289389
28	Intron 9	221	G/A	rs2297320	57	3′ Flanking	2	G/A	
29	Intron 10	153	T/G	rs1289394					

SLC15A1, Solute carrier family 15, member 1

[a] For SNPs in the 5′ flanking region, intron, or 3′ flanking region, nucleotide positions are counted from the first intronic nucleotide at the exon/intron junction (for SNPs in the exon, nucleotide positions are counted from the first exonic nucleotide at the exon/intron junction)

Discussion

We identified 238 genetic variations (213 SNPs and 25 insertion/deletion polymorphisms) by screening the entire genomic regions, except for repetitive sequences, containing six *SLC* genes (*SLC10A1*, *SLC15A1*, *SLC22A1*, *SLC22A2*, *SLC22A4* and *SLC22A5*) in 96 chromosomes from 48 unrelated Japanese individuals. The polymorphisms published here should be useful for examining relationships between genotypes and susceptibilities to certain diseases or the efficacy or adverse effects of certain drugs.

The promoter region of the *SLC10A1* gene contains potential DNA-binding sites for transcription factors C/EBP and HNF3/HNF6 (Shiao et al. 2000). Although mutations at the C/EBP sites markedly reduce transcriptional activity (Shiao et al. 2000), we found no variations in this region in our test population.

Table 3c. Summary of genetic variations detected in the *SLC22A1* gene

No.	Location	Position[a]	Genetic variation	NCBI SNP ID	No.	Location	Position[a]	Genetic variation	NCBI SNP ID
1	Exon 1	228	T/C(Ser52Ser)	rs1867351	18	Exon 6	68	C/T(Pro341Leu)	rs2282143
2	Intron 1	7715	G/T		19	Intron 6	379	A/G	
3	Exon 2	69	C/G(Phe160Leu)	rs683369	20	Intron 6	2125	C/A	
4	Intron 2	97	G/A		21	Intron 6	(2935–2953)	$(T)_{18–20}$	
5	Intron 2	797	C/G		22	Intron 7	(6–7)	TGGTAAGT/ins	
6	Intron 2	1015	T/G	rs614890	23	Intron 7	(1780–1781)	T/ins	
7	Intron 2	1768	T/C		24	Intron 8	3247	G/T	
8	Intron 3	1244	C/T		25	Intron 8	4215	T/C	rs654993
9	Intron 4	865	G/T		26	Intron 8	4316	G/A	rs2197296
10	Intron 4	990	C/T	rs806383	27	Intron 8	10521	G/A	
11	Intron 4	1028	A/G		28	Intron 9	43	C/T	rs2297374
12	Intron 4	1040	T/G		29	Intron 10	393	G/C	
13	Intron 4	1485	C/T		30	Intron 10	2421	C/T	rs622591
14	Intron 4	1997	G/A		31	3′ Flanking	1627	G/A	rs651164
15	Exon 5	9	C/T(Pro283Leu)		32	3′ Flanking	1755	T/C	
16	Exon 5	20	C/G(Arg287Gly)		33	3′ Flanking	1799	G/del	
17	Intron 5	149	G/A	rs2282142					

SLC22A1, Solute carrier family 22, member 1
[a] For SNPs in the 5′ flanking region, intron, or 3′ flanking region, nucleotide positions are counted from the first intronic nucleotide at the exon/intron junction (for SNPs in the exon, nucleotide positions are counted from the first exonic nucleotide at the exon/intron junction)

Table 3d. Summary of genetic variations detected in the *SLC22A2* gene

No.	Location	Position[a]	Genetic variation	NCBI SNP ID	No.	Location	Position[a]	Genetic variation	NCBI SNP ID
1	Exon 1	534	G/T(Thr130Thr)	rs624249	17	Intron 9	−529	A/T	rs316006
2	Intron 1	883	A/C	rs638360	18	Intron 9	−444	G/A	rs316005
3	Intron 2	32	C/G	rs2774230	19	Intron 9	−396	A/G	
4	Intron 2	1329	G/del		20	Intron 9	−386	A/C	
5	Intron 2	1867	C/del		21	Intron 9	−337	A/C	rs316004
6	Intron 2	1882	G/A	rs316009	22	Intron 9	−86	A/del	
7	Intron 2	5909	C/A	rs152275	23	Exon 10	5	G/A(Val502Val)	rs316003
8	Intron 3	80	G/A	rs316016	24	Intron 10	1725	G/A	
9	Intron 3	1047	G/A	rs316017	25	Intron 10	−225	A/T	rs2450973
10	Intron 3	1086	C/T	rs316018	26	Intron 10	−215	C/T	rs2450974
11	Intron 4	1859	T/C	rs2279463	27	Intron 10	−195	C/T	
12	Intron 5	175	G/A	rs316021	28	Exon 11	328	T/del(3′UTR)	
13	Intron 6	115	G/C	rs167217	29	Exon 11	427	A/T(3′UTR)	
14	Intron 7	421	C/T	rs315993	30	Exon 11	455	G/A(3′UTR)	
15	Intron 9	(340–343)	CTCT/del		31	3′ Flanking	34	T/A	
16	Intron 9	363	T/G	rs315990	32	3′ Flanking	62	A/C	rs2450975

SLC22A2, Solute carrier family 22, member 2
[a] For SNPs in the 5′ flanking region, intron, or 3′ flanking region, nucleotide positions are counted from the first intronic nucleotide at the exon/intron junction (for SNPs in the exon, nucleotide positions are counted from the first exonic nucleotide at the exon/intron junction)

Among the four novel nonsynonymous polymorphisms, one, Gly419Ala in *SLC15A1*, was located in the large extracellular loop that carries potential *N*-glycosylation sites (Liang et al. 1995; Covitz et al. 1998). On the other hand, two polymorphisms in *SLC22A1*, Pro283Leu and Arg287Gly, were located in the intracellular loop that carries potential phosphorylation sites for protein kinase C (Zhang et al. 1997). The fourth, Gly462Glu, was located in a TMD of *SLC22A4*. Any of these four polymorphisms could have phenotypic consequences.

Comparison of amino acids in the four organic cation transporters (SLC22A1, SLC22A2, SLC22A4, and SLC22A5) revealed conservation of 4 cysteines (Cys), 13 prolines (Pro), 3 aspartic acids (Asp), 6 glutamic acids (Glu), and 7 arginines (Arg). These residues are thought to maintain secondary structures of proteins and/or bind charged substrates (Burckhardt and Wolff 2000). The two nonsynonymous SNPs in *SLC22A1*, Pro283Leu and Arg287Gly, involved conserved residues, suggesting that these polymorphisms could be associated with altered susceptibility to certain diseases.

All data for the genetic variations reported here are available through our website (http://snp.ims.u-tokyo.ac.jp/).

Table 3e. Summary of genetic variations detected in the *SLC22A4* gene

No.	Location	Position[a]	Genetic variation	NCBI SNP ID	No.	Location	Position[a]	Genetic variation	NCBI SNP ID
1	5′ Flanking	−987	A/G	rs162887	30	Intron 4	1055	G/A	
2	5′ Flanking	−380	C/G	rs460089	31	Intron 4	2071	G/C	rs273915
3	5′ Flanking	−90	G/C	rs460271	32	Intron 4	2383	A/T	rs273914
4	Intron 1	6602	C/T		33	Exon 5	93	C/T(Thr306Ile)	rs272893
5	Intron 1	6631	A/G	rs270612	34	Intron 5	(1197–1202)	ACAACA/del	
6	Intron 1	6790	C/T		35	Intron 5	(2071–2083)	$(T)_{11–13}$	
7	Intron 1	14019	G/A		36	Intron 5	2282	A/G	rs272889
8	Intron 1	14136	T/C		37	Intron 5	2327	C/T	rs272888
9	Intron 1	14266	G/T		38	Intron 5	2617	G/A	rs272887
10	Intron 1	14412	C/T		39	Intron 5	2744	T/C	rs272886
11	Intron 1	15776	G/A		40	Intron 5	2781	G/A	
12	Intron 1	15817	A/G		41	Intron 5	4257	A/G	rs273909
13	Intron 1	15889	G/A		42	Intron 6	5	G/A	rs2304081
14	Intron 1	16063	A/G		43	Intron 6	(882–917)	$(AC)_{15–18}$	
15	Intron 2	1105	C/A		44	Intron 6	924	A/C	
16	Intron 2	1229	A/G	rs270607	45	Intron 6	1111	G/C	rs272884
17	Intron 2	1265	G/A	rs2073838	46	Intron 6	1155	G/A	rs272883
18	Intron 3	784	C/T	rs2073839	47	Exon 7	136	C/G(Thr394Thr)	rs272879
19	Intron 3	1022	T/C		48	Intron 7	511	T/C	
20	Intron 3	1217	G/A		49	Exon 8	124	G/A(Gly462Glu)	
21	Intron 3	1406	A/G	rs270606	50	Intron 8	76	C/T	rs272878
22	Intron 3	1596	G/A		51	Intron 8	3514	G/A	
23	Intron 3	1720	G/A		52	Intron 8	3715	G/A	rs272873
24	Intron 3	2104	G/A		53	Intron 8	3902	T/C	
25	Intron 3	7056	A/G	rs272842	54	Intron 8	(4064–4089)	$(T)_{18–26}$	
26	Intron 3	7239	T/C	rs270602	55	Intron 8	4171	G/A	rs272872
27	Intron 3	7536	T/C	rs270601	56	Intron 8	4288	C/T	rs2306772
28	Intron 3	8323	G/C		57	3′ Flanking	115	T/A	
29	Intron 4	926	G/T		58	3′ Flanking	1177	G/A	rs272867

SLC22A4, Solute carrier family 22, member 4

[a] For SNPs in the 5′ flanking region, intron, or 3′ flanking region, nucleotide positions are counted from the first intronic nucleotide at the exon/intron junction (for SNPs in the exon, nucleotide positions are counted from the first exonic nucleotide at the exon/intron junction)

Table 3f. Summary of genetic variations detected in the *SLC22A5* gene

No.	Location	Position[a]	Genetic variation	NCBI SNP ID	No.	Location	Position[a]	Genetic variation	NCBI SNP ID
1	5′ Flanking	−225	C/T		21	Intron 2	608	C/A	
2	5′ Flanking	−178	G/C	rs2631369	22	Intron 2	2733	C/G	rs183898
3	5′ Flanking	−147	T/G	rs2631368	23	Intron 2	4037	C/G	rs274562
4	5′ Flanking	−124	G/T		24	Intron 2	4370	G/A	
5	5′ Flanking	−13	C/G		25	Intron 3	77	G/A	rs274559
6	Exon 1	506	C/T(Leu95Leu)	rs2631365	26	Intron 3	270	A/G	rs635620
7	Intron 1	232	G/A		27	Intron 3	272	G/A	rs635619
8	Intron 1	314	C/T		28	Exon 4	155	G/A(Leu269Leu)	rs274558
9	Intron 1	1048	G/A	rs2631363	29	Intron 4	13	C/T	rs274557
10	Intron 1	1246	A/G	rs2631362	30	Intron 5	445	T/C	rs2073643
11	Intron 1	1333	A/C	rs2631361	31	Intron 5	446	T/A	rs2073644
12	Intron 1	1845	C/T	rs2631359	32	Intron 5	969	C/T	
13	Intron 1	2488	C/A	rs671473	33	Intron 6	101	A/G	rs2073645
14	Intron 1	5055	G/A		34	Intron 6	1119	C/G	rs274553
15	Intron 1	6080	A/G	rs274571	35	Intron 7	1084	C/T	rs274551
16	Intron 1	6437	G/C		36	Intron 8	812	C/A	rs274549
17	Intron 1	7181	C/T	rs274570	37	Intron 9	188	T/C	rs2074610
18	Intron 1	7727	C/T	rs2073642	38	Exon 10	931	T/C(3′UTR)	rs274548
19	Intron 2	(173–174)	TC/del		39	Exon 10	(1028–1044)	$(T)_{16–18}$(3′UTR)	
20	Intron 2	239	T/C	rs274567	40	Exon 10	1428	T/A(3′UTR)	rs274547

SLC22A5, Solute carrier family 22, member 5

[a] For SNPs in the 5′ flanking region, intron, or 3′ flanking region, nucleotide positions are counted from the first intronic nucleotide at the exon/intron junction (for SNPs in the exon, nucleotide positions are counted from the first exonic nucleotide at the exon/intron junction)

Table 4. Number and regions of SNPs detected in six *SLC* genes

				Exon				
					Coding			
Gene	5′ Flanking	Intron	3′ Flanking	5′ UTR	Nonsynonymous	Synonymous	3′ UTR	Total
SLC10A1	0	11	1	0	1	1	0	14
SLC15A1	0	43	1	1	3	1	2	51
SLC22A1	0	22	2	0	4	1	0	29
SLC22A2	0	21	2	0	0	2	2	27
SLC22A4	3	46	2	0	2	1	0	54
SLC22A5	5	29	0	0	0	2	2	38
Total	8	172	8	1	10	8	6	213

UTR, untranslated region

Table 5. Novel SNPs detected in exons of six *SLC* genes

Region	Gene	Location	Position	SNP
5′ UTR	*SLC15A1*	Exon 1	25	C/T
Coding				
Nonsynonymous	*SLC15A1*	Exon 16	107	G/C(Gly419Ala)
	SLC22A1	Exon 5	9	C/T(Pro283Leu)
		Exon 5	20	C/G(Arg287Gly)
	SLC22A4	Exon 8	124	G/A(Gly462Glu)
Synonymous	*SLC10A1*	Exon 1	307	G/A(Thr75Thr)
3′ UTR	*SLC15A1*	Exon 23	790	A/G
	SLC22A2	Exon 11	427	A/T
		Exon 11	455	G/A

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