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Catalog of 178 variations in the Japanese population among eight human genes encoding G protein-coupled receptors (GPCRs)

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Abstract We screened DNAs from 48 Japanese individuals for single-nucleotide polymorphisms (SNPs) in eight genes encoding G protein-coupled receptors (GPCRs) by directly sequencing the entire relevant genomic regions except for repetitive-sequence elements. This approach identified 147 SNPs and 31 insertion/deletion polymorphisms among the eight *GPCR* genes. On average, we identified one SNP in every 584 nucleotides. Of the 147 SNPs, 69 were identified in *AGTR1*, 12 in *AGTR2*, nine in *AGTRL1*, 20 in *AVPR1A*, nine in *AVPR2*, 16 in *DRD1*, six in *ITGA2B*, and six in *PTGIR*. Twenty-one SNPs were located in 5' flanking regions, 76 in introns, 32 in exons, and 18 in 3' flanking regions. These variants should contribute to investigations of possible correlations between genotypes and phenotypes as regards susceptibility to disease or responsiveness to drug therapy.

Keywords Single-nucleotide polymorphism (SNP) · *AGTR* · *AVPR* · *DRD1* · *ITGA2B* · *PTGIR* · G protein-coupled receptor (GPCR)

Introduction

Polymorphic sites within genes encoding G protein-coupled receptor (GPCRs) may yield possible correla-

tions between genotypes and disease-susceptibility phenotypes or responsiveness to drug therapy (Rana et al. 2001). A number of investigators have already reported numerous polymorphisms in all domains of many *GPCR* genes (Rana et al. 2001; Small et al. 2003). Eight *GPCR* genes selected for the work reported here are described in the following paragraphs:

- Angiotensin II receptors types 1 and 2 (*AGTR1* and *AGTR2* respectively), mediated by the renin-angiotensin system, play important roles in cardiovascular pathophysiology (Wagenaar et al. 2002) and are considered the most important receptors in that context (Whitebread et al. 1989). Stimulation of *AGTR1* leads to physiological effects such as vasoconstriction, inflammation, and proliferation – all of those processes being involved in cardiovascular disease (Griendling et al. 1996; Wagenaar et al. 2002). A polymorphism in the 3' untranslated region (UTR) of the *AGTR1* gene has been associated with increased risk of essential hypertension (Bonnardeaux et al. 1994; Hingorani et al. 1995; Wang et al. 1997; Kainulainen et al. 1999). For its part, *AGTR2* not only plays a role in cardiovascular functions (Hein et al. 1995) but also mediates programmed cell death (Yamada et al. 1996). Mutations in *AGTR2* cause X-linked mental retardation (Vervoort et al. 2002).
- Angiotensin receptor-like 1 (*AGTRL1*), also known as APJ, was originally isolated from human genomic DNA by polymerase chain reactions (O'Dowd et al. 1993).
- Arginine vasopressin receptor 1A (*AVPR1A*) mediates contraction and proliferation of cells, aggregation of platelets, and lysis of glycogen (Jard 1983). A number of investigators have examined potential associations of *AVPR1A* genotypes with altered susceptibility to essential hypertension (Thibonnier et al. 2000) and autism (Kim et al. 2002).
- Arginine vasopressin receptor 2 (*AVPR2*) mediates antidiuretic effects (Jard 1983). Mutations in the *AVPR2* gene are responsible for X-linked congenital

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nephrogenic diabetes insipidus (Bichet et al. 1997; Oksche and Rosenthal 1998; Morello and Bichet 2001; Rana et al. 2001).

- Dopamine receptor D1 (*DRD1*) regulates growth and differentiation of neurons (Lankford et al. 1988), and mediates several behavioral responses (Clark and White 1987). A number of investigators have examined potential associations of *DRD1* genotypes with altered susceptibilities to psychiatric diseases (Liu et al. 1995; Cichon et al. 1996; Kojima et al. 1999), drug addiction (Comings et al. 1997), alcoholism (Heinz et al. 1996; Hietala et al. 1997), and essential hypertension (Sato et al. 2000).
- Integrin alpha 2b (*ITGA2B*), also called platelet glycoprotein IIb, plays a key role in platelet aggregation (French and Seligsohn 2000). Mutations in the *ITGA2B* gene cause Glanzmann's thrombasthenia, an autosomal recessive disorder of platelets [Glanzmann Thrombasthenia Database (<http://med.mssm.edu/glanzmannndb/>)].
- Prostaglandin I2 receptor (*PTGIR*), also known as prostacyclin receptor, plays important roles in relaxation of vascular smooth muscle and in preventing blood coagulation (Smyth and FitzGerald 2002). A polymorphism (Arg212His) associated with impaired binding and activation of this receptor has been reported (Stitham et al. 2002).

To investigate in detail the nature of apparent genotype/phenotype correlations involving the eight genes described above, we began by searching for additional SNPs in their promoter regions, exons, and introns (except for repetitive elements), and report here a total of 178 genetic variations among 96 Japanese chromosomes, of which 97 had 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 protein-coupled receptor (PCR) primers to amplify DNA fragments from all eight *GPCR* 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 and discussion

Exon-intron boundaries in eight selected *GPCR* genes 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 genes by means of direct DNA sequencing.

Subsequent re-sequencing of about 86 kilobases (kb) of genomic DNA (34.4 kb for the *AGTR1* gene, 7.9 kb for *AGTR2*, 5.7 kb for *AGTRL1*, 9.8 kb for *AVPRIA*, 6.0 kb for *AVPR2*, 6.8 kb for *DRD1*, 11.0 kb for *ITGA2B*, and 4.2 kb for *PTGIR*) identified 147 SNPs and 31 insertion/deletion polymorphisms (Table 2). Fig. 1a–h documents the location of each variation we found; detailed information about nucleotide positions and substitutions is summarized in Table 3, 4, 5, 6, 7, 8, 9, and 10. On average, we identified one SNP in every 584 nucleotides. Of the 178 genetic variations identified by our screening procedures, including insertion/

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

Gene name	Chromosomal localization	Accession number	
		Genomic sequence	cDNA sequence
<i>AGTR1</i>	3q21-q25	AC024897.23	NM_000685.3 NM_009585.2 NM_004835.2 NM_031850.1 NM_032049.1 NM_000686.2
<i>AGTR2</i>	Xq22-q23	AC069480.2	U03642.1
<i>AGTRL1</i>	11q12	AP001786.4	XM_006934.3
<i>AVPRIA</i>	12q14-q15	AC025525.3	NM_000054.2
<i>AVPR2</i>	Xq28	U52112.1	X55760.1
<i>DRD1</i>	5q35.1	AC091393.1	XM_045985.1
<i>ITGA2B</i>	17q21.32	AC019152.5	XM_028273.1
<i>PTGIR</i>	19q13.3	AC025983.3	

Table 2 Summary of genetic variations in eight G protein-coupled receptor (*GPCR*) genes. SNP single-nucleotide polymorphism

Gene	All genetic variations	SNPs	Insertion/deletion polymorphisms	Novel	Total base pairs sequenced (kb)	Frequency (bp/1SNP)
<i>AGTR1</i>	84	69	15	45	34.4	499
<i>AGTR2</i>	15	12	3	8	7.9	658
<i>AGTRL1</i>	12	9	3	7	5.7	633
<i>AVPRIA</i>	25	20	5	18	9.8	490
<i>AVPR2</i>	9	9	0	4	6.0	667
<i>DRD1</i>	17	16	1	10	6.8	425
<i>ITGA2B</i>	9	6	3	3	11.0	1833
<i>PTGIR</i>	7	6	1	2	4.2	700
Total	178	147	31	97	85.8	(average) 584

Fig. 1 Locations of single-nucleotide polymorphisms (SNPs) in the *AGTR1* (a), *AGTR2* (b), *AGTRL1* (c), *AVPR1A* (d), *AVPR2* (e), *DRD1* (f), *ITGA2B* (g), and *PTGIR* (h) genes (vertical lines). Open boxes, exons; hatching, unsequenced regions of repetitive elements; ATG, initiation codons; TGA, TAG, and TAA, stop codons

Table 3 Summary of genetic variations detected in the *AGTR1* gene. *AGTR* angiotensin receptor 1, *NCBI* National Center for Biotechnology Information, *SNP* single nucleotide polymorphism, *UTR* untranslated region, *del* deletion, *ins* insertion

No.	Location	Position ^a	Genetic variation	NCBI SNP ID
1	5' Flanking	-(283–274)	(A) _{9–11}	
2	Intron 1	868	T/C	
3	Intron 1	(869–871)	(T) _{2–4}	
4	Intron 1	1128	G/C	rs2640539
5	Intron 1	(1457–1460)	TAAG/del	
6	Intron 1	1642	C/G	
7	Intron 1	2037	T/C	
8	Intron 1	2254	T/C	rs3772633
9	Intron 1	3279	T/C	rs2638363
10	Intron 1	4602	C/T	rs2638362
11	Intron 1	(7313–7314)	CTTT/ins	
12	Intron 1	7480	G/A	
13	Intron 1	(8087–8095)	(T) _{8–9}	
14	Intron 1	8229	G/A	rs2131127
15	Intron 1	9042	T/A	rs1964102
16	Intron 1	9464	A/G	rs1964102
17	Intron 1	(9485–9497)	TAGACATTTCTTA/del/GTAGC/ins	
18	Exon 2	(25–28)	(A) _{4–5} (5'UTR)	
19	Intron 2	59	A/G	rs2276736
20	Intron 2	174	G/A	rs2276735
21	Intron 2	353	T/C	
22	Intron 2	658	T/C	rs3772630
23	Intron 2	747	C/T	rs3772629
24	Intron 2	1082	T/G	
25	Intron 2	(1144–1145)	TG/del	
26	Intron 2	1220	T/C	
27	Intron 2	1317	G/T	rs3821499
28	Intron 2	1528	G/T	rs3772628
29	Intron 2	2542	A/G	rs2638360
30	Intron 2	4314	G/A	
31	Intron 2	4432	G/C	
32	Intron 2	4440	A/G	
33	Intron 2	4953	A/G	rs931490
34	Intron 2	(5294–5311)	(AT) _{8–9}	
35	Intron 2	6760	A/C	rs4681444
36	Intron 2	6778	T/C	rs3772626
37	Intron 2	6918	A/G	rs3772625
38	Intron 2	7150	A/G	rs1492103
39	Intron 2	7186	C/T	rs1492102
40	Intron 2	7852	A/G	
41	Intron 2	7972	C/G	rs3772623
42	Intron 2	8819	G/T	
43	Intron 2	8886	A/C	rs4681446
44	Intron 2	9698	C/T	rs718858
45	Intron 2	9939	T/C	rs3772622
46	Intron 2	10392	C/T	rs909383
47	Intron 2	10494	C/T	rs3772620
48	Intron 2	10643	A/T	rs731252
49	Intron 2	(11267–11275)	(T) _{8–10}	
50	Intron 2	12010	A/T	
51	Intron 2	(12243–12256)	(CA) _{6–7}	
52	Intron 2	12377	C/T	rs3772616
53	Intron 2	(12691–12695)	GTTAC/del	
54	Intron 2	15806	G/A	
55	Intron 2	18823	G/A	
56	Intron 2	21150	G/A	
57	Intron 2	21942	A/G	
58	Intron 3	1132	G/C	rs385338
59	Intron 3	3115	C/T	
60	Intron 3	3213	C/T	
61	Intron 3	3323	T/G	
62	Intron 3	4569	G/A	rs3772615
63	Intron 3	4604	C/T	rs3772614
64	Intron 3	4685	T/C	rs3772613
65	Intron 3	4838	A/C	rs3772612
66	Intron 3	4876	G/C	rs3772611

Table 3 (Continued)

No.	Location	Position ^a	Genetic variation	NCBI SNP ID
67	Intron 3	4994	C/G	rs275649
68	Intron 3	5094	A/G	
69	Intron 3	5222	C/T	
70	Intron 3	5302	G/A	
71	Intron 3	5458	A/G	
72	Intron 3	5789	T/del	
73	Intron 3	6065	A/G	
74	Intron 3	6794	G/C	
75	Intron 3	6994	G/T	
76	Intron 3	7175	C/A	
77	Exon 4	56	T/C(5'UTR)	rs1800766
78	Exon 5	620	T/C(Leu191Leu) ^b	
79	Exon 5	1213	A/C(3'UTR) ^b	
80	Exon 5	1831	A/G(3'UTR)	
81	Exon 5	1925	A/G(3'UTR) ^b	
82	Exon 5	(1930–1931)	AT/ins(3'UTR)	rs5182 rs5185
83	3' Flanking	(454–455)	AT/del	
84	3' Flanking	511	T/C	

^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)

^b SNPs previously reported by Bonnardeaux et al. (1994)

Table 4 Summary of genetic variations detected in the *AGTR2* gene. *AGTR2* angiotensin receptor 2, *NCBI* National Center for Biotechnology Information, *SNP* single nucleotide polymorphism

No.	Location	Position ^a	Genetic variation	NCBI SNP ID
1	5' Flanking	–151	T/C	rs1403543 rs3736556
2	5' Flanking	–125	G/C	
3	5' Flanking	–(122–114)	(A) _{8–9}	
4	Intron 1	123	G/A	
5	Intron 2	55	A/T	
6	Intron 2	(209–219)	(T) _{10–12}	rs5193 rs5194
7	Intron 2	(1122–1130)	(T) _{8–9}	
8	Exon 3	1326	G/T(3'UTR)	
9	Exon 3	1332	G/A(3'UTR)	rs5950587 rs1546754
10	Exon 3	1628	A/C(3'UTR) ^b	
11	3' Flanking	424	G/T	
12	3' Flanking	531	C/G	
13	3' Flanking	634	T/C	
14	3' Flanking	1611	C/T	
15	3' Flanking	1929	C/T	

^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)

^b SNP previously reported by Katsuya et al. (1997)

deletion polymorphisms, 97 (54%) had not been reported previously.

Among the 147 SNPs mapped in our experiments, 21 were located in 5' flanking regions, 76 in introns, 32 in exons, and 18 in 3' flanking regions (Table 11). Among the 32 SNPs detected in exons, six were located in 5'UTRs, 13 in coding regions, and 13 in 3'UTRs. Four of the 13 SNPs detected in coding regions would cause substitution of amino acids, and two of those had not been reported before (Gly250Glu in *AVPR2*, and Ala128Thr in *PTGIR*) (Table 12).

Table 5 Summary of genetic variations detected in the *AGTRL1* gene. *AGTRL1* angiotensin receptor-like 1, *NCBI* National Center for Biotechnology Information, *SNP* single nucleotide polymorphism

No.	Location	Position ^a	Genetic variation	NCBI SNP ID
1	5' Flanking	–(1796–1813)	(T) _{11–18}	rs948847 rs746886 rs2282625 rs2282624 rs2282623
2	5' Flanking	–1433	A/T	
3	5' Flanking	–1176	C/T	
4	5' Flanking	–799	G/A	
5	5' Flanking	–279	G/A	
6	5' Flanking	–(47–55)	(A) _{8–9}	
7	Exon 1	445	A/C(Gly45Gly)	
8	Intron 1	(1045–1048)	GTGT/del	
9	Intron 1	1155	C/T	
10	Intron 1	1338	C/T	
11	Intron 1	1355	G/A	
12	Intron 1	1440	G/A	

^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)

Because *AGTRL1* is expressed in vascular smooth-muscle cells and regulates vasoconstriction in response to angiotensin II, a number of investigators have examined potential associations of *AGTRL1* genotypes with altered susceptibility to essential hypertension (Duncan et al. 2001). A polymorphism in the 3'UTR of this gene has been associated with increased risk of essential hypertension (Bonnardeaux et al. 1994; Hingorani et al. 1995; Wang et al. 1997; Kainulainen et al. 1999). However, other investigators have been unable to confirm the association between this variant and hypertension (Schmidt et al. 1997; Takami et al. 1998; Kikuya et al. 2003; Ono et al. 2003). Our results

Table 6 Summary of genetic variations detected in the *AVPR1A* gene. *AVPR1A* arginine vasopressin receptor 1A, *NCBI* National Center for Biotechnology Information, *SNP* single nucleotide polymorphism

No.	Location	Position ^a	Genetic variation	NCBI SNP ID
1	5' Flanking	-1058	C/T	rs3759292
2	5' Flanking	-723	T/C	
3	5' Flanking	-649	A/G	
4	Exon 1	(16–21)	(T) _{6–7} (5'UTR)	rs3021528
5	Exon 1	605	T/G(5'UTR) ^b	
6	Exon 1	911	C/T(5'UTR) ^b	
7	Exon 1	1733	C/T(5'UTR)	rs3741865
8	Exon 1	2382	C/T(Phe136Phe) ^b	rs1042615
9	Intron 1	(40–67)	(GT) _{13–15} ^c	rs3803107
10	Intron 1	462	A/G	
11	Intron 1	1295	C/T	
12	Intron 1	1509	A/G	rs3803107
13	Intron 1	1933	T/A	
14	Exon 2	592	C/T(3'UTR)	
15	Exon 2	950	G/T(3'UTR)	rs3803107
16	Exon 2	1130	C/T(3'UTR)	
17	Exon 2	1131	G/A(3'UTR)	
18	3' Flanking	523	T/C	rs3803107
19	3' Flanking	(800–812)	(T) _{11–13}	
20	3' Flanking	1453	A/del	
21	3' Flanking	1570	C/G	rs3803107
22	3' Flanking	1758	C/T	
23	3' Flanking	1941	A/G	
24	3' Flanking	2094	T/G	rs3803107
25	3' Flanking	(2320–2326)	(A) _{6–7}	

^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)

^b SNPs previously reported by Kim et al. (2002)

^c SNP previously reported by Thibonnier et al. (2000)

Table 7 Summary of genetic variations detected in the *AVPR2* gene. *AVPR2* arginine vasopressin receptor 2, *NCBI* National Center for Biotechnology Information, *SNP* single nucleotide polymorphism

No.	Location	Position ^a	Genetic variation	NCBI SNP ID
1	5' Flanking	-2680	G/A	rs4898458
2	5' Flanking	-2216	G/A	rs4898372
3	5' Flanking	-15	A/C	
4	Exon 2	10	G/A(Gly12Glu)	
5	Exon 2	724	G/A(Gly250Glu)	rs5201
6	Exon 3	17	G/A(Leu309Leu) ^b	
7	Exon 3	83	C/T(Ser331Ser)	
8	3' Flanking	643	C/T	rs5202
9	3' Flanking	1335	C/T	

^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)

^b SNP previously reported by Pan et al. (1992)

should contribute to a better understanding of ethnic differences that might influence correlations between genotypes and phenotypes with respect to susceptibility to hypertension.

Table 8 Summary of genetic variations detected in the *DRD1* gene. *DRD1* dopamine receptor D1, *NCBI* National Center for Biotechnology Information, *SNP* single nucleotide polymorphism

No.	Location	Position ^a	Genetic variation	NCBI SNP ID
1	5' Flanking	-1942	T/C	rs265981
2	5' Flanking	-1826	C/A	
3	5' Flanking	-1754	T/C	
4	5' Flanking	-976	G/C	rs5326
5	5' Flanking	-524	C/T	
6	Exon 1	183	G/A(5'UTR) ^b	
7	Exon 1	229	G/A(5'UTR) ^b	rs4532
8	Exon 1	474	G/A(Leu66Leu) ^c	rs1799914
9	Exon 1	1679	T/C(3'UTR) ^b	rs686
10	Exon 1	2480	A/G(3'UTR)	rs4867798
11	Exon 1	3210	G/A(3'UTR)	
12	3' Flanking	(112–120)	(T) _{8–9}	rs703748
13	3' Flanking	126	A/G	
14	3' Flanking	505	C/T	
15	3' Flanking	748	C/T	rs703748
16	3' Flanking	955	A/C	
17	3' Flanking	1010	C/A	

^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)

^b SNPs previously reported by Cichon et al. (1994)

^c SNP previously reported by Liu et al. (1995)

Table 9 Summary of genetic variations detected in the *ITGA2B* gene. *ITGA2B* integrin, alpha 2b, *NCBI* National Center for Biotechnology Information, *SNP* single nucleotide polymorphism

No.	Location	Position ^a	Genetic variation	NCBI SNP ID
1	5' Flanking	-931	A/T	rs3760364
2	Intron 20	138	T/del	rs850730
3	Intron 21	(34–35)	CAGGGGCTC/ins	
4	Intron 21	594	G/C	
5	Intron 22	107	G/A	rs850731
6	Intron 22	134	A/G	rs850732
7	Intron 22	(397–407)	(A) _{10–11}	rs5911
8	Exon 26	20	T/G(Ile874Ser)	
9	Exon 30	3	T/C(Val1021Val)	

^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 10 Summary of genetic variations detected in the *PTGIR* gene. *PTGIR* prostaglandin I2 receptor, *NCBI* National Center for Biotechnology Information, *SNP* single nucleotide polymorphism

No.	Location	Position ^a	Genetic variation	NCBI SNP ID
1	5' Flanking	-1390	G/A	rs3760759
2	5' Flanking	-(1326–1327)	CCT/ins	rs3760758
3	5' Flanking	-1241	A/G	
4	5' Flanking	-1238	T/C	
5	Exon 2	171	G/C(Val53Val)	rs2229128
6	Exon 2	394	G/A(Ala128Thr)	rs2229129
7	Exon 3	216	A/C(Ser328Ser)	

^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 11 Number and regions of single nucleotide polymorphisms (SNPs) detected in eight *GPCR* genes. *GPCR* G protein-coupled receptor, *UTR* untranslated region

Gene	5' Flanking	Intron	3' Flanking	Exon				Total
				5'UTR	Coding		3'UTR	
					Nonsynonymous	Synonymous		
<i>AGTR1</i>	0	63	1	1	0	1	3	69
<i>AGTR2</i>	2	2	5	0	0	0	3	12
<i>AGTRL1</i>	4	4	0	0	0	1	0	9
<i>AVPR1A</i>	3	4	5	3	0	1	4	20
<i>AVPR2</i>	3	0	2	0	2	2	0	9
<i>DRD1</i>	5	0	5	2	0	1	3	16
<i>ITGA2B</i>	1	3	0	0	1	1	0	6
<i>PTGIR</i>	3	0	0	0	1	2	0	6
Total	21	76	18	6	4	9	13	147

Table 12 Novel single nucleotide polymorphisms (SNPs) detected in Exon s in eight *GPCR* genes. *GPCR* G protein-coupled receptor, *UTR* untranslated region

Region		Gene	Location	Position	SNP
Coding	Nonsynonymous	<i>AVPR2</i>	Exon 2	724	G/A(Gly250Glu)
		<i>PTGIR</i>	Exon 2	394	G/A(Ala128Thr)
3'UTR		<i>AGTR1</i>	Exon 5	1831	A/G
		<i>AVPR1A</i>	Exon 2	950	G/T
			Exon 2	1130	C/T
			Exon 2	1131	G/A
		<i>DRD1</i>	Exon 1	3210	G/A

DRD1 mediates several behavioral responses (Clark and White 1987). Although potential correlations between *DRD1* genotypes and disease susceptibilities have been investigated extensively (Liu et al. 1995; Cichon et al. 1994; Heinz et al. 1996; Comings et al. 1997; Hietala et al. 1997; Kojima et al. 1999; Sato et al. 2000), no conclusive results have emerged as yet.

Our screening experiments detected two novel nonsynonymous polymorphisms (Gly250Glu in *AVPR2*, and Ala128Thr in *PTGIR*). As both were located in cytoplasmic domains, these polymorphisms could have phenotypic consequences (Birnbauer et al. 1992; Boie et al. 1994; Stitham et al. 2003). These and other polymorphisms published herein may have significant value for researchers who wish to examine relationships between *GPCR* genotypes and susceptibilities to certain diseases.

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