

Supplementary Table 1**Changes in gene expression in pons/medulla after chronic levetiracetam treatment.**

Rats received levetiracetam, 150 mg/kg, or control solution perorally twice per day for 90 days. Changes in gene expression were noted for 65 genes in pons/medulla, of which 41 were identified or similar to known genes or predicted (P) gene sequences.

Source		log2	
accession	symbol	ratio	gene name
Ion channels, transporters and extracellular signaling			
AI408417	Pdcl	1.15	phosducin-like
BC088395	Dao1	1.02	D-amino acid oxidase
BC091136	Cxcr3	0.81	chemokine (C-X-C motif) receptor 3
AF080453	Slc23a2	0.77	solute carrier family 23 (nucleobase transporters), member 2
AF070475	Slc4a7	0.74	solute carrier family 4, Na+/HCO3- cotransporter, member 7
AW529457	Kcna4	0.61	K voltage-gated channel, shaker-related subfamily, member 4
BF415436	Pcdh9 (P)	0.60	Protocadherin 9
BC083173	Acvrl1	-0.59	activin A receptor type II-like 1
NM_017346	Cacnb1	-0.61	Ca channel,

			voltage-dependent, beta 1 subunit
AF247451	Hcn2	-0.78	hyperpolarization activated cyclic nucleotide-gated K channel 2
Intracellular signal transduction			
AI177433	Ppp1cb	0.74	Protein phosphatase 1, catalytic subunit, beta isoform
CB579357	Spred1 (P)	0.68	Sprouty protein with EVH-1 domain 1, related sequence
AY724501	Kctd3 (P)	0.65	K channel tetramerisation domain containing 3
AF305618	Khdrbs2	0.63	KH domain containing, RNA binding, signal transduction associated 2
BC091203	Prkx	0.62	Protein kinase, X- linked
CR473766	LOC502685	-0.60	similar to interferon regulatory factor 10
CB579601	Phldb1	-0.63	pleckstrin homology-like

			domain, family B, member 1
CB327478	Arhgef1	-0.68	Rho guanine nucleotide exchange factor (GEF) 1
Transcription/translation			
CB717774		1.27	Similar to zinc finger protein 426 (Zfp426)
CO563017	Lsm1 (P)	0.70	LSM1 homolog, U6 small nuclear RNA associated
AW253109	Gle11 (P)	0.68	GLE1 RNA export mediator-like (yeast)
AI236628	RGD1565867	0.63	Similar to 60S ribosomal protein L7a
AF372090	Psip1	0.61	PC4 and SFRS1 interacting protein 1
AI411264	Vars2l	-0.61	valyl-tRNA synthetase 2-like
BQ199692	Hdac10	-0.65	histone deacetylase 10
BC087668	Dbp	-0.66	D site albumin promoter binding protein
CB547923	Dnmt2 (P)	-0.89	DNA methyltransferase 2

Replication/DNA repair

BI288826	Ccnh	0.84	cyclin H
BU760481	Ccna1	0.75	cyclin A1
AW534902	Smc2l1 (P)	0.63	SMC2 structural maintenance of chromosomes 2- like 1 (yeast)
BI288925	Nap1l2	0.61	nucleosome assembly protein 1- like 2
AI007875	Xrcc1	-0.70	X-ray repair complementing defective repair in Chinese hamster cells 1

Cytoskeleton/cell adhesion

BE101868	Itgb8 (P)	0.75	Integrin beta 8
CK838524	Des	0.64	desmin
BC092587	Itga7	0.62	integrin alpha 7

Metabolism

BF402481	LOC361014	0.70	similar to peptide N-glycanase
AI548891	Papd4	0.63	PAP associated domain containing 4
AA945172	Lap3	0.63	leucine aminopeptidase 3
XM_576452	LOC501040	0.60	similar to nicotinamide nucleotide adenylyltransferase

3

AI112140	Serinc1	0.60	serine incorporator 1
BM386322	Hsd17b12	-0.60	hydroxysteroid (17-beta) dehydrogenase 12

Supplementary Table 2**Differentially expressed transcripts in hippocampus after chronic phenytoin**

Source Accession	Symbol	log2ratio	Rat UniGene Title
Ion channels, transporters, extracellular signaling			
AY724501	Kctd3	0.72	Potassium channel tetramerisation domain containing 3 (P)
CB327348	Grin1	0.69	Glutamate receptor, ionotropic, N-methyl D-aspartate 1
M59980	Kcnd2	0.63	Potassium voltage gated channel, Shal-related family, member 2
XM_238093	Ltbp4	0.63	Latent transforming growth factor beta binding protein 4 (P)
CV797322	Cx3cl1	0.6	Chemokine (C-X3-C motif) ligand 1

J05167	Slc4a3	0.59	Solute carrier family 4, member 3
AI170314	Cfh	-0.65	Complement component factor H
CA508381	C2	-0.7	Complement component 2
X03036	Crh	-0.88	Corticotropin releasing hormone
BQ189922	Adrb3	-1.06	Adrenergic receptor, beta 3
Intracellular signal transduction			
AF451975	Caskin1	0.74	Cask-interacting protein 1
AF112257	Ryr2	0.64	Ryanodine receptor 2, cardiac
CR460619	Sipa1l1	0.62	Signal-induced proliferation- associated 1 like 1
Transcription/translation			
CB324150	RGD:708405	0.86	CTD-binding SR- like rA1
BI281745	Pbx1	0.86	Pre-B-cell leukemia transcription factor 1 (P)
AA851841	Sart3	0.74	Squamous cell carcinoma antigen recognized by T- cells 3 (P)
BI285893	Helz	0.62	Helicase with zinc finger domain (P)
BQ781853	Rai1	0.61	Retinoic acid

BC087665	Rsrc1	-0.65	induced 1 (P) arginine-serine-rich coiled-coil 1
Replication/DNA repair			
BI288925	LOC317247	-0.73	Nap1l2
Cytoskeleton/cell adhesion			
BF386446	Slit3	1.11	Slit Homolog 3
BF409144	Igsv4a	0.65	Immunoglobulin superfamily, member 4A (P)
NM_022401	Plec1	0.64	Plectin 1
CK840124	Lama2	0.61	Laminin, alpha 2 (P)
CB701422	Mapre3	0.61	Microtubule- associated protein, RP/EB family, member 3
AI677633	Epb4.9	-0.69	Erythrocyte protein band 4.9 (P)
BF410497	Ank3	-0.79	Ankyrin 3, epithelial isoform g
Metabolism			
AW521418	Atpaf1	-0.61	ATP synthase mitochondrial F1 complex assembly
BC091358	LOC500954	-0.64	Ubiquitin-Like 5 Protein
AA945172	Lap3	-0.71	Leucine aminopeptidase 3 (P)
CO563017	Lsm1	-0.73	LSM1 homolog, U6 small nuclear RNA

associated (P)

Supplementary Table 3

Differentially-expressed transcripts in frontal cortex after chronic phenytoin

Source accession	Gene Symbol	log2 ratio	rat unigene title
Ion channels, transporters and extracellular signaling			
CX570045	Sypl	1.61	synaptophysin-like protein; pantophysin
AF332142	Pcyox1	1.50	Chloride ion pump-associated 55 kDa protein
AI228929	Bai3	1.28	Brain-specific angiogenesis inhibitor 3 (P)
BF404398	RGD:1562096	1.06	Similar to opioid growth factor receptor
XM_574923	Bbs7	1.05	Bardet-Biedl syndrome 7 (P)
X03036	Crh	1.01	Corticotropin releasing hormone
AA817752	Snx2	0.98	Sorting nexin 2 (P)
AI009372	Fgf12	0.96	Fibroblast growth factor 12
AI232887	Mtx2	0.92	Metaxin 2 (P)
BF404562	Gabrg2	0.88	Gamma-aminobutyric acid A receptor, gamma 2
AI171975	Sh3yl1	0.88	SEC24 related gene family, member A (<i>S. cerevisiae</i>) (P)
CB695754	Nr2f1	0.81	Nuclear receptor subfamily 2, group F, member 1
XM_214331	Klhl2	0.76	Kelch-like 2, Mayven (<i>Drosophila</i>) (P)
CB556667	Klhl7	0.76	Kelch-like 7 (<i>Drosophila</i>)

			(P)
AA819421	Nup153	0.76	Nucleoporin 153kD
AW526521	Gpm6a	0.71	Glycoprotein m6a
CB733855	Golga3	0.69	Golgi autoantigen, golgin subfamily a, 3 (P)
CB323230	RGD:735095	0.65	Similar to Protein KIAA1688 homolog
BF552272	Ppil4	0.59	Peptidylprolyl isomerase (cyclophilin)-like 4 (P)
BF283385	Aaas	-0.66	Achalasia, adrenocortical insufficiency, alacrimia (P)
AI409651	Clcn6	-1.01	Similar to putative chloride channel protein CLC6
Intracellular signal transduction			
AI408417	Pdcl	1.51	phosducin-like
AF305618	Khdrbs2	1.50	KH domain containing, RNA binding, signal transduction associated 2
U78517	Rapgef4	1.43	CAMP-regulated guanine nucleotide exchange factor II
CB692530	Ranbp6	1.25	RAN binding protein 6 (P)
BG667328		1.07	Similar to protein phosphatase 2C domain containing protein
BC086357	RGD1308119	0.99	Similar to F-box protein FBL2 (P)
AI045974	Sh3yl1	0.99	Sh3 domain YSC-like 1 (P)
BI293175	Riok2	0.93	RIO kinase 2 (yeast) (P)
AI144754	Ddx23	0.89	Rho family GTPase 1 (P)
AW920244	Hook3	0.86	Hook homolog 3

AA964459	Dyrk2	0.85	Dual-specificity tyrosine-(Y)-phosphorylation regulated kinase 2 (P)
AY769991	LOC493574	0.83	Notch1-induced protein
CB729338	Pard6g	0.81	Par-6 partitioning defective 6 homolog gamma (C. elegans) (P)
AI169016	Plcl1	0.80	Phospholipase C-like 1
XM_235823	RGD1309884	0.79	Similar to translokin (P)
AA945483	Lrba	0.74	LPS-responsive beige-like anchor (P)
XM_342634	LOC362317	0.74	Similar to krev interaction trapped-1A
CF113908	Hrmt1l3	0.73	arginine N-methyltransferase 3 (PRMT3)
BF281863		0.70	strongly similar to serum/glucocorticoid regulated kinase 3
AW144433	Akap10	0.70	A kinase (PRKA) anchor protein 10 (P)
BF561395	Nkd2	0.68	Naked cuticle 2 homolog (Drosophila) (P)
CB544812	Map3k4	0.68	Mitogen activated protein kinase kinase kinase 4 (P)
CB579357	Spred1	0.67	Sprouty protein with EVH-1 domain 1, related sequence (P)
CB693316	Cpne1	0.66	Copine I (P)
AY004875	Arfip1	0.64	ADP-ribosylation factor interacting protein 1

AI177433	Ppp1cb	0.64	Protein phosphatase 1, catalytic subunit, beta isoform
XM_575385	RGD:1563764	0.61	Similar to PHD finger protein 14 isoform 1
XM_578400	RGD:1565949	0.61	Similar to neuronal interacting factor X 1 (NIX1)
AF275266	Pdrp	-0.64	PDRP protein
XM_342612	Centg3	-0.81	Centaurin, gamma 3 (P)
XM_343552	Ptpn18	-0.89	Protein tyrosine phosphatase, non-receptor type 18 (P)
AF451975	Caskin1	-0.99	Cask-interacting protein 1
Transcription/translation			
CB742460	Zfml	1.50	Zinc finger, matrin-like (P)
CK218800	Fmr1	1.45	Fragile X mental retardation syndrome 1 homolog
XM_575140	Rbms1	1.44	RNA binding motif, single stranded interacting protein 1 (P)
AI178112	Ndnl2	1.32	Necdin-like 2 (P)
AI172236	Crsp9	1.23	Cofactor required for Sp1 transcriptional activation, subunit 9 (P)
XM_224894	Cnot7	1.16	CCR4-NOT transcription complex, subunit 7 (P)
AA800994	Ptbp2	1.12	Polypyrimidine tract binding protein 2
XM_227104	Zfp131	1.08	Zinc finger protein 131 (P)
AI100897	Vars2	1.03	Valyl-tRNA synthetase 2

BC087155	RGD1310161	1.02	Similar to DNA segment, Chr 8, ERATO Doi 233, expressed (P)
XM_214003	Mrps18c	0.96	Mitochondrial ribosomal protein S18C (P)
XM_224510	RGD1308297	0.96	Similar to CG10084-PA (P)
BC070932	Taf9l	0.94	TAF9-like RNA polymerase II
AF372090	Psip1	0.94	PC4 and SFRS1 interacting protein 1
BF415922	Dhx9	0.92	DEAH (Asp-Glu-Ala-His) box polypeptide 9 (P)
BF545357	Zipro1	0.91	Zinc finger proliferation 1 (P)
AI235601	RGD:1563860	0.88	Similar to ribosomal protein S6 kinase 2
XM_341180	Mtf2	0.87	Metal-response element-binding transcription factor 2
AJ278466	Cdx2	0.85	Caudal type homeo box 2
AI236628		0.84	Similar to 60S ribosomal protein L7a
BI293915	Qki	0.83	Similar to QUAKING isoform 6
AA944589	Cpsf6	0.82	Cleavage and polyadenylation specific factor 6, 68kDa (P)
BC093607	LOC317163	0.82	Eukaryotic translation initiation factor 1A (P)
CF978846	Ap1s2	0.81	adaptor related protein complex 1, sigma 2 subunit

			(P)
XM_342684	Hnrrpa2b1	0.79	Heterogeneous nuclear ribonucleoprotein A2/B1
			(P)
XM_347237	LOC368070	0.77	Similar to pinin
NM_017086	Egr3	0.75	Early growth response 3
BF281146	Nr3c1	0.73	Nuclear receptor subfamily 3, group C, member 1
AA942929	Npas2	0.73	Neuronal PAS domain protein 2 (P)
BE108412	Terf1	0.72	Similar to telomeric repeat binding factor 1 [Rattus norvegicus] P
AI179013	Rbm3	0.71	RNA binding motif (RNP1, RRM) protein 3
BQ781897	Gnl2	0.71	Guanine nucleotide binding protein-like 2
BF283760	Ldb2	0.71	LIM domain binding 2 (P)
XM_233812	LOC313837	0.70	Similar Glutaminyl-tRNA cyclotransferase
BF416550		0.68	Similar to WW-domain oxidoreductase
XM_226380	Smarca5	0.67	SWI/SNF related (P)
AI232908	Rg9mtd3	0.65	RNA (guanine-9-) methyltransferase domain containing 3 (P)
AI230884	Clp1	0.65	Cardiac lineage protein 1
BF547277	Mycbp	0.63	C-myc binding protein (P)
XM_223786	Zfp503	0.63	Zinc finger protein 503 (P)
BF418812	Tceal1	0.63	Transcription elongation factor A (SII)-like 1

BG670370	Isgf3g	0.62	Interferon dependent positive acting transcription factor 3 gamma (P)
BI294916	Klf2	0.60	Rattus norvegicus Kruppel-like factor (Klf2), mRNA (P)
CK841084	Whsc2	-0.61	Wolf-Hirschhorn syndrome candidate 2 (P)
Replication			
BI288925	LOC317247	1.41	Similar to Nap1l2
CF109508	Trp53bp2	1.03	Transformation related protein 53 binding protein 2 (P)
CK223547	Smc5l1	1.00	structural maintenance of chromosomes 5-like 1 (P)
AW534902	Smc2l1	0.98	SMC2 structural maintenance of chromosomes 2-like 1 (yeast) (P)
BI298690	Ccnc	0.85	Cyclin C
CB793611	Ccnt2	0.79	Cyclin T2 (P)
AI501936	LOC317575	0.74	Similar to Smarca1 protein
Cytoskeleton/cell adhesion			
BE107259	Fndc3a	2.44	Fibronectin type III domain containing 3 (P)
BF415436	Pcdh9	1.82	Protocadherin 9 (P)
BE101868	Itgb8	1.19	Integrin beta 8 (predicted)
AI599327	Itgb3bp	1.08	Integrin beta 3 binding protein (beta3-endonexin) (P)
BF391491	Col10a1	1.06	5'-nucleotidase, cytosolic

			II-like 1 (P)
CB765491		0.97	Phosphatidylinositol glycan, class B (P)
BE120827	Ipp	0.93	IAP promoted placental gene (P)
CX569401	RGD1564871	0.91	Similar to Thioredoxin domain containing protein 6
BE118227	Cbl11	0.90	Casitas B-lineage lymphoma-like 1 (P)
Metabolism			
AA945172	Lap3	3.96	Leucine aminopeptidase 3 (P)
NM_021769	Sult1d1	2.12	Sulfotransferase family 1D, member 1
CB326787	Ptgs2	1.86	Prostaglandin-endoperoxide synthase 2
BQ782625	RGD:708530	1.58	Cytochrome P450, family 4, subfamily v, polypeptide 3 (P)
CB614058	Psmc6	1.33	Proteasome (prosome, macropain) 26S subunit, ATPase, 6 (P)
AA943306	Gnpda2	1.26	Glucosamine-6-phosphate deaminase 2 (P)
CF113680	Mthfd1l	1.22	Methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 1-
			like (P)
BC081751	Yme111	1.16	YME1-like 1 (<i>S. cerevisiae</i>)
U13176	Ube2d2	1.11	Ubiquitin-conjugating enzyme E2D 2

BF547130	Fbxl3a	0.95	F-box and leucine-rich repeat protein 3a (P)
AI171206	Zfp364	0.94	Zinc finger protein 364 (P)
BI284033	Car6	0.93	Carbonic anhydrase 6 (P)
AI069981	Senp7	0.91	SUMO1/sentrin specific protease 7 (P)
AA925355	Rkhd1	0.88	Ring finger (C3HC4 type) and KH domain containing 1 (P)
AI177273	LOC361181	0.88	Similar to cullin 4A
AI010637	LOC361014	0.87	Similar to peptide N-glycanase
CN542202	Mgat2	0.87	Alpha-1,6-mannosyl-glycoprotein 2-beta-N-acetylglucosaminyltransferase
AI170993	Adamts9	0.85	disintegrin-like metalloprotease with thrombospondin type 1 motif, 9 (P)
BI273816	Cyp20a1	0.84	Cytochrome P450, family 20, subfamily A, polypeptide 1
XM_233345	Zcchc11	0.84	Zinc finger, CCHC domain containing 11 (P)
BC083823	Fbxo30	0.83	F-box only protein 30
BF283070	Cyp7b1	0.79	Cytochrome P450, family 7, subfamily b, polypeptide 1
BC079007	RGD:1303146	0.77	Similar to calcyclin binding protein
AB067814	RGD:620449	0.77	Seven in absentia 1A
AW918051	LOC316122	0.76	CGI-58-like protein

AA997435	LOC500629	0.74	Similar to alcohol dehydrogenase PAN2
BG666167	Adam32	0.73	A disintegrin and metalloproteinase domain 9 (P)
CB580139	LOC501157	0.67	Similar to Ribulose-5-phosphate-3-epimerase
XM_574749	Herc4	0.65	Hect domain and RLD 4 (P)
AI235574		0.65	Similar to ubiquitin-protein ligase E3-alpha
AA996520	MGC109340	0.65	Similar to Microsomal signal peptidase 23 kDa subunit
CR477228	Psmd12	0.63	Proteasome 26S non-ATPase subunit 12
AI233261	Gclm	0.63	Glutamate cysteine ligase, modifier subunit
CB794901	Cmpk	0.63	Cytidylate kinase
CK842957	Parg	0.61	Poly (ADP-ribose) glycohydrolase
AA851922	Lypla1	0.60	Lysophospholipase 1
XM_341334	Ebpl	0.60	Emopamil binding protein-like (P)
AA893261	Inpp5f	0.59	Inositol polyphosphate-5-phosphatase F (P)
CB324902	B4galt7	-0.62	Xylosylprotein beta1,4-galactosyltransferase, polypeptide 7 (P)
BC091209	Rnaseh1	-0.86	Ribonuclease H1 (P)