

Genome-wide gene expression profiles of clear cell renal cell carcinoma: Identification of molecular targets for treatment of renal cell carcinoma

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Abstract. In order to clarify the molecular mechanism involved in renal carcinogenesis, and to identify molecular targets for diagnosis and treatment, we analyzed genome-wide gene expression profiles of 15 surgical specimens of clear cell renal cell carcinoma (RCC), compared to normal renal cortex, using a combination of laser microbeam microdissection (LMM) with a cDNA microarray representing 27,648 genes. We identified 257 genes that were commonly up-regulated and 721 genes that were down-regulated in RCCs. None of top 24 up-regulated genes that showed most significant differences in informative RCC-cases were included in previous reports describing expression profiles of RCC using RNAs isolated from bulk tissues. These findings suggest that it is important to purify as much as possible the populations of cancerous and normal epithelial cells obtained from surgical specimens. Among the significantly-transactivated genes, we focused on Semaphorin 5B (*SEMA5B*) and knocked-down its expression in RCC cells by small-interfering RNA (siRNA). Effective down-regulation of its expression levels in RCC cells significantly attenuated RCC cell viability. In conclusion, our data should be helpful for a better understanding of the tumorigenesis of RCC and should contribute to the development of diagnostic tumor markers and molecular-targeting therapy for patients with RCC.

Introduction

Renal cell carcinoma (RCC) accounts for approximately 3% of all malignancies (1). At present, renal cell carcinoma at an early stage can be curable by surgical resection, which is the most effective treatment for localized RCC tumors. However, no effective treatment option is available to patients at an advanced stage because this disease is usually resistant to both chemotherapy and radiotherapy. The proportion of the patients showing good response to chemotherapy alone is 4-6% (2). Although immunotherapy is also available, the response rate is limited to 10-15% and severe adverse reactions are often observed; for example, about 14% of the cases with metastatic RCC respond to a single treatment of interferon- α (3). Hence, no significant improvement of overall prognosis of patients with this disease has been observed.

The prognosis of RCC is influenced most significantly by tumor stage and histological grade (2-6). At present the diagnosis of RCC is made by imaging tools such as ultrasonography and computed tomography, but any tumor markers specific to RCC are not yet available in general clinical practice for diagnosis. Histopathologically, RCC is considered to be a mixture of heterogeneous diseases and constitutes from various distinct histological types such as clear cell (70%), papillary (15-20%), chromophobe (4-6%), collecting duct (<1%) and unclassified (4-5%) (7).

We chose the most predominant type, clear cell renal cell carcinoma (ccRCC), for this study and performed genome-wide expression profile analysis of ccRCC. We studied the gene expression profiles of 15 ccRCC cells using cDNA microarrays consisting of 27,648 genes in a combination with laser microbeam microdissection technology to collect pure populations of ccRCC cells as well as non-cancerous renal cortex cells. Genome-wide gene expression profiles of tumors can provide comprehensive information of molecular mechanism underlying renal carcinogenesis, and possibly lead to find molecular tumor markers that are applicable for earlier diagnosis and also serve as targets for development of novel effective therapies.

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Patients and methods

Patients, tissue samples and RCC cell lines. Tissue samples of surgically-resected RCC and their corresponding clinical information were obtained from patients with written informed consent at three hospitals participating in this study, Juntendo University School of Medicine, Kochi Medical School, and Kyoto Prefectural University of Medicine. Total of 15 cancer patients (6 women and 9 men; median age, 66; range, 36-75 years; Table I) who had been confirmed histologically with ccRCC were selected for this study. Clinical stage of each patient was judged according to the Union International Centre Cancer tumor-node-metastasis classification. Two to three pieces of cancer tissue had been taken from each patient at the time of radical nephrectomy. Normal tissue was obtained from the distant region from cancer area in the resected kidney tissue. These samples were immediately embedded in TissueTek OCT compound (Sakura, Tokyo, Japan), frozen, and stored at -80°C . The frozen tissues were sliced into $8\text{-}\mu\text{m}$ sections using a cryostat (Sakura) and then stained with H&E for histological examination. The human renal cell carcinoma (RCC) cell lines, Caki-1, Caki-2, 786-O, A-498, ACHN, 769-P, and A-704 were purchased from American Type Culture Collection (ATCC; Rockville, MD). OS-RC-2, TUHR10TKB, and TUHR14TKB were provided by the RIKEN Bio-Resource Center (Tsukuba, Japan). RXF-631L was gifted from Dr Takao Yamori, Div. of Molecular Pharmacology, Cancer Chemotherapy Center, Japanese Foundation for Cancer Research (Tokyo, Japan). All cells were grown in monolayers in appropriate medium supplemented with 10% (A-704; 15%) fetal bovine serum (Cansera International, Ontario, Canada) and 1% antibiotic/antimycotic solution (Sigma-Aldrich). Cells were maintained at 37°C in atmosphere of humidified air with 5% CO_2 . Normal human renal proximal tubule epithelial cells (RPTEC) were grown in optimized medium purchased from Cambrex Bio Science, Inc. (Walkersville, MD).

Laser microbeam microdissection, extraction of RNA and T7-based RNA amplification. Preparation of sections, laser microbeam microdissection (LMM), extraction of total RNA, T7-based amplification, and labeling of probes were performed as described previously (8). Like many solid tumors, RCCs contain other cell types in addition to carcinoma cells. Especially, ccRCC is generally well vascularized, and infiltrating immune cells are frequently seen on histological sections. To obtain precise gene expression profiles of cancer cells, we used LMM technology to collect pure populations of ccRCC cells as well as non-cancerous renal cortex. A mixture of normal renal cortex cells in kidney tissues from 11 patients was prepared as a universal control. To guarantee the quality of RNAs, total RNA extracted from adjacent frozen tissue of each case were electrophoresed on a denaturing agarose gel, and the quality was validated by the presence of rRNA bands. We labeled $2.5\ \mu\text{g}$ aliquots of RNA amplified by the T7-RNA amplification method from each cancerous or non-cancerous tissue sample, respectively, with Cy5-dCTP or Cy3-dCTP (Amersham Biosciences, Buckinghamshire, UK).

cDNA microarray and analysis of data. The procedures for hybridization, washing, scanning (detection of signals), and

Table I. Clinicopathological features of ccRCC clinical samples used for cDNA microarray analysis.

No.	Age	Sex	pT	Grade
1	57	M	1b	G2
2	70	M	2	G2
3	68	M	1a	G2
4	73	F	1b	G3>G2
5	54	M	1b	G2
6	71	F	1a	G1
7	69	F	3a	G2>G3
8	47	F	1b	G2>G3
9	75	M	3a	G2
10	41	M	1a	G1
11	54	F	2	G2>G1
12	74	F	3a	G2
13	66	M	1b	G2
14	62	M	1a	G2
15	36	M	1a	G2

normalization of data were carried out as previously described (9). We fabricated a genome-wide cDNA microarray containing 27,648 cDNAs selected from the UniGene Database of the National Center for Biotechnology Information. We quantified the signal intensities of Cy3 and Cy5 from the 27,648 spots and analyzed the signals by substituting backgrounds, using ArrayVision software (Imaging Research, Inc., St. Catharines, Ontario, Canada). Subsequently, the fluorescence intensities of Cy5 (RCC tumor) and Cy3 (control) for each target spot were adjusted so that the mean Cy5/Cy3 ratio of the 52 house-keeping genes became one. Because data derived from low-signal intensities are less reliable, we determined a cut-off value on each slide, and we excluded genes from further analysis when both the Cy3 and the Cy5 dyes yielded signal intensities lower than that of the cut-off. For other genes, we calculated the Cy5/Cy3 ratio using the raw data of each sample. After leaving out the unreliable spots, we selected up-regulated or down-regulated genes based on their Cy5/Cy3 ratios (r): up-regulated ($r > 5.0$) and down-regulated ($r < 0.2$).

Identification of genes that were up- or down-regulated commonly from normal renal cortex to RCC. We defined genes, that revealed altered expression in ccRCCs according to the following criteria: a) genes for which we were able to obtain expression data $>50\%$ of the cases examined; and b) genes whose expression ratio was >5.0 or <0.2 in $>50\%$ of informative cases.

Semi-quantitative reverse transcription-PCR. RNAs from the purified populations of ccRCC cells and from normal renal cortex cells were extracted using RNeasy Micro Kits (Qiagen, Valencia, CA) and were treated with DNase I according to the recommendation of the manufacturer. Extracted RNAs were subjected to two rounds of RNA amplification using

Table II. Primer sequences for semi-quantitative RT-PCR experiments.

Gene	Forward primer	Reverse primer
<i>FDFT1</i>	5'-AGTCAAATGCAGGTGAGAAGAAG-3'	5'-TCATTCTAGCCAGGATCATACTAAG-3'
<i>SEMA5B</i>	5'-TGACCTGTGCTTAGAAGTCCTTT-3'	5'-GTGTGTGTTTCTGAACAGATGAA-3'
<i>ADORA3</i>	5'-CCTGAAGGGTGCCTAGTTGA-3'	5'-ACTCAAAAACATCCACAGGTGA-3'
<i>SLC1A3</i>	5'-GGCTGTGGTGCAGTAACCAT-3'	5'-CATCTACAAAAGTAATGCTTCCCAGT-3'
<i>STC2</i>	5'-TCCCTCACGTTATTGGAAGC-3'	5'-TCCACATCCTTCTCAAAGG-3'
<i>ENPP3</i>	5'-ATGATGGCCATTTTGTATGCT-3'	5'-GCTCTCCACGTTGGTAGGTC-3'
<i>VWF</i>	5'-CACCAATGGCTCTGTTGTGT-3'	5'-TAAGAGCTCAGCCTTTATTGTGG-3'
<i>NNMT</i>	5'-GCTACTACATGATTGGTGAGCAG-3'	5'-CTTTAATTGAGGTACAGGCATC-3'

Table III. Sequences of specific double-stranded oligonucleotides inserted into siRNA expression vector.

psi-U6BX-SEMA5B#1 (non-silencing)	5'-CACCCGTAAACAGCATCGCGGCTTTCAAGAGAAGCCGCGATGCTGTTTACG-3'
	5'-AAAACGTAAACAGCATCGCGGCTTCTCTTGAAGCCGCGATGCTGTTTACG-3'
psi-U6BX-SEMA5B#2	5'-CACCGCAGCAACGTTGCAGCACATTCAAGAGATGTGCTGCAACGTTGCTGC-3'
	5'-AAAAGCAGCAACGTTGCAGCACATCTCTTGAATGTGCTGCAACGTTGCTGC-3'
psi-U6BX-Mock	5'-CACCGTGTCTTCAAGCTTGAAGACTA-3'
	5'-AAAATAGTCTTCAAGCTTGAAGACAC-3'
psi-U6BX-Scramble	5'-CACCGCGCGCTTTGTAGGATTCGTTCAAGAGACGAATCCTACAAAAGCGCGC-3'
	5'-AAAAGCGCGCTTTGTAGGATTCGTTCTTGAACGAATCCTACAAAAGCGCGC-3'

T7-based *in vitro* transcription (Epicentre Technologies, Madison, WI), and amplified RNAs were reverse transcribed to single-stranded cDNAs using random primer with Superscript II reverse transcriptase (Invitrogen, Carlsbad, CA). We prepared appropriate dilutions of each single-stranded cDNA for subsequent PCR amplification and monitored their reactions using Farnesyl-diphosphate farnesyl-transferase 1 (*FDFT1*) as a quantitative control because this showed the smallest Cy5/Cy3 fluctuations in our RCC-microarray data. PCR amplification was performed using single-strand cDNAs as templates and gene specific primers (Table II). To examine the expression level of SEMA5BV1 and SEMA5BV2 in RCC cells, we performed RT-PCR experiments using the following primer sets: 5'-CTGGAAACAGCAGCCAGAG-3' and 5'-CAGTGCTGGCAAGACAGGTA-3'. PCR reactions were optimized for the number of cycles to ensure product intensity within the logarithmic phase of amplification.

Northern blot analysis. For Northern blot analysis, a 1 μ g aliquot of each mRNA isolated using mRNA Purification Kit (Amersham Biosciences) and human normal-tissue polyA(+) RNAs (Clontech, Palo Alto, CA) were separated on a 1% denaturing agarose gel and transferred to a nylon membrane.

Human multiple tissue northern (MTN) blots (BD Biosciences, Palo Alto, CA) as well as our own RCC blots containing mRNA from 11 RCC cell lines (Caki-1, Caki-2, 786-O, A-498, ACHN, 769-P, A-704, RXF-631L, OS-RC-2, TUHR10TKB, and TUHR14TKB), four normal organs (heart, lung, liver and kidney) and normal renal proximal tubule epithelial cells (RPTEC), were hybridized for 16 h with a ³²P-labeled PCR product of *SEMA5B* cDNA. The cDNA probes of *SEMA5B* were prepared by RT-PCR using the primers 5'-CTGTGGA CCTACTGGGCATT-3' and 5'-GTGTGTGTTTCTGAACA GATGAA-3'. Pre-hybridization, hybridization and washing were performed according to the supplier's recommendations. The blots were autoradiographed with intensifying screens at -80°C for 14 days.

Effect of small-interfering RNA on growth of RCC cells. To evaluate the biological functions of *SEMA5B* in RCC cells, we used a psi-U6BX3.0 vector for expression of short-hairpin RNA against the target gene, as described previously (10). The U6 promoter was cloned upstream of the gene-specific sequence (19-nucleotide sequence from the target transcript, separated from the reverse complement of the same sequence by a short spacer, TTCAAGAGA), with five thymidines as a

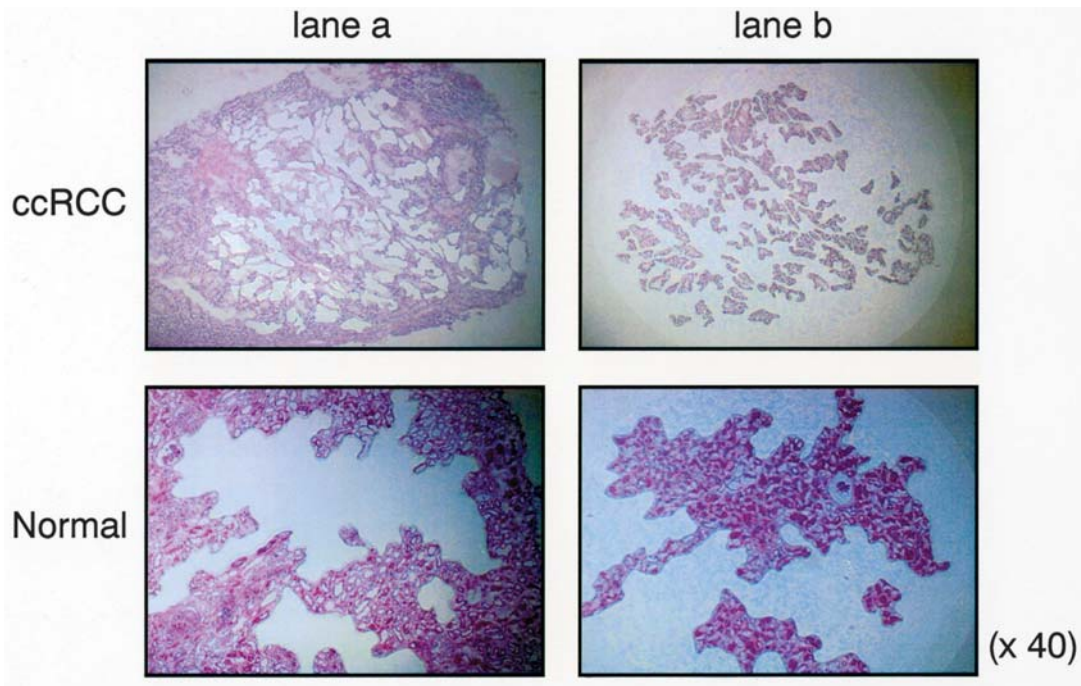


Figure 1. Purified cells by laser microbeam microdissection. Normal renal cortex cells (Normal), clear cell renal cell carcinoma cells (ccRCC) from single specimen were microdissected from H&E stained sections. Lane a, post microdissected tissue; lane b, microdissected cells.

termination signal and a neo-cassette for selection by Geneticin (Sigma). Plasmids designed to express small interfering RNA (siRNA) were prepared by cloning of double-stranded oligonucleotides into psi-U6BX vector (Table III). Human RCC cell line, OS-RC-2, which express *SEMA5B* at a high level, were plated onto 10-cm dishes (1×10^6 cells per dish), and transfected with psiU6BX vectors that included the target sequences for scramble sequences, *SEMA5B* using Lipofectamine 2000 (Invitrogen). The transfected OS-RC-2 cells were selected in medium containing 0.7 mg/ml of neomycin (Geneticin; Gibco BRL, Carlsbad, CA). Next, total RNA was extracted from the cells at 5 days after Geneticin selection, and then the knockdown effect of siRNAs was examined by a semi-quantitative RT-PCR using specific primer sets: forward, 5'-AACTTAGAGGTGGGAGCAG-3' and reverse, 5'-CACAACCATGCCTTACTTTATC-3' as an internal control, and 5'-TGACCTGTGCTTAGAAGTCCTTT-3' and 5'-CTGTGTGTTCTGAAACAGATGAA-3' for *SEMA5B*. In 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay, cell viability was evaluated using Cell-counting kit-8 (DOJINDO, Kumamoto, Japan) at 7 or 14 days after the transfection according to the protocol of the supplier. After 21 days of the incubation, these cells were fixed with 4% paraformaldehyde, and stained with Giemsa solution for colony formation assay.

Results

Identification of commonly up-regulated or down-regulated genes in ccRCCs. We carried out LMM to purify cancer cells from tumor tissue and also normal renal cortex cells as controls (Fig. 1), and performed gene expression analysis using cDNA microarray consisting of 27,648 cDNA sequences. We then selected genes from our data set according to the criteria that the Cy5/Cy3 ratio of a given gene was >5.0 in $>50\%$ of

informative cases (see Materials and methods). Using this filter, we identified 257 genes that were commonly up-regulated in ccRCC compared with normal renal cortex cells (Table IV). Among them, the biological functions of 182 genes were already known to some extent. Of them, *HIG2* (hypoxia inducible gene 2), *NNMT* (nicotinamide N-methyltransferase), *IGFBP3* (insulin-like growth factor binding protein 3), *VEGF* (vascular endothelial growth factor), and *VWF* (Von Willebrand factor) had already been reported as genes involved in renal tumorigenesis (11-15), supporting the high quality of our microarray data. The up-regulated genes represented a variety of functions including genes associated with signal-transduction pathways (*ADORA3*, *EDA2R*), or genes involved in various metabolic pathways (*SCD*, *ENPP3*), transport systems (*SLC1A3*, *ABCG1*), angiogenesis (*VEGF*), apoptosis (*FTS*), and cell adhesion (*CDH2*). In particular, 92 of the up-regulated genes were expressed at a level >10 -fold higher than in normal cortex cells; for example, *ADORA3* (adenosine A3 receptor), *SLC1A3* (solute carrier family 1, member 3) and *STC2* (stanniocalcin 2) were up-regulated >10 -fold in $>90\%$ of the informative cases.

We also identified 721 genes whose expression ratios were <0.2 in $\geq 50\%$ of the informative ccRCCs (Table V). Among these down-regulated genes, 532 genes had been functionally characterized to some extent. They included *WT1* (Wilms tumors 1), *CDKN1C* (cyclin-dependent kinase inhibitor 1C), and *GAS1* (growth arrest-specific 1), which have been implicated in growth suppression or apoptosis (16-19). In particular, *WT1* and *CDKN1C* were significantly down-regulated in all the 15 RCC cases, and *GAS1* was also significantly down-regulated in 14 of 15 cases, indicating down-regulation of those genes may be related to RCC-tumorigenesis.

To further validate the expression data obtained by RCC-microarray analysis, we performed semi-quantitative RT-PCR

Table IV. Genes commonly up-regulated in RCCs.

Accession no.	Symbol	Gene name	>5-fold/ present	Present	>5-fold
NM_000677	ADORA3	Adenosine A3 receptor	1.00	13	13
NM_001445	FABP6	Fatty acid binding protein 6, ileal (gastrotropin)	1.00	13	13
AF070609	SLC1A3	DKFZP547J0410 protein	1.00	12	12
AA868809	CHC1L	Chromosome condensation 1-like	1.00	12	12
AF195765	RAMP	RA-regulated nuclear matrix-associated protein	1.00	12	12
AK027663	STC2	Stanniocalcin 2	1.00	11	11
AK023320	FTS	Fused toes homolog (mouse)	1.00	11	11
AK024965	DAB2	Disabled homolog 2, mitogen-responsive phosphoprotein (Drosophila)	1.00	11	11
BM685969	HIG2	Hypoxia-inducible protein 2	1.00	11	11
AA342991		Similar to polyadenylate-binding protein 4 (Poly(A)-binding protein 4) (PABP 4) (inducible poly(A)-binding protein) (iPABP) (Activated-platelet protein-1) (APP-1)	1.00	11	11
AA442590	ENPP3	Ectonucleotide pyrophosphatase/phosphodiesterase 3	1.00	11	11
AA128378	KIAA0303	Microtubule associated serine/threonine kinase family member 4	1.00	10	10
AK022473	FTO	Fatso	1.00	10	10
NM_001003927	EVI2A	Ecotropic viral integration site 2A	1.00	10	10
NM_001884	HAPLN1	Hyaluronan and proteoglycan link protein 1	1.00	9	9
AA156409	MCPH1	Microcephaly, primary autosomal recessive 1	1.00	9	9
AI142832	MGC34923	Hypothetical protein MGC34923	1.00	9	9
N24715		Full length insert cDNA clone YX74D05	1.00	9	9
AA258620	PLXNC1	Plexin C1	1.00	9	9
AK021778	PTPRK	Protein tyrosine phosphatase, receptor type, K	1.00	9	9
W57613		Transcribed locus, weakly similar to NP_062553.1 hypothetical protein FLJ11267 [Homo sapiens]	1.00	9	9
M31165	TNFAIP6	Tumor necrosis factor, alpha-induced protein 6	1.00	9	9
BM992179	CYB5	Cytochrome b-5	1.00	8	8
CR749811		Similar to hypothetical protein MGC38937	1.00	8	8
AK023507	CMKOR1	Chemokine orphan receptor 1	0.92	13	12
U78556	CRA (MTMR11)	Cisplatin resistance associated	0.92	12	11
NM_005505	SCARB1	Scavenger receptor class B, member 1	0.91	11	10
AI821270	DARS	Aspartyl-tRNA synthetase	0.91	11	10
BU736022	FABP7	Fatty acid binding protein 7, brain	0.91	11	10
AI741514	ALPK2	Alpha-kinase 2	0.91	11	10
H87865	RFP2	Ret finger protein 2	0.91	11	10
AK025204	ABI3BP	ABI gene family, member 3 (NESH) binding protein	0.91	11	10
AF013249	LAIR1	Leukocyte-associated Ig-like receptor 1	0.90	10	9
BX112530	TLK1	Tousled-like kinase 1	0.90	10	9
AL832259	LOC284749	Hypothetical protein LOC284749	0.90	10	9
AF430643	GBP5	Guanylate binding protein 5	0.90	10	9
R38549	LOC150271	Hypothetical LOC388889	0.89	9	8
AK126261		Similar to RIKEN cDNA E030024N20 gene	0.89	9	8
BU622474		Similar to D(1B) dopamine receptor (D(5) dopamine receptor) (D1beta dopamine receptor)	0.89	9	8
BF115786	ZCCHC11	Zinc finger, CCHC domain containing 11	0.88	8	7
W86513		Transcribed locus, weakly similar to XP_517256.1 UDP glycosyltransferase 2 family, polypeptide B4 [Pan troglodytes]	0.88	8	7
R77952	PSMA3	Proteasome (prosome, macropain) subunit, alpha type, 3	0.88	8	7
BC008718	BIRC5	Baculoviral IAP repeat-containing 5 (survivin)	0.88	8	7
AK001149	FLJ10287	Hypothetical protein FLJ10287	0.88	8	7
AL832281	LOC340351	Hypothetical protein LOC340351	0.88	8	7
AK021954	NRCAM	Neuronal cell adhesion molecule	0.88	8	7
AI368204	ENPP3	Ectonucleotide pyrophosphatase/phosphodiesterase 3	0.86	14	12
BC034919	EDA2R	Ectodysplasin A2 receptor	0.85	13	11
BQ949386	FCGR1A	Fc fragment of IgG, high affinity Ia, receptor for (CD64)	0.83	12	10
BC033746	PNCK	Pregnancy upregulated non-ubiquitously expressed CaM kinase	0.83	12	10

Table IV. Continued.

Accession no.	Symbol	Gene name	>5-fold/ present	Present	>5-fold
AI023320		Hypothetical LOC387790	0.83	12	10
H88362	EHBP1	EH domain binding protein 1	0.83	12	10
AK123603	FLJ12443	Hypothetical protein FLJ12443	0.82	11	9
BC050423	TMEM22	Transmembrane protein 22	0.82	11	9
AA827683		Transcribed locus, moderately similar to NP_775735.1 l(3)mbt-like 4 (Drosophila) [Homo sapiens]	0.82	11	9
NM_002193	INHBB	Inhibin, beta B (activin AB beta polypeptide)	0.80	15	12
NM_005063	SCD	Stearoyl-CoA desaturase (delta-9-desaturase)	0.80	15	12
AY048757	ABCG1	ATP-binding cassette, sub-family G (WHITE), member 1	0.80	15	12
NM_005428	VAV1	Vav 1 oncogene	0.80	10	8
CR608325	PLA2G7	Phospholipase A2, group VII (platelet-activating factor acetylhydrolase, plasma)	0.80	10	8
BC036680	FBXL16	F-box and leucine-rich repeat protein 16	0.80	10	8
BU742664		Full length insert cDNA clone ZE12B03	0.80	10	8
BQ007156		Transcribed locus	0.80	10	8
N49962	BCL2	B-cell CLL/lymphoma 2	0.79	14	11
AK090411	RGPR	Regucalcin gene promotor region related protein	0.79	14	11
AA872040	INHBB	Inhibin, beta B (activin AB beta polypeptide)	0.79	14	11
NM_018685	ANLN	Anillin, actin binding protein (scraps homolog, Drosophila)	0.78	9	7
BC047724	C10orf128	Chromosome 10 open reading frame 128	0.78	9	7
BX648468	DKFZP564J0863	DKFZP564J0863 protein	0.78	9	7
AA282540	OSBPL8	Oxysterol binding protein-like 8	0.78	9	7
NM_019043	APBB1IP	Amyloid beta (A4) precursor protein-binding, family B, member 1 interacting protein	0.78	9	7
AA826148	NRCAM	Neuronal cell adhesion molecule	0.78	9	7
BC015050	OIP5	Opa-interacting protein 5	0.78	9	7
NM_000878	IL2RB	Interleukin 2 receptor, beta	0.78	9	7
U79242	GRM5	Glutamate receptor, metabotropic 5	0.78	9	7
AB018345	KIAA0802	KIAA0802	0.77	13	10
XM_058513	LRRK2	Leucine-rich repeat kinase 2	0.77	13	10
U29171	CSNK1D	Casein kinase 1, delta	0.75	12	9
BM665350	AIG1	Androgen-induced 1	0.75	12	9
N46844		CDNA: FLJ20892 fis, clone ADKA03430	0.75	12	9
NM_178229	IQGAP3	IQ motif containing GTPase activating protein 3	0.75	12	9
BX641066	KLF8	Kruppel-like factor 8	0.75	8	6
NM_003042	SLC6A1	Solute carrier family 6 (neurotransmitter transporter, GABA), member 1	0.75	8	6
AA781195	PRAME	Preferentially expressed antigen in melanoma	0.75	8	6
BC033490	LOC285016	Hypothetical protein LOC285016	0.75	8	6
X57548	CDH2	Cadherin 2, type 1, N-cadherin (neuronal)	0.73	15	11
BC002536	PFKP	Phosphofructokinase, platelet	0.73	15	11
NM_000552	VWF	Von Willebrand factor	0.73	15	11
NM_021201	MS4A7	Membrane-spanning 4-domains, subfamily A, member 7	0.73	15	11
BC036661	CMKOR1	Chemokine orphan receptor 1	0.73	15	11
H03641	FAM13A1	Family with sequence similarity 13, member A1	0.73	15	11
BC000234	NNMT	Nicotinamide N-methyltransferase	0.73	15	11
AA187749	PFKP	Phosphofructokinase, platelet	0.73	15	11
BU625507	SLC16A3	Solute carrier family 16 (monocarboxylic acid transporters), member 3	0.73	15	11
AI074524	LRRK2	Leucine-rich repeat kinase 2	0.73	15	11
BC065522	VEGF	Vascular endothelial growth factor	0.73	15	11
AL137588	ZNF395	Zinc finger protein 395	0.73	15	11
AW978675	GNRH1	Gonadotropin-releasing hormone 1 (lutetizing-releasing hormone)	0.73	11	8
BC024278	LOC255326	Hypothetical protein LOC255326	0.73	11	8
AA907927	MDS009	X 009 protein	0.73	11	8
AL080215	TFPI	Tissue factor pathway inhibitor (lipoprotein-associated coagulation inhibitor)	0.73	11	8
AA653431		Transcribed locus	0.71	14	10
NM_022349	MS4A6A	Membrane-spanning 4-domains, subfamily A, member 6A	0.71	14	10

Table IV. Continued.

Accession no.	Symbol	Gene name	>5-fold/ present	Present	>5-fold present
CA429220	SKP2	S-phase kinase-associated protein 2 (p45)	0.71	14	10
NM_018092	NETO2	Neuropilin (NRP) and tolloid (TLL)-like 2	0.71	14	10
AY358124	SEMA5B	Sema domain, seven thrombospondin repeats (type 1 and type 1-like), transmembrane domain (TM) and short cytoplasmic domain (semaphorin) 5B	0.71	14	10
R78576	COG6	Component of oligomeric golgi complex 6	0.70	10	7
Y18046	FGFR1OP	FGFR1 oncogene partner	0.70	10	7
XM_496823		Similar to RIKEN cDNA A630077B13 gene; RIKEN cDNA 2810048G17	0.70	10	7
AK026403	TLN2	Talin 2	0.70	10	7
AA570186		Hypothetical gene supported by AK096951; BC066547	0.69	13	9
H88117	DKFZP564J102	DKFZP564J102 protein	0.69	13	9
AL832896	CAPN12	Calpain 12	0.69	13	9
BC045651	P2RY5	Purinergic receptor P2Y, G-protein coupled, 5	0.67	15	10
BC000013	IGFBP3	Insulin-like growth factor binding protein 3	0.67	15	10
NM_002133	HMOX1	Heme oxygenase (decycling) 1	0.67	15	10
R55185	IRX3	Iroquois homeobox protein 3	0.67	15	10
BC007372	TRIM52	Tripartite motif-containing 52	0.67	15	10
T79802		MRNA full length insert cDNA clone EUROIMAGE 1534000	0.67	15	10
NM_052947	ALPK2	Alpha-kinase 2	0.67	15	10
N91945	KIAA0746	KIAA0746 protein	0.67	15	10
AL162079	SLC16A1	Solute carrier family 16 (monocarboxylic acid transporters), member 1	0.67	15	10
U88878	TLR2	Toll-like receptor 2	0.67	15	10
AK021624	C5orf13	Chromosome 5 open reading frame 13	0.67	15	10
BQ268701			0.67	12	8
BC009924	NPTX2	Neuronal pentraxin II	0.67	12	8
BC037568	EOMES	Eomesodermin homolog (<i>Xenopus laevis</i>)	0.67	12	8
AK091335	MARCH-I	Membrane-associated RING-CH protein I	0.67	12	8
R60655	RNF32	Ring finger protein 32	0.67	9	6
AK023966		CDNA FLJ13904 fis, clone THYRO1001895	0.67	9	6
AK090397	MGC15875	Hypothetical protein MGC15875	0.67	9	6
AK022173	LAF4	Lymphoid nuclear protein related to AF4	0.67	9	6
AA766314	RASSF6	Ras association (RalGDS/AF-6) domain family 6	0.64	14	9
AA159605		Transcribed locus	0.64	14	9
L06797	CXCR4	Chemokine (C-X-C motif) receptor 4	0.64	11	7
AA971400	MGC47816	Hypothetical protein MGC47816	0.64	11	7
AF376061	CARD12	Caspase recruitment domain family, member 12	0.64	11	7
Z11502	ANXA13	Annexin A13	0.63	8	5
AB011123	TNIK	TRAF2 and NCK interacting kinase	0.63	8	5
BG196354		Transcribed locus	0.63	8	5
AK124752	PCDH21	Protocadherin 21	0.63	8	5
BU191922	FLJ23861	Hypothetical protein FLJ23861	0.63	8	5
AA938691		Transcribed locus	0.63	8	5
BQ709650		Transcribed locus	0.63	8	5
NM_000560	CD53	CD53 antigen	0.62	13	8
M13699	CP	Ceruloplasmin (ferroxidase)	0.62	13	8
D87448	TOPBP1	Topoisomerase (DNA) II binding protein 1	0.62	13	8
M24486	P4HA1	Procollagen-proline, 2-oxoglutarate 4-dioxygenase (proline 4-hydroxylase) alpha polypeptide I	0.60	15	9
J04162	FCGR3B	Fc fragment of IgG, low affinity IIIb, receptor for (CD16)	0.60	15	9
AF059617	PLK2	Polo-like kinase 2 (<i>Drosophila</i>)	0.60	15	9
BC000013	IGFBP3	Insulin-like growth factor binding protein 3	0.60	15	9
M73554	CCND1	Cyclin D1 (PRAD1: parathyroid adenomatosis 1)	0.60	15	9
M15395	ITGB2	Integrin, beta 2 (antigen CD18 (p95), lymphocyte function-associated antigen 1; macrophage antigen 1 (mac-1) beta subunit)	0.60	15	9
NM_000292	PHKA2	Phosphorylase kinase, alpha 2 (liver)	0.60	15	9
K02765	C3	Complement component 3	0.60	15	9

Table IV. Continued.

Accession no.	Symbol	Gene name	>5-fold/ present	Present	>5-fold
BM991954		Transcribed locus, weakly similar to XP_311626.1 <i>Anopheles gambiae</i> str. PEST ENSANGG00000020300 gene	0.60	15	9
AK057151		CDNA FLJ32589 fis, clone SPLEN2000443	0.60	15	9
AK124656	ENO2	Enolase 2 (gamma, neuronal)	0.60	15	9
BQ448718	CDC2L6	Cell division cycle 2-like 6 (CDK8-like)	0.60	15	9
AY260577	C14orf58	Chromosome 14 open reading frame 58	0.60	15	9
BC005832	KIAA0101	KIAA0101	0.60	15	9
NM_002610	PDK1	Pyruvate dehydrogenase kinase, isoenzyme 1	0.60	15	9
Z22970	CD163	CD163 antigen	0.60	15	9
AB058765	KIAA1862	KIAA1862 protein	0.60	15	9
M81141	HLA-DQB1	Major histocompatibility complex, class II, DQ beta 1	0.60	15	9
BM988473	CCND1	Cyclin D1 (PRAD1: parathyroid adenomatosis 1)	0.60	15	9
H83622	COMMD10	COMM domain containing 10	0.60	15	9
AW976457	MBNL1	Muscleblind-like (<i>Drosophila</i>)	0.60	15	9
AK025273	EGLN3	Egl nine homolog 3 (<i>C. elegans</i>)	0.60	15	9
U57962	CG018	Hypothetical gene CG018	0.60	15	9
L11932	SHMT2	Serine hydroxymethyltransferase 2 (mitochondrial)	0.60	10	6
AA398762	PHKA2	Phosphorylase kinase, alpha 2 (liver)	0.60	10	6
AA632745		Transcribed locus	0.60	10	6
AK096712	FLJ11850	Hypothetical protein FLJ11850	0.60	10	6
NM_013448	BAZ1A	Bromodomain adjacent to zinc finger domain, 1A	0.60	10	6
BX482647	PARP14	Poly(ADP-ribose) polymerase family, member 14	0.60	10	6
BC035802	GZMK	Granzyme K (serine protease, granzyme 3; tryptase II)	0.58	12	7
AA398096	PFKFB4	6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 4	0.58	12	7
AI290343	STC2	Stanniocalcin 2	0.58	12	7
BC065544	C14orf106	Chromosome 14 open reading frame 106	0.58	12	7
BM724257	PLEKHM2	Pleckstrin homology domain containing, family M (with RUN domain) member 2	0.58	12	7
NM_002664	PLEK	Pleckstrin	0.57	14	8
AA521342	DDX31	DEAD (Asp-Glu-Ala-Asp) box polypeptide 31	0.57	14	8
AK123519	ARHGAP26	Rho GTPase activating protein 26	0.57	14	8
BG621779	EGFR	Epidermal growth factor receptor (erythroblastic leukemia viral (v-erb-b) oncogene homolog, avian)	0.57	14	8
BX392279		Transcribed locus, strongly similar to XP_496781.1 transposon-derived Buster3 transposase-like [<i>Homo sapiens</i>]	0.57	14	8
CR599886	ADSL	Adenylosuccinate lyase	0.57	14	8
AI015709		Transcribed locus	0.57	14	8
AA831021	CLK4	CDC-like kinase 4	0.57	14	8
NM_004932	CDH6	Cadherin 6, type 2, K-cadherin (fetal kidney)	0.57	14	8
BM464532	HIST1H1C	Histone 1, H1c	0.56	9	5
AY358175	GBGT1	Globoside alpha-1,3-N-acetylgalactosaminyltransferase 1	0.56	9	5
AF146761	SLAMF8	SLAM family member 8	0.56	9	5
BQ025155	C10orf9	Chromosome 10 open reading frame 9	0.56	9	5
AK026746	C14orf140	Chromosome 14 open reading frame 140	0.56	9	5
AB020701	SORBS1	Sorbin and SH3 domain containing 1	0.56	9	5
S60415	CACNB2	Calcium channel, voltage-dependent, beta 2 subunit	0.55	11	6
BC084567	POLS	Polymerase (DNA directed) sigma	0.55	11	6
W60419	POLI	Polymerase (DNA directed) iota	0.55	11	6
H60869			0.55	11	6
BX537890	KLF7	Kruppel-like factor 7 (ubiquitous)	0.55	11	6
AI076475		Hypothetical gene supported by AK026189	0.55	11	6
BX484485	MLL3	B melanoma antigen family, member 4	0.55	11	6
AK021481	GPC6	Glypican 6	0.55	11	6
AK026747	LOC54103	Hypothetical protein LOC54103	0.55	11	6
BM662950	FCER1G	Fc fragment of IgE, high affinity I, receptor for; gamma polypeptide	0.54	13	7
N22318	LRCH1	Leucine-rich repeats and calponin homology (CH) domain containing 1	0.54	13	7

Table IV. Continued.

Accession no.	Symbol	Gene name	>5-fold/ present	Present	>5-fold
N51406	FLJ14503	Hypothetical protein FLJ14503	0.54	13	7
AL832660	C7orf29	Chromosome 7 open reading frame 29	0.54	13	7
AK021801		CDNA FLJ11739 fis, clone HEMBA1005497	0.54	13	7
AK024900	AP2B1	Adaptor-related protein complex 2, beta 1 subunit	0.54	13	7
AB002367	DCAMKL1	Doublecortin and CaM kinase-like 1	0.54	13	7
M57730	EFNA1	Ephrin-A1	0.53	15	8
U63917	GPR30	G protein-coupled receptor 30	0.53	15	8
BQ027924	SLC15A4	Solute carrier family 15, member 4	0.53	15	8
BX648117	ZNF6	Zinc finger protein 6 (CMPX1)	0.53	15	8
AA811043	RNASET2	Ribonuclease T2	0.53	15	8
T40467	MAPRE2	Microtubule-associated protein, RP/EB family, member 2	0.53	15	8
R27957	FCHO2	FCH domain only 2	0.53	15	8
NM_024830	FLJ12443	Hypothetical protein FLJ12443	0.53	15	8
CR600491	NOL3	Nucleolar protein 3 (apoptosis repressor with CARD domain)	0.53	15	8
AB002365	KIAA0367	KIAA0367	0.53	15	8
AL049987	FLJ40092	FLJ40092 protein	0.53	15	8
AK022479	HDHD1A	Haloacid dehalogenase-like hydrolase domain containing 1A	0.53	15	8
AJ224864	CMRF-35H	Leukocyte membrane antigen	0.53	15	8
AI146812			0.53	15	8
AI916271		Transcribed locus	0.53	15	8
AK095793	PRKXP1	Protein kinase, X-linked, pseudogene 1	0.50	14	7
AY423763	KLHL17	Kelch-like 17 (Drosophila)	0.50	14	7
CA308403	WIPI49	WD40 repeat protein interacting with phosphoInositides of 49 kDa	0.50	14	7
AA904502	MSL3L1	Male-specific lethal 3-like 1 (Drosophila)	0.50	14	7
BX648568	CARD8	Caspase recruitment domain family, member 8	0.50	14	7
AA830668			0.50	14	7
XM_040486	ZMAT1	Zinc finger, matrin type 1	0.50	14	7
AI619500		Transcribed locus	0.50	14	7
NM_003044	SLC6A12	Solute carrier family 6 (neurotransmitter transporter, betaine/GABA), member 12	0.50	14	7
AL832950	FLJ31033	Hypothetical protein FLJ31033	0.50	14	7
X00570	APOC1	Apolipoprotein C-I	0.50	12	6
M36284	GYPC	Glycophorin C (Gerbich blood group)	0.50	12	6
NM_024164	TPSB2	Tryptase alpha/beta 1	0.50	12	6
BU623171		CDNA clone IMAGE:3029742, partial cds	0.50	12	6
AB040120	SLC39A8	Solute carrier family 39 (zinc transporter), member 8	0.50	12	6
BC042143	FLJ32009	Hypothetical protein FLJ32009	0.50	12	6
AA780074	CSS3	Chondroitin sulfate synthase 3	0.50	12	6
M60445	HDC	Histidine decarboxylase	0.50	12	6
BC039999	C9orf76	Chromosome 9 open reading frame 76	0.50	10	5
AA205305	ANKRA2	Ankyrin repeat, family A (RFXANK-like), 2	0.50	10	5
NM_000544	TAP2	Transporter 2, ATP-binding cassette, sub-family B (MDR/TAP)	0.50	10	5
BQ787632	SPON1	Spondin 1, extracellular matrix protein	0.50	8	4
AA663031			0.50	8	4
BC028421	MGC33630	Hypothetical protein MGC33630	0.50	8	4
AA883488	KIAA0408	KIAA0408	0.50	8	4
BU620736	MAGI-3	Membrane-associated guanylate kinase-related (MAGI-3)	0.50	8	4
BC010943	OSMR	Oncostatin M receptor	0.50	8	4
AK096798	RDH13	Retinol dehydrogenase 13 (all-trans and 9-cis)	0.50	8	4
AK092260		CDNA FLJ34941 fis, clone NT2RP7007480	0.50	8	4
AF274048	UHRF1	Ubiquitin-like, containing PHD and RING finger domains, 1	0.50	8	4

We selected genes whose normalized expression ratios (RCC/normal renal cortex cells) were >5.0 in more than 50% of the 15 RCC cases examined. Accession numbers, gene symbols, and gene names were retrieved from the Unigene Database.

Table V. Genes commonly down-regulated in RCC.

Accession no.	Symbol	Gene name	<0.2-fold/ present	Present	<0.2-fold
BC034227	D4S234E	DNA segment on chromosome 4 (unique) 234 expressed sequence	1.00	15	15
U96131	TRIP13	Thyroid hormone receptor interactor 13	1.00	15	15
NM_000336	SCNN1B	Sodium channel, nonvoltage-gated 1, beta (Liddle syndrome)	1.00	15	15
AF047433	ITGB4BP	Integrin beta 4 binding protein	1.00	15	15
AK091961	UMOD	Uromodulin (uromucoid, Tamm-Horsfall glycoprotein)	1.00	15	15
NM_003984	SLC13A2	Solute carrier family 13 (sodium-dependent dicarboxylate transporter), member 2	1.00	15	15
J04132	CD3Z	CD3Z antigen, zeta polypeptide (TiT3 complex)	1.00	15	15
D86977	DHX38	DEAH (Asp-Glu-Ala-His) box polypeptide 38	1.00	15	15
BC030975	IL1RL1	Interleukin 1 receptor-like 1	1.00	15	15
CR612744	FABP1	Fatty acid binding protein 1, liver	1.00	15	15
BM805032	PRSS2	Protease, serine, 2 (trypsin 2)	1.00	15	15
BC004312	IGFBP2	Insulin-like growth factor binding protein 2, 36 kDa	1.00	15	15
M95549	SLC5A2	Solute carrier family 5 (sodium/glucose cotransporter), member 2	1.00	15	15
X51630	WT1	Wilms tumor 1	1.00	15	15
L20977	ATP2B2	ATPase, Ca ⁺⁺ transporting, plasma membrane 2	1.00	15	15
BQ012846	IL1RL1	Interleukin 1 receptor-like 1	1.00	15	15
M61900			1.00	15	15
AB209692	SLC22A8	Solute carrier family 22 (organic anion transporter), member 8	1.00	15	15
AA747835	LOC150568	Hypothetical protein LOC150568	1.00	15	15
BM677885	RASL11B	RAS-like, family 11, member B	1.00	15	15
NM_000076	CDKN1C	Cyclin-dependent kinase inhibitor 1C (p57, Kip2)	1.00	15	15
AF052098	LGI2	Leucine-rich repeat LGI family, member 2	1.00	15	15
AK057510	HPD	4-hydroxyphenylpyruvate dioxygenase	1.00	15	15
W73825	TCF21	Transcription factor 21	1.00	15	15
BC059363	SIAT7C	ST6 (alpha-N-acetyl-neuraminyl-2,3-beta-galactosyl-1,3)-N-acetylgalactosaminide alpha-2,6-sialyltransferase 3	1.00	15	15
BC063430	CPXM	Carboxypeptidase X (M14 family)	1.00	15	15
D87465	SPOCK2	Sparc/osteonectin, cwcv and kazal-like domains proteoglycan (testican) 2	1.00	15	15
AB209692	SLC22A8	Solute carrier family 22 (organic anion transporter), member 8	1.00	15	15
AA527435	LOC63928	Hepatocellular carcinoma antigen gene 520	1.00	15	15
H11294			1.00	15	15
J03565	CR2	Complement component (3d/Epstein Barr virus) receptor 2	1.00	15	15
BX248009	SERPINA4	Serine (or cysteine) proteinase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 4	1.00	15	15
AW190289		Transcribed locus, weakly similar to NP_775735.1 l(3)mbt-like 4 [Homo sapiens]	1.00	15	15
AK091926	SLC13A2	Solute carrier family 13 (sodium-dependent dicarboxylate transporter), member 2	1.00	15	15
BC071780	UNQ846	SRSR846	1.00	15	15
AB029496	LOC56920	Semaphorin sem2	1.00	15	15
AK093732		CDNA FLJ36413 fis, clone THYMU2010816	1.00	15	15
H18687	CLDN11	Claudin 11 (oligodendrocyte transmembrane protein)	1.00	15	15
AF216941	CLIC5	Chloride intracellular channel 5	1.00	15	15
BC030244	TNNC1	Troponin C, slow	1.00	15	15
AL049313	CLIC5	Chloride intracellular channel 5	1.00	15	15
AL049990		mRNA; cDNA DKFZp564G112 (from clone DKFZp564G112)	1.00	15	15
AF073920	RGS6	Regulator of G-protein signalling 6	1.00	14	14
BX647484	SLC12A1	Solute carrier family 12 (sodium/potassium/chloride transporters), member 1	1.00	14	14
NM_015354	NUP188	Nucleoporin 188 kDa	1.00	14	14
AA703185	MGC24039	Hypothetical protein MGC24039	1.00	14	14
AA533963	CPNE4	Copine IV	1.00	14	14
AF225426	FMN2	Formin 2	1.00	14	14
BX108635		Similar to RIKEN cDNA C330003B14	1.00	14	14
AW977053	CAS1	O-acetyltransferase	1.00	14	14
AK131204	BTLA	B and T lymphocyte associated	1.00	14	14
AA931406			1.00	14	14
AY327407	C2orf10	Hypothetical protein PRO2964	1.00	14	14

Table V. Continued.

Accession no.	Symbol	Gene name	<0.2-fold/ present	Present	<0.2-fold
NM_000807	GABRA2	Gamma-aminobutyric acid (GABA) A receptor, alpha 2	1.00	13	13
V00495	ALB	Albumin	1.00	13	13
AY335938	IRX1	Iroquois homeobox protein 1	1.00	13	13
AI820955		Transcribed locus	1.00	13	13
AW967446			1.00	13	13
R34577	FLJ21657	Hypothetical protein FLJ21657	1.00	13	13
NM_198956	SP8	Sp8 transcription factor	1.00	13	13
AA938971		Transcribed locus	1.00	13	13
AB023193	NTNG1	Netrin G1	1.00	13	13
NM_030806	C1orf21	Chromosome 1 open reading frame 21	1.00	13	13
M24122	MYL3	Myosin, light polypeptide 3, alkali; ventricular, skeletal, slow	1.00	12	12
BQ962682	GOLGA3	Golgi autoantigen, golgin subfamily a, 3	1.00	12	12
AA609323		Transcribed locus	1.00	12	12
AI732791	XRN1	5'-3' exoribonuclease 1	1.00	12	12
BC018099		Homo sapiens, clone IMAGE:4796019, mRNA	1.00	12	12
AW189299			1.00	12	12
BC025687	CAMK4	Calcium/calmodulin-dependent protein kinase IV	1.00	11	11
AF131834		Clone 24841 mRNA sequence	1.00	11	11
H84909	MGC34774	Ribosomal protein L13A-like	1.00	11	11
AA541526	WDFY3	WD repeat and FYVE domain containing 3	1.00	11	11
AA179211			1.00	11	11
L07868	ERBB4	V-erb-a erythroblastic leukemia viral oncogene homolog 4 (avian)	1.00	11	11
BC029130	C6orf35	Chromosome 6 open reading frame 35	1.00	10	10
H19830	DKFZP434G156	Hypothetical protein DKFZp434G156	1.00	10	10
NM_017495	RNPC1	RNA-binding region (RNP1, RRM) containing 1	1.00	10	10
BQ000754	OR7E47P	Olfactory receptor, family 7, subfamily E, member 47 pseudogene	1.00	10	10
NM_020039	ACCN2	Amiloride-sensitive cation channel 2, neuronal	1.00	10	10
BC012984	ALS2CR19	Amyotrophic lateral sclerosis 2 (juvenile) chromosome region, candidate 19	1.00	10	10
AF352729	STRA6	Stimulated by retinoic acid gene 6 homolog (mouse)	1.00	10	10
R00532	PAH	Phenylalanine hydroxylase	1.00	10	10
NM_002277	KRTHA1	Keratin, hair, acidic, 1	1.00	10	10
AA883874	CXXC4	CXXC finger 4	1.00	10	10
AA809349		Transcribed locus, weakly similar to XP_529819.1 PREDICTED: hypothetical protein XP_529819 [Pan troglodytes]	1.00	10	10
AF062595	AK5	Adenylate kinase 5	1.00	10	10
NM_080912	ASGR2	Asialoglycoprotein receptor 2	1.00	9	9
AA759203	XTP7	Protein 7 transactivated by hepatitis B virus X antigen (HBxAg)	1.00	9	9
AF191687			1.00	9	9
AK091765		CDNA FLJ34446 fis, clone HLUNG2002050	1.00	9	9
AA830448		Transcribed locus	1.00	9	9
BF513800		Transcribed locus	1.00	9	9
M74558	SIL	TAL1 (SCL) interrupting locus	1.00	8	8
AK095384	PDE4C	Phosphodiesterase 4C, cAMP-specific (phosphodiesterase E1 dunce homolog, Drosophila)	1.00	8	8
T67409	AFM	Afamin	1.00	8	8
NM_004378	CRABP1	Cellular retinoic acid binding protein 1	1.00	8	8
AW188090		Transcribed locus, weakly similar to NP_080901.1 RIKEN cDNA 1700067P10 [Mus musculus]	1.00	8	8
AL713793	DAPP1	Dual adaptor of phosphotyrosine and 3-phosphoinositides	1.00	8	8
AA663781		Transcribed locus	1.00	8	8
NM_013259	TAGLN3	Transgelin 3	1.00	8	8
AA757932	MINPP1	Multiple inositol polyphosphate histidine phosphatase, 1	1.00	8	8
CA426475	HBE1	Hemoglobin, epsilon 1	1.00	8	8
AI220328		Transcribed locus	1.00	8	8
NM_003117	SPAM1	Sperm adhesion molecule 1 (PH-20 hyaluronidase, zona pellucida binding)	1.00	8	8

Table V. Continued.

Accession no.	Symbol	Gene name	<0.2-fold/ present	Present	<0.2-fold
BM677716	ATP8A2	ATPase, aminophospholipid transporter-like, Class I, type 8A, member 2	1.00	8	8
BC068590	LOC150356	Hypothetical protein BC012882	1.00	8	8
BX088758		Transcribed locus	1.00	8	8
AA954092	RHBDL2	Rhomboid, veinlet-like 2 (<i>Drosophila</i>)	1.00	8	8
AK095036	SPAG16	Sperm associated antigen 16	1.00	8	8
AA617917	C20orf65	Chromosome 20 open reading frame 65	1.00	8	8
BX107944		Transcribed locus	1.00	8	8
AI911481	SUV420H2	Suppressor of variegation 4-20 homolog 2 (<i>Drosophila</i>)	1.00	8	8
AW868740	SYNPO2	Synaptopodin 2	1.00	8	8
NM_001005388	NFASC	Neurofascin	0.93	15	14
NM_001395	DUSP9	Dual specificity phosphatase 9	0.93	15	14
BC000375	CHGB	Chromogranin B (secretogranin 1)	0.93	15	14
U07643	LTF	Lactotransferrin	0.93	15	14
X51420	TYRP1	Tyrosinase-related protein 1	0.93	15	14
L04308	PTHR1	Parathyroid hormone receptor 1	0.93	15	14
X03350	ADH1B	Alcohol dehydrogenase 1B (class I), beta polypeptide	0.93	15	14
BC062476	ADH1C	Alcohol dehydrogenase 1C (class I), gamma polypeptide	0.93	15	14
V00494	ALB	Albumin	0.93	15	14
X02747	ALDOB	Aldolase B, fructose-bisphosphate	0.93	15	14
NM_058179	PSAT1	Phosphoserine aminotransferase 1	0.93	15	14
BM725055		Transcribed locus, weakly similar to NP_872301.1 hypothetical protein FLJ25224 [<i>Homo sapiens</i>]	0.93	15	14
AW450890	LMO3	LIM domain only 3 (rhombotin-like 2)	0.93	15	14
R40262	DUSP9	Dual specificity phosphatase 9	0.93	15	14
BC025985	IGHG4	Immunoglobulin heavy constant gamma 4 (G4m marker)	0.93	15	14
NM_032432	ABLIM2	Actin binding LIM protein family, member 2	0.93	15	14
BC075800	PRKAR2B	Protein kinase, cAMP-dependent, regulatory, type II, beta	0.93	15	14
NM_001011554	SLC13A3	Solute carrier family 13 (sodium-dependent dicarboxylate transporter), member 3	0.93	15	14
BC041846	CDH3	Cadherin 3, type 1, P-cadherin (placental)	0.93	15	14
BC063109	KCNJ1	Potassium inwardly-rectifying channel, subfamily J, member 1	0.93	15	14
BC004312	IGFBP2	Insulin-like growth factor binding protein 2, 36 kDa	0.93	15	14
AI361002	TBC1D17	TBC1 domain family, member 17	0.93	15	14
AY549722	ITLN1	Intelectin 1 (galactofuranose binding)	0.93	15	14
U05569	CRYAA	Crystallin, alpha A	0.93	15	14
NM_006617	NES	Nestin	0.93	15	14
AI929792		Transcribed locus	0.93	15	14
H04828		Transcribed locus	0.93	15	14
BQ182775	ECRG4	Esophageal cancer related gene 4 protein	0.93	15	14
NM_000893	KNG1	Kininogen 1	0.93	15	14
BC071790		cDNA clone IMAGE:4611512	0.93	15	14
N32157	TMC3	Transmembrane channel-like 3	0.93	15	14
H22566	DACH1	Dachshund homolog 1 (<i>Drosophila</i>)	0.93	15	14
AK001000	DACH1	Dachshund homolog 1 (<i>Drosophila</i>)	0.93	15	14
BC001776	CYP27B1	Cytochrome P450, family 27, subfamily B, polypeptide 1	0.93	15	14
H14263	GAS1	Growth arrest-specific 1	0.93	15	14
NM_033063	MAP6	Microtubule-associated protein 6	0.93	15	14
R59552	CHRD1	Chordin-like 1	0.93	15	14
NM_002241	KCNJ10	Potassium inwardly-rectifying channel, subfamily J, member 10	0.93	15	14
D83017	NELL1	NEL-like 1 (chicken)	0.93	14	13
AA455926	PTGER3	Prostaglandin E receptor 3 (subtype EP3)	0.93	14	13
AA806986	ATRX	Alpha thalassemia/mental retardation syndrome X-linked (RAD54 homolog, <i>S. cerevisiae</i>)	0.93	14	13
W96022		Transcribed locus	0.93	14	13
NM_001005388	NFASC	Neurofascin	0.93	14	13
AF054839	TSPAN2	Tetraspanin 2	0.93	14	13

Table V. Continued.

Accession no.	Symbol	Gene name	<0.2-fold/ present	Present	<0.2-fold
AK001590	C14orf132	Chromosome 14 open reading frame 132	0.93	14	13
H11384	CDC42EP3	CDC42 effector protein (Rho GTPase binding) 3	0.92	13	12
BU684240	EHF	Ets homologous factor	0.92	13	12
BU569535	CHODL	Chondrolectin	0.92	13	12
AF338109	PACAP	Proapoptotic caspase adaptor protein	0.92	13	12
AJ243937	GPSM3	G-protein signalling modulator 3 (AGS3-like, <i>C. elegans</i>)	0.92	12	11
AF054910	TEKT2	Tektin 2 (testicular)	0.92	12	11
NM_001275	CHGA	Chromogranin A (parathyroid secretory protein 1)	0.92	12	11
AI339506	WAC	WW domain containing adaptor with coiled-coil	0.92	12	11
AA417198		Transcribed locus, weakly similar to NP_060190.1 signal-transducing adaptor protein-2; brk kinase substrate [<i>Homo sapiens</i>]	0.92	12	11
AB188489	SYNPO2L	Synaptopodin 2-like	0.92	12	11
NM_001083	PDE5A	Phosphodiesterase 5A, cGMP-specific	0.91	11	10
AA877216		Transcribed locus	0.91	11	10
AF000560	LOC126208	Hypothetical protein LOC126208	0.90	10	9
AA809379		Transcribed locus	0.90	10	9
N51413	TMAP1	Transmembrane anchor protein 1	0.90	10	9
AA862436	THEA	Thioesterase, adipose associated	0.90	10	9
BC004888	FLJ10052	Sushi domain containing 4	0.90	10	9
AA813164	EMP2	Epithelial membrane protein 2	0.90	10	9
BX114748		Transcribed locus	0.90	10	9
BX092660	RORA	RAR-related orphan receptor A	0.90	10	9
AA741001		Transcribed locus	0.89	9	8
AA723586	FLJ31951	Hypothetical protein FLJ31951	0.89	9	8
NM_020349	ANKRD2	Ankyrin repeat domain 2 (stretch responsive muscle)	0.89	9	8
AA854756	ZYX	Zyxin	0.89	9	8
AI000771	SLC30A5	Solute carrier family 30 (zinc transporter), member 5	0.89	9	8
AA421322	IGLC2	Immunoglobulin lambda joining 3	0.88	8	7
BM805669	TTR	Transthyretin (prealbumin, amyloidosis type I)	0.88	8	7
BU738725		Transcribed locus	0.88	8	7
AK075052		CDNA FLJ90571 fis, clone OVARC1001725, highly similar to <i>Homo sapiens</i> patched related protein TRC8 (TRC8) gene	0.88	8	7
L21998	MUC2	Mucin 2, intestinal/tracheal	0.88	8	7
AA970389		Transcribed locus, weakly similar to NP_872301.1 hypothetical protein FLJ25224 [<i>Homo sapiens</i>]	0.88	8	7
AY358700	SERPINA9	Serine (or cysteine) proteinase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 9	0.88	8	7
AA935766		Transcribed locus, moderately similar to XP_372039.2 PREDICTED: similar to hypothetical protein (LIH 3 region) - human [<i>Homo sapiens</i>]	0.88	8	7
AI742927	SHPRH	SNF2 histone linker PHD RING helicase	0.88	8	7
U45955	GPM6B	Glycoprotein M6B	0.87	15	13
U17033	PLA2R1	Phospholipase A2 receptor 1, 180 kDa	0.87	15	13
X72475		Immunoglobulin kappa light chain variable region (IGKV gene), clone 25	0.87	15	13
U97519	PODXL	Podocalyxin-like	0.87	15	13
L22214	ADORA1	Adenosine A1 receptor	0.87	15	13
U29089	PRELP	Proline arginine-rich end leucine-rich repeat protein	0.87	15	13
L34041	GPD1	Glycerol-3-phosphate dehydrogenase 1 (soluble)	0.87	15	13
NM_003966	SEMA5A	Sema domain, seven thrombospondin repeats (type 1 and type 1-like), transmembrane domain (TM) and short cytoplasmic domain (semaphorin) 5A	0.87	15	13
L13740	NR4A1	Nuclear receptor subfamily 4, group A, member 1	0.87	15	13
NM_000426	LAMA2	Laminin, alpha 2 (merosin, congenital muscular dystrophy)	0.87	15	13
X74819	TNNT2	Troponin T2, cardiac	0.87	15	13
NM_000277	PAH	Phenylalanine hydroxylase	0.87	15	13
H23177	CA10	Carbonic anhydrase X	0.87	15	13
M21574	PDGFRA	Platelet-derived growth factor receptor, alpha polypeptide	0.87	15	13

Table V. Continued.

Accession no.	Symbol	Gene name	<0.2-fold/ present	Present	<0.2-fold
BC010082	ETNK2	Ethanolamine kinase 2	0.87	15	13
AI205684	HSPA2	Heat shock 70 kDa protein 2	0.87	15	13
AK075151	HSPB7	Heat shock 27 kDa protein family, member 7 (cardiovascular)	0.87	15	13
NM_003182	TAC1	Tachykinin, precursor 1 (substance K, substance P, neurokinin 1, neurokinin 2, neuromedin L, neurokinin alpha, neuropeptide K, neuropeptide gamma)	0.87	15	13
AA831240			0.87	15	13
NM_001002295	GATA3	GATA binding protein 3	0.87	15	13
BC018986	HPGD	Hydroxyprostaglandin dehydrogenase 15-(NAD)	0.87	15	13
AB073386	SGEF	Src homology 3 domain-containing guanine nucleotide exchange factor	0.87	15	13
BC067289	CTSL2	Cathepsin L2	0.87	15	13
BC041366	USP2	Ubiquitin specific protease 2	0.87	15	13
BQ044958	NRK	Nik related kinase	0.87	15	13
T50700	ALDOB	Aldolase B, fructose-bisphosphate	0.87	15	13
BQ001493	EHD3	EH-domain containing 3	0.87	15	13
NM_002725	PRELP	Proline arginine-rich end leucine-rich repeat protein	0.87	15	13
AK022877		CDNA FLJ12815 fis, clone NT2RP2002546	0.87	15	13
AA976712	LOC387914	Transmembrane protein 46	0.87	15	13
NM_002345	LUM	Lumican	0.87	15	13
AA165165		Transcribed locus	0.87	15	13
AL162042		CDNA FLJ41690 fis, clone HCASM2009405	0.87	15	13
AY358845	FLJ31166	Hypothetical protein FLJ31166	0.87	15	13
AL109700		CDNA FLJ37610 fis, clone BRCOC2011398	0.87	15	13
AB032953	ODZ2	Odz, odd Oz/ten-m homolog 2 (Drosophila)	0.87	15	13
NM_001901	CTGF	Connective tissue growth factor	0.87	15	13
AL137326	FLJ37478	Hypothetical protein FLJ37478	0.87	15	13
BC080187	LMOD1	Leiomodin 1 (smooth muscle)	0.87	15	13
U48707	PPP1R1A	Protein phosphatase 1, regulatory (inhibitor) subunit 1A	0.86	14	12
X55656	HBG2	Hemoglobin, gamma G	0.86	14	12
AB209661	ARHGEF3	Rho guanine nucleotide exchange factor (GEF) 3	0.86	14	12
NM_000618	IGF1	Insulin-like growth factor 1 (somatomedin C)	0.86	14	12
NM_020946	KIAA1608	KIAA1608	0.86	14	12
Z30137	LDB3	LIM domain binding 3	0.86	14	12
AA776749	LOC57821	Chromosome 1 open reading frame 114	0.86	14	12
AL109706		mRNA full length insert cDNA clone EUROIMAGE 362430	0.86	14	12
BC094691	HRC	Histidine rich calcium binding protein	0.85	13	11
BC011782	RAB3A	RAB3A, member RAS oncogene family	0.85	13	11
W45330		CDNA FLJ43434 fis, clone OCBBF2028055	0.85	13	11
AW964166	FTCD	Formiminotransferase cyclodeaminase	0.85	13	11
AF059203	SOAT2	Sterol O-acyltransferase 2	0.83	12	10
CA314541		Transcribed locus	0.83	12	10
NM_007356	LAMB4	Laminin, beta 4	0.83	12	10
BX101094	FLJ21128	Hypothetical protein FLJ21128	0.83	12	10
X91148	MTP	Microsomal triglyceride transfer protein (large polypeptide, 88 kDa)	0.83	12	10
BC028373	RG9MTD2	RNA (guanine-9-) methyltransferase domain containing 2	0.83	12	10
AF361494	SOSTDC1	Sclerostin domain containing 1	0.83	12	10
N24235	KIAA0789	KIAA0789 gene product	0.82	11	9
NM_004378	CRAP1	Cellular retinoic acid binding protein 1	0.82	11	9
AK128514	NDEL1	NudE nuclear distribution gene E homolog like 1 (A. nidulans)	0.82	11	9
AI093859	MLL5	Myeloid/lymphoid or mixed-lineage leukemia 5 (trithorax homolog, Drosophila)	0.82	11	9
BX648776	MSRB3	Methionine sulfoxide reductase B3	0.82	11	9
AA975173		Transcribed locus, strongly similar to XP_512017.1 PREDICTED: hypothetical protein XP_512017 [Pan troglodytes]	0.82	11	9
AK025270	C10orf137	Chromosome 10 open reading frame 137	0.82	11	9
AB033090	PAK7	P21(CDKN1A)-activated kinase 7	0.82	11	9
NM_001002260	C9orf58	Chromosome 9 open reading frame 58	0.80	15	12

Table V. Continued.

Accession no.	Symbol	Gene name	<0.2-fold/ present	Present	<0.2-fold
BI759204	KLK1	Kallikrein 1, renal/pancreas/salivary	0.80	15	12
AF053470	BLCAP	Bladder cancer associated protein	0.80	15	12
NM_005589	ALDH6A1	Aldehyde dehydrogenase 6 family, member A1	0.80	15	12
U24266	ALDH4A1	Aldehyde dehydrogenase 4 family, member A1	0.80	15	12
NM_005577	LPA	Lipoprotein, Lp(a)	0.80	15	12
BC000458	MAL	Mal, T-cell differentiation protein	0.80	15	12
BC092518	IGHG3	Immunoglobulin heavy constant mu	0.80	15	12
BM709336	AIF1	Allograft inflammatory factor 1	0.80	15	12
L38486	MFAP4	Microfibrillar-associated protein 4	0.80	15	12
M16967	F5	Coagulation factor V (proaccelerin, labile factor)	0.80	15	12
NM_000301	PLG	Plasminogen	0.80	15	12
BC048282	CLCNKA	Chloride channel Ka	0.80	15	12
M25809	ATP6V1B1	ATPase, H+ transporting, lysosomal 56/58 kDa, V1 subunit B, isoform 1 (Renal tubular acidosis with deafness)	0.80	15	12
BQ183489	SLC14A1	Solute carrier family 14 (urea transporter), member 1 (Kidd blood group)	0.80	15	12
BX537531	FBLN5	Fibulin 5	0.80	15	12
H27000	WBSCR17	Williams-Beuren syndrome chromosome region 17	0.80	15	12
AA682533	SGOL2	Shugoshin-like 2 (S. pombe)	0.80	15	12
NM_000118	ENG	Endoglin (Osler-Rendu-Weber syndrome 1)	0.80	15	12
NM_002581	PAPPA	Pregnancy-associated plasma protein A, pappalysin 1	0.80	15	12
AK027126	ASS	Argininosuccinate synthetase	0.80	15	12
BX094063	PIN4	Protein (peptidyl-prolyl cis/trans isomerase) NIMA-interacting, 4 (parvulin)	0.80	15	12
NM_012188	FOXI1	Forkhead box I1	0.80	15	12
BX423161	LHPP	Phospholysine phosphohistidine inorganic pyrophosphate phosphatase	0.80	15	12
NM_001001936	KIAA1914	KIAA1914	0.80	15	12
BC042688	RASD1	RAS, dexamethasone-induced 1	0.80	15	12
N66510	GPM6B	Glycoprotein M6B	0.80	15	12
AK223296	LILRB5	Leukocyte immunoglobulin-like receptor, subfamily B (with TM and ITIM domains), member 5	0.80	15	12
NM_032932	RAB11FIP4	RAB11 family interacting protein 4 (class II)	0.80	15	12
AL834240	KIAA1576	KIAA1576 protein	0.80	15	12
AL133118	EMCN	Endomucin	0.80	15	12
AI342255	SYNPO2	Synaptopodin 2	0.80	15	12
BQ718658		CDNA: FLJ22642 fis, clone HSI06970	0.80	15	12
BC004107	FST	Follistatin	0.80	15	12
AF070632		Clone 24405 mRNA sequence	0.80	15	12
X14640	KRT13	Keratin 13	0.80	15	12
X83618	HMGCS2	3-hydroxy-3-methylglutaryl-Coenzyme A synthase 2 (mitochondrial)	0.80	15	12
NM_004484	GPC3	Glypican 3	0.80	15	12
AI076840	MGC33926	Hypothetical protein MGC33926	0.80	15	12
BC014640	COL14A1	Collagen, type XIV, alpha 1 (undulin)	0.80	15	12
XM_032571	KIAA0888	KIAA0888 protein	0.80	15	12
AA319638	DKFZp761L1417	Hypothetical protein DKFZp761L1417	0.80	15	12
AK122672	GPCR5A	G protein-coupled receptor, family C, group 5, member A	0.80	15	12
AK055811		CDNA FLJ31249 fis, clone KIDNE2005327	0.80	15	12
AK055811		CDNA FLJ31249 fis, clone KIDNE2005327	0.80	15	12
AI261591	ATP6V1G3	ATPase, H+ transporting, lysosomal 13 kDa, V1 subunit G isoform 3	0.80	15	12
NM_007289	MME	Membrane metallo-endopeptidase (neutral endopeptidase, enkephalinase, CALLA, CD10)	0.80	15	12
X77737	SLC4A1	Solute carrier family 4, anion exchanger, member 1 (erythrocyte membrane protein band 3, Diego blood group)	0.80	15	12
AF049884	ARGBP2	Arg/Abl-interacting protein ArgBP2	0.80	10	8
U59299	SLC16A5	Solute carrier family 16 (monocarboxylic acid transporters), member 5	0.80	10	8
BC033873	BST2	Bone marrow stromal cell antigen 2	0.80	10	8
AA975742	LRP16	LRP16 protein	0.80	10	8

Table V. Continued.

Accession no.	Symbol	Gene name	<0.2-fold/ present	Present	<0.2-fold
AA191573	SYNJ2	Synaptojanin 2	0.80	10	8
BQ185194		Transcribed locus, weakly similar to XP_375099.1 PREDICTED: similar to hypothetical protein FLJ25224 [Homo sapiens]	0.80	10	8
AA804745	GBF1	Golgi-specific brefeldin A resistance factor 1	0.80	10	8
AK023979	C14orf46	Chromosome 14 open reading frame 46	0.80	10	8
AL713743	FLJ42875	FLJ42875 protein	0.79	14	11
NM_005378	MYCN	V-myc myelocytomatosis viral related oncogene, neuroblastoma derived (avian)	0.79	14	11
BC063521	HS6ST1	Heparan sulfate 6-O-sulfotransferase 1	0.79	14	11
BC031609	ATP12A	ATPase, H+/K+ transporting, nongastric, alpha polypeptide	0.79	14	11
NM_032737	LMNB2	Lamin B2	0.79	14	11
M62839	APOH	Apolipoprotein H (beta-2-glycoprotein I)	0.79	14	11
L02870	COL7A1	Collagen, type VII, alpha 1 (epidermolysis bullosa, dystrophic, dominant and recessive)	0.79	14	11
X91148	MTP	Microsomal triglyceride transfer protein (large polypeptide, 88 kDa)	0.79	14	11
AF055015	EYA2	Eyes absent homolog 2 (Drosophila)	0.79	14	11
NM_021200	PLEKHB1	Pleckstrin homology domain containing, family B (evectins) member 1	0.79	14	11
J04599	BGN	Biglycan	0.79	14	11
AA036952	Gup1	GRINL1A combined protein	0.79	14	11
AA405685	UHSKerB	Keratin associated protein 5-8	0.79	14	11
AF010236	SGCD	Sarcoglycan, delta (35 kDa dystrophin-associated glycoprotein)	0.79	14	11
NM_000596	IGFBP1	Insulin-like growth factor binding protein 1	0.79	14	11
L20316	GCGR	Glucagon receptor	0.79	14	11
AL697428	ENTH	Enthoprotin	0.78	9	7
NM_080672	PHACTR3	Phosphatase and actin regulator 3	0.78	9	7
BC022567	CHST1	Carbohydrate (keratan sulfate Gal-6) sulfotransferase 1	0.78	9	7
AW197616		Transcribed locus	0.78	9	7
NM_001007156	NTRK3	Neurotrophic tyrosine kinase, receptor, type 3	0.78	9	7
NM_012127	CIZ1	CDKN1A interacting zinc finger protein 1	0.78	9	7
NM_006566	CD226	CD226 antigen	0.78	9	7
AY161004	COX8C	Cytochrome c oxidase subunit 8C	0.78	9	7
N99340	CLIPR-59	CLIP-170-related protein	0.77	13	10
NM_001011554	SLC13A3	Solute carrier family 13 (sodium-dependent dicarboxylate transporter), member 3	0.77	13	10
AF052170	MICAL2	Microtubule associated monooxygenase, calponin and LIM domain containing 2	0.77	13	10
AA669023	PCDH9	Protocadherin 9	0.77	13	10
AA721101	LOC92162	Similar to RIKEN cDNA 2600017H02	0.77	13	10
XM_032571	KIAA0888	KIAA0888 protein	0.77	13	10
AI912733	FLJ40125	Hypothetical protein FLJ40125	0.77	13	10
M55671	PROZ	Protein Z, vitamin K-dependent plasma glycoprotein	0.75	12	9
U38254	SCNN1D	Sodium channel, nonvoltage-gated 1, delta	0.75	12	9
NM_006617	NES	Nestin	0.75	12	9
X05332	KLK3	Kallikrein 3, (prostate specific antigen)	0.75	12	9
NM_015120	ALMS1	Alstrom syndrome 1	0.75	12	9
W44613	LY6K	Lymphocyte antigen 6 complex, locus K	0.75	12	9
BX117062		LOC440008	0.75	12	9
NM_152461	ERN1	Endoplasmic reticulum to nucleus signalling 1	0.75	12	9
M38258	RARG	Retinoic acid receptor, gamma	0.75	12	9
NM_002083	GPX2	Glutathione peroxidase 2 (gastrointestinal)	0.75	8	6
U89165	NRGN	Neurogranin (protein kinase C substrate, RC3)	0.75	8	6
BU621583	KIAA0056	KIAA0056 protein	0.75	8	6
H77985	FLJ25476	FLJ25476 protein	0.75	8	6
NM_153486	LDHD	Lactate dehydrogenase D	0.75	8	6
BC007956	DKFZp727A071	Similar to tRNA synthetase class II	0.75	8	6

Table V. Continued.

Accession no.	Symbol	Gene name	<0.2-fold/ present	Present	<0.2-fold
AI359551	FLJ90119	Hypothetical protein FLJ90119	0.75	8	6
BC040176	LOC130576	Hypothetical protein LOC130576	0.75	8	6
BX538105	COLM	Collomin	0.75	8	6
N71087		CDNA FLJ37676 fis, clone BRHIP2012627	0.75	8	6
BX102181		Homo sapiens, similar to neuronal thread protein, clone IMAGE:4102657, mRNA	0.75	8	6
AK125106	SYTL5	Synaptotagmin-like 5	0.75	8	6
AA247642	SNAP23	Synaptosomal-associated protein, 23 kDa	0.75	8	6
AY791349	KIF18A	Kinesin family member 18A	0.75	8	6
AI262277	PFN2	Profilin 2	0.75	8	6
U26726	HSD11B2	Hydroxysteroid (11-beta) dehydrogenase 2	0.73	15	11
BC039065	ADH6	Alcohol dehydrogenase 6 (class V)	0.73	15	11
NM_002084	GPX3	Glutathione peroxidase 3 (plasma)	0.73	15	11
J02854	MYL9	Elongation factor Tu family protein	0.73	15	11
NM_005951	MT1H	Metallothionein 1H	0.73	15	11
NM_033018	PCTK1	PCTAIRE protein kinase 1	0.73	15	11
BQ003596	GJA5	Gap junction protein, alpha 5, 40 kDa (connexin 40)	0.73	15	11
BC023505	ECM1	Extracellular matrix protein 1	0.73	15	11
AF208070	KLHL3	Kelch-like 3 (Drosophila)	0.73	15	11
V00497	HBB	Hemoglobin, beta	0.73	15	11
AK074668	ISLR	Immunoglobulin superfamily containing leucine-rich repeat	0.73	15	11
BC092449	MGC27165	Hypothetical protein MGC27165	0.73	15	11
AI091459	FLJ20489	Hypothetical protein FLJ20489	0.73	15	11
W94882	FREM1	FRAS1 related extracellular matrix 1	0.73	15	11
U26726	HSD11B2	Hydroxysteroid (11-beta) dehydrogenase 2	0.73	15	11
AK022877		CDNA FLJ12815 fis, clone NT2RP2002546	0.73	15	11
AK123132	MSRA	Methionine sulfoxide reductase A	0.73	15	11
NM_032387	WNK4	WNK lysine deficient protein kinase 4	0.73	15	11
BX110180		Transcribed locus	0.73	15	11
BM981462	FLJ13710	Hypothetical protein FLJ13710	0.73	15	11
BC068446	FLJ34658	Hypothetical protein FLJ34658	0.73	15	11
X03635	ESR1	Estrogen receptor 1	0.73	15	11
BX537781	FNDC5	Fibronectin type III domain containing 5	0.73	15	11
D14838	FGF9	Fibroblast growth factor 9 (glia-activating factor)	0.73	15	11
AB033040	RNF150	Ring finger protein 150	0.73	15	11
BC052574	FLJ20171	Hypothetical protein FLJ20171	0.73	15	11
BQ773658		Hypothetical LOC401384	0.73	15	11
NM_020795	NLGN2	Neuroigin 2	0.73	15	11
BC017312	MGC3047	Limitrin	0.73	15	11
AA994979	ATP6V0A4	ATPase, H ⁺ transporting, lysosomal V0 subunit a isoform 4	0.73	15	11
BC090956	MGC11324	Hypothetical protein MGC11324	0.73	15	11
AB209237	NPY1R	Neuropeptide Y receptor Y1	0.73	15	11
BQ446275	HBD	Hemoglobin, delta	0.73	15	11
BU683028		CDNA FLJ10151 fis, clone HEMBA1003402	0.73	15	11
R50993			0.73	15	11
AI694359	PLG	Plasminogen	0.73	15	11
AI003542	PDE11A	Phosphodiesterase 11A	0.73	15	11
AI126777	FLJ45455	FLJ45455 protein	0.73	15	11
AF131754	SH3BGR2	SH3 domain binding glutamic acid-rich protein like 2	0.73	15	11
BU741863	SPOCK	Sparc/osteonectin, cwcv and kazal-like domains proteoglycan (testican)	0.73	15	11
AF098269	PCOLCE2	Procollagen C-endopeptidase enhancer 2	0.73	15	11
BF967878	C10orf83	Chromosome 10 open reading frame 83	0.73	15	11
CN280172	YWHAQ	Tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, theta polypeptide	0.73	15	11
U19487	PTGER2	Prostaglandin E receptor 2 (subtype EP2), 53 kDa	0.73	15	11
AK026196	MGC4172	Short-chain dehydrogenase/reductase	0.73	15	11

Table V. Continued.

Accession no.	Symbol	Gene name	<0.2-fold/ present	Present	<0.2-fold present
AB002320	HECW1	HECT, C2 and WW domain containing E3 ubiquitin protein ligase 1	0.73	15	11
AB208813	RBM5	RNA binding motif protein 5	0.73	11	8
BC042692	CTL2	CTL2 protein	0.73	11	8
AB002388	ZNF536	Zinc finger protein 536	0.73	11	8
AI075877	FLJ11539	Hypothetical protein FLJ11539	0.73	11	8
AI279516		CDNA FLJ11723 fis, clone HEMBA1005314	0.73	11	8
BX088780		Transcribed locus	0.73	11	8
AK000795	PDE3A	Phosphodiesterase 3A, cGMP-inhibited	0.73	11	8
AB209237	NPY1R	Neuropeptide Y receptor Y1	0.71	14	10
Z98489		Transcribed locus	0.71	14	10
U91963	TLL1	Tolloid-like 1	0.71	14	10
NM_024017	HOXB9	Homeo box B9	0.71	14	10
X66417	CSN3	Casein kappa	0.71	14	10
AF209747	KCNMB2	Potassium large conductance calcium-activated channel, subfamily M, beta member 2	0.71	14	10
AA629743	KIAA1712	KIAA1712	0.70	10	7
NM_015576	C1orf1	CAZ-associated structural protein	0.70	10	7
N75862	EYA4	Eyes absent homolog 4 (Drosophila)	0.70	10	7
BC030666	MGC33993	Ring finger protein 182	0.70	10	7
AK097190	LOC285286	Hypothetical protein LOC285286	0.70	10	7
BU741595	LHX4	LIM homeobox 4	0.70	10	7
AA034053		Transcribed locus	0.70	10	7
BC046365	LOC253012	Hypothetical protein LOC253012	0.70	10	7
AW977610	MYO1E	Myosin IE	0.70	10	7
AA977738		CDNA FLJ40061 fis, clone TESOP2000083	0.70	10	7
AA765718		CDNA FLJ33551 fis, clone BRAMY2009105	0.70	10	7
AA007591	SEN5	SUMO1/sentrin specific protease 5	0.70	10	7
AB032996	FAM40B	Family with sequence similarity 40, member B	0.70	10	7
NM_000112	SLC26A2	Solute carrier family 26 (sulfate transporter), member 2	0.69	13	9
AF001436	CDC42EP2	CDC42 effector protein (Rho GTPase binding) 2	0.69	13	9
BC078664	HMGA1	High mobility group AT-hook 1	0.69	13	9
W39428	FBXO2	F-box protein 2	0.69	13	9
AY044437	SFXN5	Sideroflexin 5	0.69	13	9
BC002378	KIAA0652	KIAA0652 gene product	0.69	13	9
L10320	FBP1	Fructose-1,6-bisphosphatase 1	0.67	15	10
BC028315	GABARAPL1	GABA(A) receptor-associated protein like 1	0.67	15	10
X04741	UCHL1	Ubiquitin carboxyl-terminal esterase L1 (ubiquitin thiolesterase)	0.67	15	10
M13143	KLKB1	Kallikrein B, plasma (Fletcher factor) 1	0.67	15	10
L13288	VIPR1	Vasoactive intestinal peptide receptor 1	0.67	15	10
NM_031850	AGTR1	Angiotensin II receptor, type 1	0.67	15	10
X92720	PCK2	Phosphoenolpyruvate carboxykinase 2 (mitochondrial)	0.67	15	10
AF117225	PROM1	Prominin 1	0.67	15	10
AB028952	SYNPO	Synaptopodin	0.67	15	10
AA032154	FLJ22655	Hypothetical protein FLJ22655	0.67	15	10
AF052090	NNT	Nicotinamide nucleotide transhydrogenase	0.67	15	10
D17517	TYRO3	TYRO3 protein tyrosine kinase	0.67	15	10
NM_005141	FGB	Fibrinogen, B beta polypeptide	0.67	15	10
BM994174	HBB	Hemoglobin, beta	0.67	15	10
M55513	KCNA5	Potassium voltage-gated channel, shaker-related subfamily, member 5	0.67	15	10
BX109845	SH3BGR2	SH3 domain binding glutamic acid-rich protein like 2	0.67	15	10
D42047	GPD1L	Glycerol-3-phosphate dehydrogenase 1-like	0.67	15	10
AK025198	XIST	X (inactive)-specific transcript	0.67	15	10
NM_012244	SLC7A8	Solute carrier family 7 (cationic amino acid transporter, y+ system), member 8	0.67	15	10
BX412247	EFHD1	EF hand domain family, member D1	0.67	15	10
NM_018667	SMPD3	Sphingomyelin phosphodiesterase 3, neutral membrane (neutral sphingomyelinase II)	0.67	15	10

Table V. Continued.

Accession no.	Symbol	Gene name	<0.2-fold/ present	Present	<0.2-fold present
AF205940	EMCN	Endomucin	0.67	15	10
AF007144	DIO2	Deiodinase, iodothyronine, type II	0.67	15	10
NM_006548	IMP-2	IGF-II mRNA-binding protein 2	0.67	15	10
NM_033400	ZFHX2	Zinc finger homeobox 2	0.67	15	10
AI928242	TFCP2L1	Transcription factor CP2-like 1	0.67	15	10
NM_020990		Creatine kinase, mitochondrial 1B	0.67	15	10
AF089854	TU3A	TU3A protein	0.67	15	10
AK021754		CDNA FLJ11692 fis, clone HEMBA1004983	0.67	15	10
AK025164	FLJ21511	Hypothetical protein FLJ21511	0.67	15	10
NM_001584	C11orf8	Chromosome 11 open reading frame 8	0.67	15	10
N39341	MT1G	Metallothionein 1G	0.67	15	10
NM_004673	ANGPTL1	Angiopoietin-like 1	0.67	15	10
AA206141	PRICKLE1	Prickle-like 1 (Drosophila)	0.67	15	10
NM_152296	ATP1A3	ATPase, Na ⁺ /K ⁺ transporting, alpha 3 polypeptide	0.67	15	10
NM_002667	PLN	Phospholamban	0.67	15	10
AA621124	LOC338773	Hypothetical protein LOC338773	0.67	12	8
AB058780	SIAT2	ST6 beta-galactosamide alpha-2,6-sialyltransferase 2	0.67	12	8
NM_003048	SLC9A2	Solute carrier family 9 (sodium/hydrogen exchanger), isoform 2	0.67	12	8
BG569025	ORM1	Orosomucoid 1	0.67	9	6
D49742	HABP2	Hyaluronan binding protein 2	0.67	9	6
BU728456	RIMS2	Regulating synaptic membrane exocytosis 2	0.67	9	6
CR595341	FLJ90024	Fasting-inducible integral membrane protein TM6P1	0.67	9	6
H18456		Transcribed locus	0.67	9	6
BC050354		Hypothetical gene supported by BC014163	0.67	9	6
XM_059954	C9orf57	Chromosome 9 open reading frame 57	0.67	9	6
NM_032105	PPP1R12B	Protein phosphatase 1, regulatory (inhibitor) subunit 12B	0.67	9	6
BC075838	LAMB3	Laminin, beta 3	0.64	14	9
M93107	BDH	3-hydroxybutyrate dehydrogenase (heart, mitochondrial)	0.64	14	9
J02874	FABP4	Fatty acid binding protein 4, adipocyte	0.64	14	9
M96789	GJA4	Gap junction protein, alpha 4, 37 kDa (connexin 37)	0.64	14	9
BC078664	HMGA1	High mobility group AT-hook 1	0.64	14	9
BC023152	GYG2	Glycogenin 2	0.64	14	9
NM_001015053	HDAC5	Histone deacetylase 5	0.64	14	9
BC039071	HHAT	Hedgehog acyltransferase	0.64	14	9
AL832156	CPEB1	Cytoplasmic polyadenylation element binding protein 1	0.64	14	9
AL359590	PGS1	Phosphatidylglycerophosphate synthase	0.64	14	9
NM_005503	APBA2	Amyloid beta (A4) precursor protein-binding, family A, member 2 (X11-like)	0.64	11	7
AF131821	MGLL	Monoglyceride lipase	0.64	11	7
AI822035		Transcribed locus	0.64	11	7
CR749484	LOC152519	Hypothetical protein LOC152519	0.64	11	7
BX100620		Transcribed locus	0.64	11	7
AA180985	ZNF229	Zinc finger protein 229	0.64	11	7
BC029261	MYOC	Myocilin, trabecular meshwork inducible glucocorticoid response	0.63	8	5
BC006992	RAD51AP1	RAD51 associated protein 1	0.63	8	5
U01839	FY	Duffy blood group	0.63	8	5
NM_000773	CYP2E1	Cytochrome P450, family 2, subfamily E, polypeptide 1	0.63	8	5
AK124139	KIAA1970	KIAA1970 protein	0.63	8	5
AA738314	FBXO42	F-box protein 42	0.63	8	5
BM560961	PDLIM3	PDZ and LIM domain 3	0.63	8	5
NM_138456	MGC20410	Hypothetical protein BC012330	0.63	8	5
AA112743	SGPL1	Sphingosine-1-phosphate lyase 1	0.63	8	5
AW978378	KCNN3	Potassium intermediate/small conductance calcium-activated channel, subfamily N, member 3	0.63	8	5
NM_002563	P2RY1	Purinergic receptor P2Y, G-protein coupled, 1	0.62	13	8
NM_004557	NOTCH4	Notch homolog 4 (Drosophila)	0.62	13	8

Table V. Continued.

Accession no.	Symbol	Gene name	<0.2-fold/ present	Present	<0.2-fold present
AA663484	PPP2R2B	Protein phosphatase 2 (formerly 2A), regulatory subunit B (PR 52), beta isoform	0.62	13	8
AK126536	TSK	Tsukushi	0.62	13	8
AA758171	MLL3	Myeloid/lymphoid or mixed-lineage leukemia 3	0.62	13	8
U66464	MAP4K1	Mitogen-activated protein kinase kinase kinase kinase 1	0.62	13	8
AI808724	CHRN2	Cholinergic receptor, nicotinic, beta polypeptide 2 (neuronal)	0.62	13	8
BC011873	MTRF1L	Mitochondrial translational release factor 1-like	0.62	13	8
AA777755	TFCP2	Transcription factor CP2	0.62	13	8
AF000959	CLDN5	Claudin 5 (transmembrane protein deleted in velocardiofacial syndrome)	0.60	15	9
M93284	PNLIPRP2	Pancreatic lipase-related protein 2	0.60	15	9
NM_021120	DLG3	Discs, large homolog 3 (neuroendocrine-dlg, Drosophila)	0.60	15	9
AB209756	CSRP1	Cysteine and glycine-rich protein 1	0.60	15	9
M59305	NPR3	Natriuretic peptide receptor C/guanylate cyclase C (atrionatriuretic peptide receptor C)	0.60	15	9
AB119995	CES1	Carboxylesterase 1 (monocyte/macrophage serine esterase 1)	0.60	15	9
BC050383	TMPO	Thymopoietin	0.60	15	9
BM687969	PVALB	Parvalbumin	0.60	15	9
M62829	EGR1	Early growth response 1	0.60	15	9
M76180	DDC	Dopa decarboxylase (aromatic L-amino acid decarboxylase)	0.60	15	9
AF029082	SFN	Stratifin	0.60	15	9
M87790	IGLC2	Immunoglobulin lambda joining 3	0.60	15	9
NM_012205	HAAO	3-hydroxyanthranilate 3,4-dioxygenase	0.60	15	9
NM_001068	TOP2B	Topoisomerase (DNA) II beta 180 kDa	0.60	15	9
BM458221	MT1X	Metallothionein 1X	0.60	15	9
X58022	CRHBP	Corticotropin releasing hormone binding protein	0.60	15	9
AF389338	SCD4	Stearoyl-CoA desaturase 5	0.60	15	9
NM_012190	FTHFD	Aldehyde dehydrogenase 1 family, member L1	0.60	15	9
AB018279	SV2A	Synaptic vesicle glycoprotein 2A	0.60	15	9
AA634326	TCF20	Transcription factor 20 (AR1)	0.60	15	9
BC035713	KIAA1914	KIAA1914	0.60	15	9
BM474898	SLIT2	Slit homolog 2 (Drosophila)	0.60	15	9
XM_496688	LOC152573	Hypothetical protein BC012029	0.60	15	9
AB209591	SLC7A7	Solute carrier family 7 (cationic amino acid transporter, y+ system), member 7	0.60	15	9
BC063304	NPR1	Natriuretic peptide receptor A/guanylate cyclase A (atrionatriuretic peptide receptor A)	0.60	15	9
AB031046	TCF7L1	Transcription factor 7-like 1 (T-cell specific, HMG-box)	0.60	15	9
AA156792	HEYL	Hairy/enhancer-of-split related with YRPW motif-like	0.60	15	9
NM_058186	FAM3B	Family with sequence similarity 3, member B	0.60	15	9
T95199	MT1F	Metallothionein 1F (functional)	0.60	15	9
M55618	TNC	Tenascin C (hexabrachion)	0.60	15	9
BC033736	DPT	Dermatopontin	0.60	15	9
AK095908	MFGE8	Milk fat globule-EGF factor 8 protein	0.60	15	9
BC008366	DDC	Dopa decarboxylase (aromatic L-amino acid decarboxylase)	0.60	15	9
BC066977	C1orf40	Chromosome 1 open reading frame 40	0.60	15	9
BC014564	MEST	Mesoderm specific transcript homolog (mouse)	0.60	15	9
AB067483	SLC25A25	Solute carrier family 25 (mitochondrial carrier; phosphate carrier), member 25	0.60	15	9
AB081837	FLJ20315	Hypothetical protein FLJ20315	0.60	15	9
XM_350880	PPM1H	Protein phosphatase 1H (PP2C domain containing)	0.60	15	9
BQ062201	DCXR	Dicarbonyl/L-xylulose reductase	0.60	15	9
N70019	MT1E	Metallothionein 1E (functional)	0.60	15	9
NM_002775	PRSS11	Protease, serine, 11 (IGF binding)	0.60	15	9
NM_000701	ATP1A1	Hypothetical protein MGC16179	0.60	15	9
CA427160	PDCD6	Programmed cell death 6	0.60	15	9
NM_001007470	TRPM3	Transient receptor potential cation channel, subfamily M, member 3	0.60	15	9
AW298180	MMP7	Matrix metalloproteinase 7 (matrilysin, uterine)	0.60	15	9
AF370395	EPS8L1	EPS8-like 1	0.60	15	9

Table V. Continued.

Accession no.	Symbol	Gene name	<0.2-fold/ present	Present	<0.2-fold present
CA450275	FREQ	Frequenin homolog (Drosophila)	0.60	15	9
AK096674	C14orf32	Chromosome 14 open reading frame 32	0.60	15	9
CR749297	SKIP	SPHK1 (sphingosine kinase type 1) interacting protein	0.60	15	9
AK091965	MGC15937	Similar to RIKEN cDNA 0610008P16 gene	0.60	15	9
BE080213		Full-length cDNA clone CS0DE011YI04 of Placenta of Homo sapiens (human)	0.60	15	9
J05401	CKMT2	Creatine kinase, mitochondrial 2 (sarcomeric)	0.60	15	9
AF389429	SEMA6D	Sema domain, transmembrane domain (TM), and cytoplasmic domain (semaphorin) 6D	0.60	15	9
BU619137	TGFBR3	Transforming growth factor, beta receptor III (betaglycan, 300 kDa)	0.60	15	9
AL832661	LOC143381	Hypothetical protein LOC143381	0.60	15	9
AB006000	LECT1	Leukocyte cell derived chemotaxin 1	0.60	15	9
AF389426	SEMA6D	Sema domain, transmembrane domain (TM), and cytoplasmic domain (semaphorin) 6D	0.60	15	9
M65199	EDN2	Endothelin 2	0.60	10	6
BC052996	CTNNA2	Catenin (cadherin-associated protein), alpha 2	0.60	10	6
L12579	CUTL1	Cut-like 1, CCAAT displacement protein (Drosophila)	0.60	10	6
AA642294	GNG7	Guanine nucleotide binding protein (G protein), gamma 7	0.60	10	6
NM_004291	CART	Cocaine- and amphetamine-regulated transcript	0.60	10	6
AA715708		Chromosome 18 open reading frame 49	0.60	10	6
AK026244	GPR107	G protein-coupled receptor 107	0.60	10	6
N64389		Transcribed locus	0.60	10	6
AB040529	MAGED4	Melanoma antigen family D, 4	0.58	12	7
AK127945	HYAL2	Hyaluronoglucosaminidase 2	0.58	12	7
AK057972	LOC51066	Fls485	0.58	12	7
R56087	KIAA0984	KIAA0984 protein	0.58	12	7
AK126055	C9orf84	Chromosome 9 open reading frame 84	0.58	12	7
Z21707	ZNF197	Zinc finger protein 197	0.58	12	7
AA195950	NRAP	Nebulin-related anchoring protein	0.58	12	7
AI823969	MGST1	Microsomal glutathione S-transferase 1	0.58	12	7
AA994999	SYNE2	Spectrin repeat containing, nuclear envelope 2	0.58	12	7
NM_005828	HAN11	WD repeat domain 68	0.58	12	7
BX091957		Zinc finger, DHHC-type containing 20	0.58	12	7
NM_000260	MYO7A	Myosin VIIA (Usher syndrome 1B (autosomal recessive, severe))	0.57	14	8
NM_012342	BAMBI	BMP and activin membrane-bound inhibitor homolog (Xenopus laevis)	0.57	14	8
AW135188		Transcribed locus, weakly similar to XP_509271.1 PREDICTED: similar to RIKEN cDNA 4921537D05 [Pan troglodytes]	0.57	14	8
T83961	FLJ21986	Hypothetical protein FLJ21986	0.57	14	8
T50062		Transcribed locus	0.57	14	8
AA451886	CYP1B1	Cytochrome P450, family 1, subfamily B, polypeptide 1	0.57	14	8
BC060866	LOC163782	Ankyrin repeat domain 38	0.57	14	8
BC057792	CA4	Carbonic anhydrase IV	0.56	9	5
D12485	ENPP1	Ectonucleotide pyrophosphatase/phosphodiesterase 1	0.56	9	5
NM_004209	SYNGR3	Synaptogyrin 3	0.56	9	5
AL834231	MTPN	Myotrophin	0.56	9	5
R42757	IGSF4	Immunoglobulin superfamily, member 4	0.56	9	5
NM_016143	NSFL1C	NSFL1 (p97) cofactor (p47)	0.56	9	5
BM996064	TJP3	Tight junction protein 3 (zona occludens 3)	0.56	9	5
AK056793	LOC145694	Hypothetical protein LOC145694	0.56	9	5
AK095632	ABTB2	Ankyrin repeat and BTB (POZ) domain containing 2	0.56	9	5
U47413	CCNG1	Cyclin G1	0.55	11	6
AK122881	PRICKLE1	Prickle-like 1 (Drosophila)	0.55	11	6
AK092766	OLFML3	Olfactomedin-like 3	0.55	11	6
J04599	BGN	Biglycan	0.55	11	6
NM_001008779	SPDY1	Speedy homolog 1 (Drosophila)	0.55	11	6

Table V. Continued.

Accession no.	Symbol	Gene name	<0.2-fold/ present	Present	<0.2-fold present
BC094740	LIMS3	LIM and senescent cell antigen-like domains 3	0.55	11	6
AA524150	SDC4	Syndecan 4 (amphiglycan, ryudocan)	0.55	11	6
AA994364	FLJ32421	Chromosome 1 open reading frame 58	0.55	11	6
AA766649		Transcribed locus	0.55	11	6
NM_002989	CCL21	Chemokine (C-C motif) ligand 21	0.55	11	6
BC011262	PHGDH	Phosphoglycerate dehydrogenase	0.54	13	7
NM_001620	MGC5395	AHNAK nucleoprotein (desmoyokin)	0.54	13	7
L02867	HUMPPA	Paraneoplastic antigen	0.54	13	7
NM_005723	TM4SF9	Tetraspanin 5	0.54	13	7
D17408	CNN1	Calponin 1, basic, smooth muscle	0.54	13	7
BC034222	HRLP5	H-rev107-like protein 5	0.54	13	7
BF673741	TUSC3	Tumor suppressor candidate 3	0.54	13	7
NM_015393	DKFZP564O0823	DKFZP564O0823 protein	0.54	13	7
BC041168	LCN12	Lipocalcin 12	0.54	13	7
H08298	C13orf7	Chromosome 13 open reading frame 7	0.54	13	7
AK021708	PDZRN3	PDZ domain containing RING finger 3	0.54	13	7
AK024898		CDNA: FLJ21245 fis, clone COL01184	0.54	13	7
NM_005928	MFGE8	Milk fat globule-EGF factor 8 protein	0.53	15	8
U23435	ABI2	Abl interactor 2	0.53	15	8
BC029050	ARG2	Arginase, type II	0.53	15	8
D29013	POLB	Polymerase (DNA directed), beta	0.53	15	8
AF036268	SH3GL2	SH3-domain GRB2-like 2	0.53	15	8
NM_001482	GATM	Glycine amidinotransferase (L-arginine:glycine amidinotransferase)	0.53	15	8
BU730105	MT2A	Metallothionein 2A	0.53	15	8
L15388	GRK5	G protein-coupled receptor kinase 5	0.53	15	8
NM_001690	ATP6V1A	ATPase, H+ transporting, lysosomal 70 kDa, V1 subunit A	0.53	15	8
BC053578	GSTA1	Glutathione S-transferase A1	0.53	15	8
NM_004394	DAP	Death-associated protein	0.53	15	8
NM_004293	GDA	Guanine deaminase	0.53	15	8
AJ001016	RAMP3	Receptor (calcitonin) activity modifying protein 3	0.53	15	8
J05581	MUC1	Mucin 1, transmembrane	0.53	15	8
AI356291	GPT2	Glutamic pyruvate transaminase (alanine aminotransferase) 2	0.53	15	8
NM_000118	ENG	Endoglin (Osler-Rendu-Weber syndrome 1)	0.53	15	8
NM_005953	MT2A	Metallothionein 2A	0.53	15	8
BC007290	TSPAN1	Tetraspanin 1	0.53	15	8
AA521405	SPAP1	Fc receptor-like 2	0.53	15	8
AA719352		Transcribed locus	0.53	15	8
AY358336	LOC255743	Likely ortholog of mouse nephronectin	0.53	15	8
R78436			0.53	15	8
AK123393	CCDC3	Coiled-coil domain containing 3	0.53	15	8
NM_170677	MEIS2	Meis1, myeloid ecotropic viral integration site 1 homolog 2 (mouse)	0.53	15	8
NM_005843	STAM2	Signal transducing adaptor molecule (SH3 domain and ITAM motif) 2	0.53	15	8
AA621665			0.53	15	8
CB529051	G0S2	Putative lymphocyte G0/G1 switch gene	0.53	15	8
W67837	EMP2	Epithelial membrane protein 2	0.53	15	8
NM_006988	ADAMTS1	A disintegrin-like and metalloprotease (reprolysin type) with thrombospondin type 1 motif, 1	0.53	15	8
AA490011	LTBP1	Latent transforming growth factor beta binding protein 1	0.53	15	8
N58556	DKFZp547K1113	Hypothetical protein DKFZp547K1113	0.53	15	8
W84893	AGTRL1	Angiotensin II receptor-like 1	0.53	15	8
BC032508	FLJ10781	Hypothetical protein FLJ10781	0.53	15	8
AA055976	SLIT2	Slit homolog 2 (Drosophila)	0.53	15	8
AF097431	LEPRE1	Leucine proline-enriched proteoglycan (leprecan) 1	0.53	15	8
AK055782	PDLIM2	PDZ and LIM domain 2 (mystique)	0.53	15	8
AF407165	PPP1R14C	Protein phosphatase 1, regulatory (inhibitor) subunit 14C	0.53	15	8

Table V. Genes commonly down-regulated in RCC.

Accession no.	Symbol	Gene name	<0.2-fold/ present	Present	<0.2-fold
BC042636	ZNF134	Zinc finger protein 134 (clone pHZ-15)	0.53	15	8
BC038457	DKFZP586H2123	Regeneration associated muscle protease	0.53	15	8
AA056734	IQSEC3	IQ motif and Sec7 domain 3	0.53	15	8
BC033183	CHST3	Carbohydrate (chondroitin 6) sulfotransferase 3	0.53	15	8
BQ447358		BTB/POZ-zinc finger protein-like	0.53	15	8
BC052998	DDR2	Discoidin domain receptor family, member 2	0.53	15	8
AF191652	NUDT4	Nudix (nucleoside diphosphate linked moiety X)-type motif 4 pseudogene 2	0.53	15	8
M81883	GAD1	Glutamate decarboxylase 1 (brain, 67 kDa)	0.53	15	8
AA528243	RTN4RL1	Reticulon 4 receptor-like 1	0.53	15	8
NM_182964	NAV2	Neuron navigator 2	0.53	15	8
BU743008		Similar to implantation-associated protein	0.53	15	8
AK095203	PDE3A	Phosphodiesterase 3A, cGMP-inhibited	0.53	15	8
CR627284	LEPR	Leptin receptor	0.53	15	8
AF504647		Cilia-associated protein (CYS1)	0.53	15	8
AA626775	PCDHA9	Protocadherin alpha 9	0.53	15	8
NM_021963	NAP1L2	Nucleosome assembly protein 1-like 2	0.53	15	8
BC090061	DKFZP761H1710	Hypothetical protein DKFZp761H1710	0.53	15	8
AK023744	EPS15L1	Epidermal growth factor receptor pathway substrate 15-like 1	0.53	15	8
NM_002864	PZP	Pregnancy-zone protein	0.53	15	8
AF245505	DKFZp564I1922	Matrix-remodelling associated 5	0.53	15	8
BC052210	GARP	Leucine rich repeat containing 32	0.53	15	8
AL049338	PTPRD	Protein tyrosine phosphatase, receptor type, D	0.53	15	8
CF146489	NKX3-1	NK3 transcription factor related, locus 1 (Drosophila)	0.53	15	8
AA429665		Transcribed locus	0.53	15	8
BU608866	KIF5A	Kinesin family member 5A	0.53	15	8
AK025651	PNAS-4	Chromosome 1 open reading frame 121	0.53	15	8
AA767342	KCNC3	Potassium voltage-gated channel, Shaw-related subfamily, member 3	0.53	15	8
AA972840		Similar to hypothetical protein	0.53	15	8
AA918686	PFKFB2	6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 2	0.53	15	8
AK128814		CDNA FLJ46049 fis, clone SYNOV2020463	0.53	15	8
BX640908	EVI1	Ecotropic viral integration site 1	0.53	15	8
AA995921	UPP2	Uridine phosphorylase 2	0.53	15	8
NM_000963	PTGS2	Prostaglandin-endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase)	0.53	15	8
AF169802	CYB5R2	Cytochrome b5 reductase b5R.2	0.53	15	8
BC015178	C18orf10	Chromosome 18 open reading frame 10	0.53	15	8
AI002365	PDGFRB	Platelet-derived growth factor receptor, beta polypeptide	0.53	15	8
AF030880	SLC26A4	Solute carrier family 26, member 4	0.53	15	8
AL117612	MAL2	Mal, T-cell differentiation protein 2	0.53	15	8
AB018260	RHOBTB2	Rho-related BTB domain containing 2	0.53	15	8
L13972	SIAT4A	ST3 beta-galactoside alpha-2,3-sialyltransferase 1	0.53	15	8
BC064700	ESRRG	Estrogen-related receptor gamma	0.53	15	8
NM_000930	PLAT	Plasminogen activator, tissue	0.53	15	8
NM_002182	IL1RAP	Interleukin 1 receptor accessory protein	0.50	14	7
NM_080542	COLQ	Collagen-like tail subunit (single strand of homotrimer) of asymmetric acetylcholinesterase	0.50	14	7
U53347	SLC1A5	Solute carrier family 1 (neutral amino acid transporter), member 5	0.50	14	7
AK091288	C9orf19	Chromosome 9 open reading frame 19	0.50	14	7
AA634140	ME2	Malic enzyme 2, NAD(+)-dependent, mitochondrial	0.50	14	7
BC039733	PTX3	Pentraxin-related gene, rapidly induced by IL-1 beta	0.50	14	7
W20074	PNPLA4	Patatin-like phospholipase domain containing 4	0.50	14	7
N90724	IGSF4	Immunoglobulin superfamily, member 4	0.50	14	7
NM_006548	IMP-2	IGF-II mRNA-binding protein 2	0.50	14	7
NM_153683	KL	Klotho	0.50	14	7
NM_004910	PITPNM1	Phosphatidylinositol transfer protein, membrane-associated 1	0.50	12	6

Table V. Genes commonly down-regulated in RCC.

Accession no.	Symbol	Gene name	<0.2-fold/ present	Present	<0.2-fold
NM_001756	SERPINA6	Serine (or cysteine) proteinase inhibitor, clade A (alpha-1 antitrypsin), member 6	0.50	12	6
D31888	RCOR1	REST corepressor 1	0.50	12	6
R61832	SNRPB2	Small nuclear ribonucleoprotein polypeptide B"	0.50	12	6
H03606	NPL	N-acetylneuraminase pyruvate lyase (dihydrodipicolinate synthase)	0.50	12	6
R12478			0.50	12	6
AA807166	TSGA10	Testis specific, 10	0.50	12	6
U81523	LEFTY2	Left-right determination factor 2	0.50	12	6
AI281932		Hypothetical LOC400134	0.50	12	6
AA043381	HOXD10	Homeo box D10	0.50	12	6
NM_152243	CDC42EP1	CDC42 effector protein (Rho GTPase binding) 1	0.50	12	6
AK024275	FLJ14213	Hypothetical protein FLJ14213	0.50	12	6
NM_199248	CACNB1	Calcium channel, voltage-dependent, beta 1 subunit	0.50	10	5
AF020543	PPT2	Palmitoyl-protein thioesterase 2	0.50	10	5
NM_002881	RALB	V-ral simian leukemia viral oncogene homolog B (ras related; GTP binding protein)	0.50	10	5
AF064255	SLC27A5	Solute carrier family 27 (fatty acid transporter), member 5	0.50	10	5
AA732989	ADAMTS2	A disintegrin-like and metalloprotease (reprolysin type) with thrombospondin type 1 motif, 2	0.50	10	5
AW977392		Full-length cDNA clone CS0DI042YD07 of Placenta Cot 25-normalized of Homo sapiens (human)	0.50	10	5
BC051340	CD164L1	CD248 antigen, endosialin	0.50	10	5
AK095271	LOC128977	Hypothetical protein LOC128977	0.50	10	5
BC006093	MMP9	Matrix metalloproteinase 9 (gelatinase B, 92 kDa gelatinase, 92 kDa type IV collagenase)	0.50	10	5
BX648671	MGC61571	Hypothetical protein MGC61571	0.50	10	5
NM_002505	NFYA	Nuclear transcription factor Y, alpha	0.50	8	4
AL713770	FAM31C	Family with sequence similarity 31, member C	0.50	8	4
AA808804	FLJ23469	Isochorismatase domain containing 2	0.50	8	4
AA442410	EMP1	Epithelial membrane protein 1	0.50	8	4
AA196034	TMEM38A	Transmembrane protein 38A	0.50	8	4
BX647751	WDR20	WD repeat domain 20	0.50	8	4
R49126	MGC24039	Hypothetical protein MGC24039	0.50	8	4
AI016895			0.50	8	4
AW452669	IARS	Isoleucine-tRNA synthetase	0.50	8	4

We selected genes whose normalized expression ratios (RCC/normal renal cortex cells) were <0.2 in >50% of the 15 RCC cases examined. Accession numbers, gene symbols, and gene names were retrieved from the Unigene Database.

experiments for 6 genes that were most significantly over-expressed in almost all of the informative cases: *ADORA3*, *SLC1A3*, *STC2*, *ENPP3*, *VWF*, and *NNMT*. The results of the semi-quantitative RT-PCR analysis were highly concordant with the microarray data in the great majority of the tested cases (Fig. 2).

Identification of semaphorin 5B (SEMA5B) as a molecular target for ccRCC therapy. Among the up-regulated genes in RCC, we focused on semaphorin 5B, *SEMA5B*, for further biological analysis because it was overexpressed very commonly in RCC, but not expressed in any of the normal human tissues examined. To validate the expression pattern of this gene, we performed semi-quantitative RT-PCR using 10 clinical RCC cases and confirmed that *SEMA5B* was

up-regulated in all of the 10 RCC cases examined, but its expression was undetectable in normal renal cortex (Fig. 3A). Subsequent Northern blot analysis using a *SEMA5B* cDNA fragment as a probe revealed that an approximately 5-kb transcript was highly expressed in RCC cell lines, A704, OS-RC-2, and TUHR14TKB, but was hardly detectable in RPTEC cells derived from normal human renal proximal tubule epithelial cells (Fig. 3B, upper panel), or in normal human tissues except fetal brain and kidney (Fig. 3B, lower panel). Expression of this gene was not elevated frequently in cancers of the breast, esophagus, lung, colon, bladder, pancreatic or prostate cancer according to our previous expression profile data (data not shown).

To obtain the full-length cDNA sequence of *SEMA5B*, we performed RT-PCR using RCC cell lines, OS-RC-2 or A704,

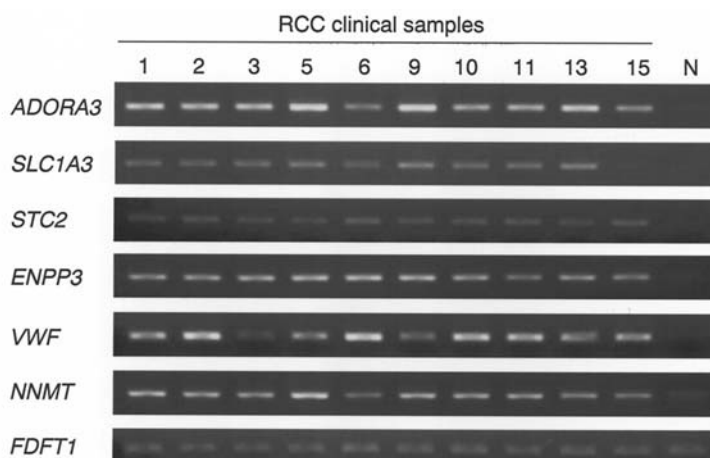


Figure 2. Semi-quantitative RT-PCR analysis of representative up-regulated genes. Expression of six representative up-regulated genes in microdissected ccRCC cells (clinical cases, Nos. 1-3, 5, 6, 9, 11, 13 and 15) and normal renal cortex cells (N) examined by semi-quantitative RT-PCR. *FDFT-1* was used as a quantitative control because this showed the smallest Cy5/Cy3 fluctuations in our RCC-microarray data.

as a template. We identified two transcriptional variants *SEMA5BV1* (GenBank accession No. NM_001031702) and *SEMA5BV2* (GenBank accession; NM_018987) each having 4,494 and 4,725 nucleotides, with an open reading frame of 3,456 and 3,279 nucleotides that encode 1,151- and 1,092-amino-acid peptides, respectively. A comparison of cDNA sequences with the genomic DNA sequence revealed that both cDNA sequences (Fig. 3C, *SEMA5BV1* and *SEMA5BV2*, respectively) consists of 23 exons spanning an approximately 120 kb genomic region on chromosome 3p21.1. *SEMA5BV1* and *V2* are transcribed from different first exons, 1a and 1b, and share the remaining exons although exons 16, 20 and 21 are differently spliced in the two transcripts. Exon 16 of *V2* was three nucleotides shorter than that of the *V1* at the 3' end, and exon 20 of *V2* was also three nucleotides shorter than that of *V1* at the 5' end. Exon 21 of *V2* was 131 nucleotides longer than that of *V1* at the 3' portion, generating an earlier stop codon within exon 22. The translational initiation codon for both variants is commonly present in exon 2. To examine which variant was dominantly expressed in ccRCC cells, we performed RT-PCR experiments and found that *SEMA5BV1* was highly up-regulated in ccRCC cells, whereas *SEMA5BV2* was undetectable in all RCC cell lines (Fig. 3D). Hence, we further perform functional analysis for the *SEMA5BV1* transcript.

Inhibition of growth of RCC cells by specific small-interfering RNA against SEMA5B. To assess whether *SEMA5B* is essential for growth or survival of RCC cells, we constructed plasmids to express siRNAs against *SEMA5B* (si-#1 and si-#2) as well as control plasmids (siRNAs for Scramble and Mock vector), and transfected each of them into OS-RC-2 RCC cell line, which endogenously express high levels of *SEMA5B* mRNA. Among the siRNA constructs examined, si-#2 effectively reduced expression of *SEMA5B* mRNA compared with control siRNAs (si-Scramble and si-Mock) (Fig. 4A). We observed significant decreases in the number of colonies (Fig. 4B) and in the numbers of viable cells measured by MTT assay for the cells treated with si-#2 (Fig. 4C). To exclude a possibility

of off-target effect by *SEMA5B*-siRNA (si-#2), we generated two forms of siRNA with 3-bp replacement and found that neither of them suppressed *SEMA5B* expression in OS-RC-2 cells (data not shown). These findings indicated an important role of *SEMA5B* in RCC cell survival and/or growth.

Discussion

Recent progress in molecular biology has improved our understanding of the genesis of a wide range of human neoplasms. In RCC, several groups have reported microarray-based molecular profiling (12,20-25). Although these studies have highlighted candidate genes that might be useful as diagnostic markers, data based on expression of mRNAs isolated from tumor masses might not exactly reflect changes during the course of renal carcinogenesis since tumor masses are generally mixtures of various cell populations such as inflammatory cells, stroma cells, and fibroblasts in addition to cancer cells and the proportions of each cell type vary significantly from one individual to another. In addition, RCCs is considered to originate from renal proximal tubule epithelial cells in renal cortex. Therefore, microarray data published previously are likely to have been influenced significantly by cellular heterogeneity among control preparations. In this study, we performed laser microbeam microdissection (LMM) to obtain pure populations of renal cancer cells as well as control normal renal cortex cells. Compared with one representative expression profile data of clear cell RCC (ccRCC) using RNAs from bulk tumor tissues by means of micorarray (21), only 4 of the 85 (5%) genes which were commonly up-regulated in >75% of informative ccRCC cases in our data (Table IV) were overlapped to bulk-expression profile data (21). These discrepancies were attributed to the fact that RCC cells are histopathologically heterogeneous, and expression profiles from bulk tissues could be significantly influenced by contamination with non-cancerous cells. Surprisingly, none of the top 24 genes that were most significantly up-regulated in our gene list (Table IV) was included in the previous results of ccRCC-expression profiles from bulk tissues (12,21). This

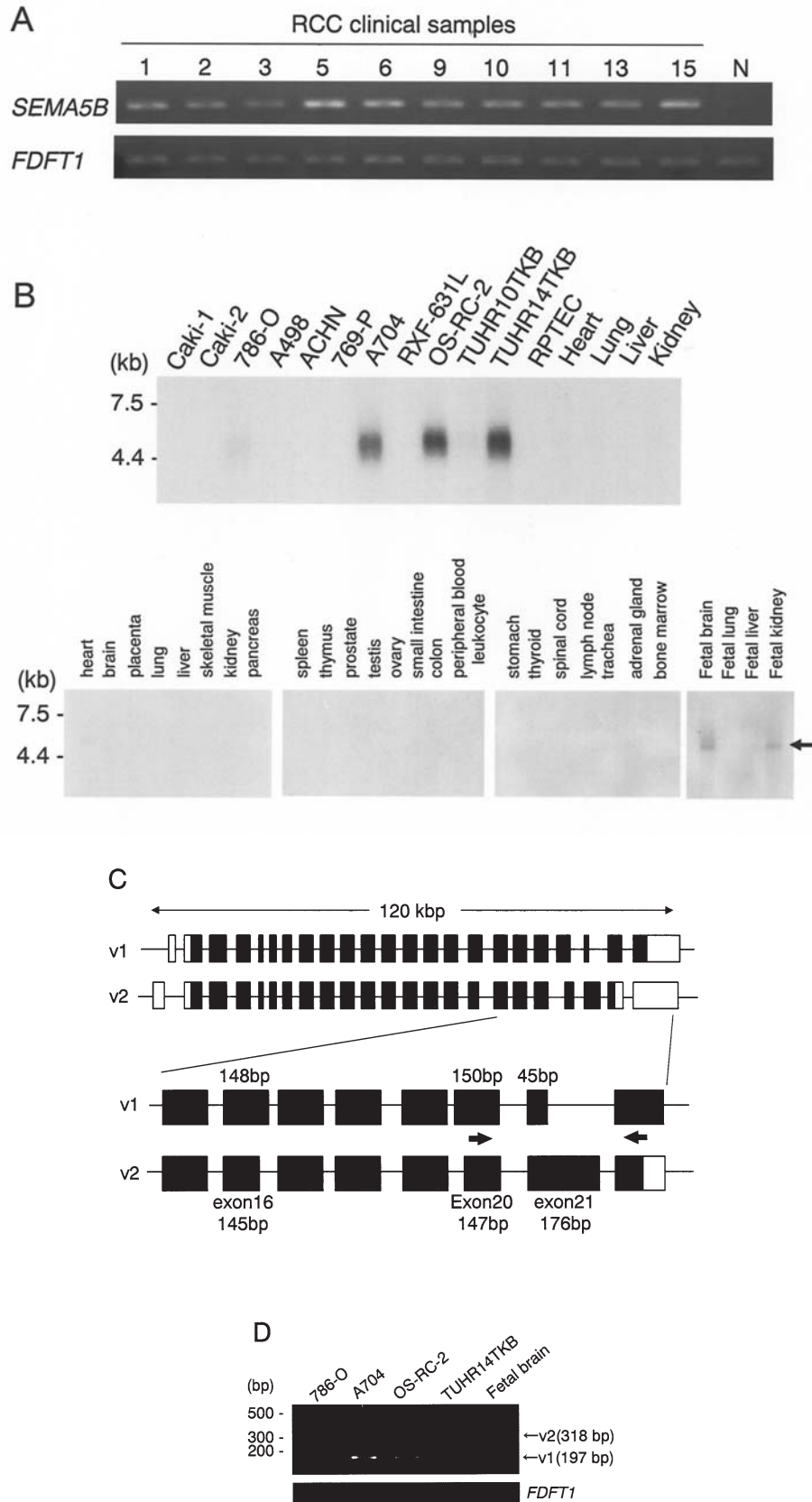


Figure 3. Expression of *SEMA5B* in RCC cells and normal tissues. (A) Expression of *SEMA5B* in microdissected ccRCC cells (clinical cases, Nos. 1-3, 5, 6, 9-11, 13 and 15) and normal renal cortex cells (N) examined by semi-quantitative RT-PCR. (B) Northern blot analysis of the *SEMA5B* expression in RCC cells and in normal human tissues. Upper panel; RCC cell lines, Caki-1, Caki-2, 786-O, A-498, ACHN, 769-P, A-704, RXF-631L, OS-RC-2, TUHR10TKB, and TUHR14TKB; normal human renal proximal tubule epithelial cells, RPTEC. Lower panel, multiple tissue Northern (MTN) blot. (C) Genomic structure of *SEMA5BV1* and *SEMA5BV2* spanning at 120 kb on chromosome 3p21.1. Arrows, positions of primers used in RT-PCR analysis. Closed boxes correspond to exons of the coding regions. Open boxes correspond to the non-coding exonic regions. (D) Semi-quantitative RT-PCR analysis of *SEMA5B* using RNAs prepared from three RCC cell lines (786-O, A704, OS-RC-2 and TUHR14TKB) and fetal brain poly A+ RNA. Primer sequences for RT-PCR are as follows: forward, 5'-CTGGAAACAGCAGCCAGAG-3' and 5'-CAGTGCTGCAAGACAGGTA-3'. PCR products amplified from *SEMA5BV1* or *SEMA5BV2* as illustrated.

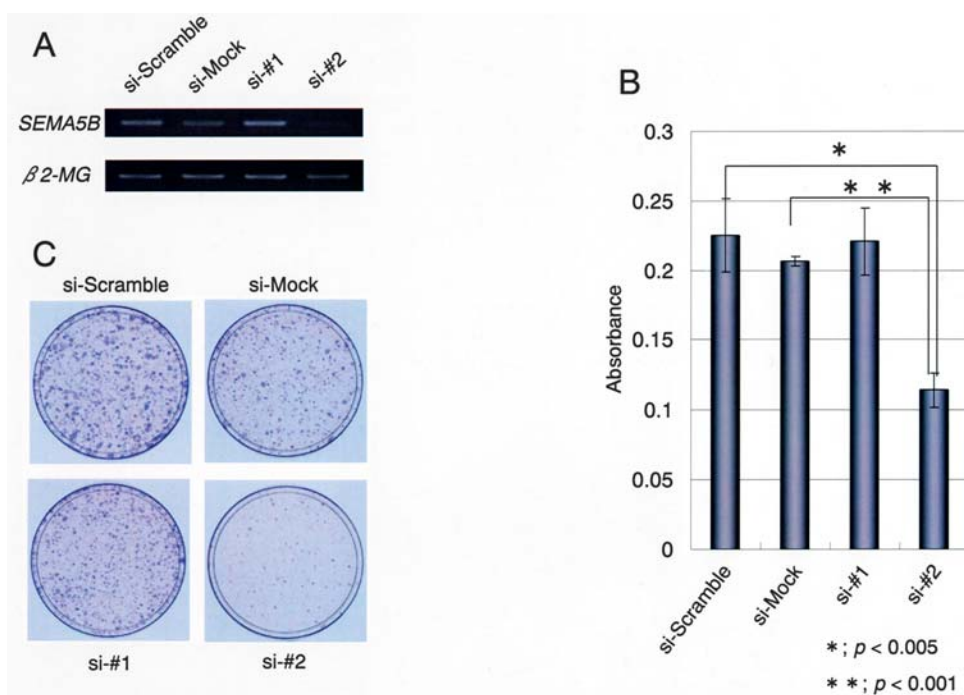


Figure 4. siRNA knockdown effect of *SEMA5B* on RCC cell growth and cell viability. Two *SEMA5B* siRNA expression vectors (si-#1, #2) and control vectors (si-Scramble and si-Mock) were transfected into OS-RC-2 cells. (A) RT-PCR experiments for examining the *SEMA5B* transcript level in the cells treated with siRNA. $\beta 2$ -MG expression level was used as quantitative control. si-#2 vector revealed a knockdown effect; si-#1, si-Scramble, and si-Mock failed to show any effect on the level of the *SEMA5B* transcript. Transfection with si-#2 vector resulted in reduction of the number of colonies (B), and numbers of viable cells (C), compared with the cells transfected with si-#1, si-Scramble, and si-Mock ($p < 0.005$ and $p < 0.001$, respectively; unpaired t-test).

evidence suggests our microarray data are much reliable as compared with others. We attribute this discrepancy to the fact that previous expression profiles from bulk cells could be significantly influenced by contamination of renal medullas in normal kidney tissues used as a control. For example, genes highly expressed in renal medulla, but not in renal proximal tubule epithelial cells in renal cortex, may be selected as down-regulated or unchanged genes in expression profiles from bulk tissues. Taking these points into consideration, it is crucial to perform the LMM system to purify as much as possible the populations of cancerous and normal epithelial cells obtained from surgical specimens.

Genes with altered expression in most of ccRCCs may serve as molecular diagnostic markers and candidates of RCC-therapeutic targets or may play causal roles in renal carcinogenesis. Among up-regulated genes, *NNMT* (nicotinamide N-methyltransferase), *IGFBP3* (insulin-like growth factor binding protein 3), *ENPP3* (ectonucleotide pyrophosphatase/phosphodiesterase 3), *VEGF* (vascular endothelial growth factor), and *VWF* (Von Willebrand factor) were included in our study as well as others. *NNMT* has been reported to be more frequently increased in ccRCCs than in other types of RCCs and to correlate with good prognosis in RCCs (12). It was shown by immunohistochemical staining that *IGFBP-3* leads to dysregulation of the IGF-axis within ccRCC (27,28). *IGFBP-3* was also shown to be involved in the regulation of RCC cell proliferation in an autocrine manner (27,28). Ecto-nucleotide pyrophosphatase/phosphodiesterase-I enzyme (*ENPP*), cleaves phosphodiester and phosphosulfate bonds of a variety of substrates. Mammalian *ENPP* comprises a family of three closely related proteins: *ENPP1*, *ENPP2*, and

ENPP3. The function of *ENPP3* is unknown, but it was reported that the expression of *ENPP3* was higher in tumor tissues than in surrounding tissues and the specific form of the *ENPP3* protein was detected in the sera of patients with bile duct carcinoma (BDC) and that *ENPP3* enhanced cell migration. Therefore, *ENPP3* may be related to the invasiveness of neoplastic BDC and can be applicable as a tumor marker (29). Serum *VEGF* and *VWF* levels were indicated to be predictive markers for immunomodulatory agents including interleukin-2 and IFN- α ; the patients with higher levels of *VEGF* and *VWF* revealed poor response to these treatments comparing to those showing lower serum levels of these proteins (15). Furthermore, *ABCG1* [ATP-binding cassette, sub-family G (WHITE), member 1] and *STC2* (stanniocalcin 2) *ABCG1*, mediates the transport of cholesterol in general. *ABCG1* was reported to be up-regulated in head and neck squamous cell carcinoma by microarray analysis and differential display (29).

On the contrary, among the down-regulated genes, *WT1* (Wilms tumors 1), *CDKN1C* (cyclin-dependent kinase inhibitor 1C), and *GAS1* (growth arrest-specific 1), have been implicated in growth suppression or apoptosis (16-19). Niu *et al* have reported that expression of *WT1* was significantly down-regulated in RCC tumors as compared with corresponding normal kidney tissues (16), although no significant correlation was noted between the mRNA level and the clinicopathological features of RCCs. *CDKN1C* has been known to induce cell cycle arrest by inhibiting the activity of cyclin dependent kinases. Epigenetic silencing of this gene has been reported in solid tumors such as colorectal, gastric, hepatocellular, and pancreatic cancers (17), suggesting that *CDKN1C* functions as

a tumor suppressor gene. *GAS1* was also significantly down-regulated in 14 of 15 cases in this study. Induction of *GAS1* has been reported to suppress cell proliferation and/or leading to apoptosis in neuron cells, and expression of *GAS1* decreased glial proliferation (19).

Among the up-regulated genes in our list, in this study we focused on Semaphorin 5B (*SEMA5B*) as a possible molecular target for RCC therapy due to frequent transactivation in RCCs and its undetectable level of expression in any of the normal human adult tissues we examined. We demonstrated that the knock-down of its expression level with siRNA resulted in the specifically significant suppression of RCC cell growth, suggesting its essential role in enhancement of cell growth. *SEMA5B* is a family of cell-surface and secreted glycoproteins that belong to a diverse group of genes encoding growth guidance cues (32). Semaphorins and their receptors, plexins, were originally identified in the nervous system, where they are required to establish the correct neuronal network. Their repertoire has been expanded to several non-neural processes, including cardiac and skeletal development, the immune response and epithelial morphogenesis. More recently, semaphorins have been implicated in tumour growth and metastasis (33). We demonstrated that *SEMA5B* is frequently expressed in the clear cell type of RCC as well as RCC cell lines, implying that targeting the *SEMA5B* might be a promising approach for development of novel therapeutic drugs.

Taken together, the up-regulated genes identified through our precise RCC-expression profiles should shed light on a better understanding of renal carcinogenesis and provide useful information to discover possible novel molecular targets for development of RCC treatment and also diagnostic tumor markers.

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