Supplementary Data

Table S1

SGCE coding-region sequence variants (SVs) in each exon (nonsynonymous, frameshift, nonsense)

Exon	Nucleotide (NM_001099401.1) ENST00000445866	Protein (NP_001092871.1)	SV in ExAC database	Average alleles checked	Variant/AA ratio (adjusted)*
1	112-220	1-36	17	116008	0.47
2	221-343	37-77	17	120876	0.40
3	344-501	78-130	12	115661	0.23
4	502-574	131-154	14	113264	0.60
5	575-773	155-220	20	120841	0.29
6	774-936	221-275	15	115108	0.27
7	937-1148	276-345	25	114536	0.36
8	1149-1175	346-354	4	120635	0.43
9	1176-1364	355-417	17	121264	0.26
10	1365-1439	418-442	2	110	0.08**
11	1440-1483	443-457	3	121055	0.19
12	1484-1497	458-462	2	121380	0.38
Brain specific	**NM_001099400.1**	**NP_001092870.1**			
11b	1382-1416	424-435	1	23032	0.08**
12b	1417-1464	436-451	4	121369	0.24

*Adjusted relative to the 116008 alleles that included exon 1. **Not adjusted due to small sample size.

Table S2

Primers for genotyping, QRT-PCR, and Sanger sequencing

Primer	Sequence (5’→3’)	Locus	Usage	Product (bp)
Sgce_Int_G1F	atgggtcgctccatgtgta	NC_000072 4684570 - 551	mouse genotyping	
Sgce_Int_G1R	gccccagacattttcctgta	NC_000072 4684019 - 037	mouse genotyping	552 (with Sgce_Int_G1F)
Sgce_KO_V2L	gttcgcttctcgcttctgtt	Gene trap vector	mouse genotyping	393 (with Sgce_Int_G1R)
Sgce_Q85F	gggtgaatttccaccttatcc	NM_001130189 320 - 340	QRT-PCR	
Sgce_Q85R	actgtacggggtcctttgg	NM_001130189 446 - 428	QRT-PCR for all isoforms	127 (with Sgce_Q85F)
Sgce_Q98F	tcccatgcacacagacaact	NM_001130189 1286 - 1305	QRT-PCR	
Sgce_Q98R	gggatctgagtctggtgtgg	NM_001130189 1369 - 1350	QRT-PCR for long isoforms	84 (with Sgce_Q98F)
Sgce_E9F	ttcgagacatgtccaaaaaca	NM_001130189 1201 - 1221	QRT-PCR	
Sgce_E11bR	agttgtcaaacgaaaatctcctg	NM_001130189 1406 - 1384	brain-specific isoform	206 (with Sgce_E9F)
β_Gal_R1	gttgcaccacagatgaaacg	Gep-SD5 Vector 1214 - 1195	fusion transcript	716 (with Sgce_E9F)
β_Gal_R2	ggcgattaagttgggtaacg	Gep-SD5 Vector 828 - 809	fusion transcript	329 (with Sgce_E9F)
Nr4a3_Q52F	cagtgtcgggatggttaagg	NM_015743 1653 - 1672	QRT-PCR	
Nr4a3_Q52R	tagtgggctctttggtttgg	NM_015743 1740 - 1621	QRT-PCR	88 (with Nr4a3_Q52F)
Dusp1_Q17F	gtgcctgacagtgcagaatc	NM_013642 606 - 625	QRT-PCR	
Dusp1_Q17R	cactgcccaggtacaggaag	NM_013642 705 - 686	QRT-PCR	100 (with Dusp1_Q17F)
Cdkn1a_Q21F	tccacagcgatatccagaca	NM_007669 67 - 86	QRT-PCR	
Cdkn1a_Q21R	ggacatcaccaggattggac	NM_007669 126 - 107	QRT-PCR	60 (with Cdkn1a_Q21F)
Eomes_Q9F	accggcaccaaactgaga	NM_010136 1319 - 1336	QRT-PCR	
Eomes_Q9R	aagctcaagaaaggaaacatgc	NM_010136 1382 - 1361	QRT-PCR	64 (with Eomes_Q9F)
Spry4_Q17F	gtggagcgatgcttgtgac	NM_011898 65 - 83	QRT-PCR	
Spry4_Q17R	caccaagggacaggcttcta	NM_011898 125 - 106	QRT-PCR	61 (with Spry4_Q17F)
Slc41a3_Q5F	gccctcatgagcagtttctt	NM_027868 871 - 890	QRT-PCR	
Slc41a3_Q5R	gaccagaggcgtcagatacc	NM_027868 930 - 911	QRT-PCR	60 (with Slc41a3_Q5F)
S100a13_Q17F	ttagctgcatcccaccttct	NM_009113 268 - 287	QRT-PCR	
S100a13_Q17R	tgctgccatcagtataccaaa	NM_009113 342 - 322	QRT-PCR	75 (with S100a13_Q17F)
Socs2_Q60F	cgcgagctcagtcaaaca	NM_007706 583 - 600	QRT-PCR	
Socs2_Q60R	agttccttctggagcctctttt	NM_007706 669 - 648	QRT-PCR	87 (with Socs2_Q60F)
Capza2_Q12F	agccatcagtttcaagcaaaa	NM_007604 502 - 522	QRT-PCR	
Capza2_Q12R	aatgccaaccacctgtgtg	NM_007604 597 - 579	QRT-PCR	96 (with Capza2_Q12F)
Mios_Q9F	cagagtggcattcgcttgta	NM_145374 2129 - 2148	QRT-PCR	
Mios_Q9R	tcatttcattggtcagcttttc	NM_145374 2205 - 2184	QRT-PCR	77 (with Mios_Q9F)
Ica1_Q48F	aagcaatcgtgctctatcaaaa	NM_010492 710 - 731	QRT-PCR	
Ica1_Q48R	ggaagccttgagatcgaaga	NM_010492 796 - 777	QRT-PCR	87 (with Ica1_Q48F)
Nr4a2_Q64F	tcagagcccacgtcgatt	NM_013613 1551 - 1568	QRT-PCR	
Nr4a2_Q64R	tagtcagggtttgcctggaa	NM_013613 1623 - 1604	QRT-PCR	73 (with Nr4a2_Q64F)
Pomt2_Q60F	tggagacctcagcctttcac	NM_153415 1279 - 1298	QRT-PCR	
Pomt2_Q60R	cacaggatgcgagcagttag	NM_153415 1338 - 1319	QRT-PCR	60 (with Pomt2_Q60F)
Sgca_Q66F	catcgaggtcacagcctaca	NM_009161 559 - 578	QRT-PCR	
Sgca_Q66R	aactcagcttggtatggcaac	NM_009161 666 - 646	QRT-PCR	108 (with Sgca_Q66F)
Sgcb_Q11F	tggtcatcactggcaacaac	NM_011890 428 - 447	QRT-PCR	
Sgcb_Q11R	caacactcagcttggtcgtc	NM_011890 490 - 471	QRT-PCR	63 (with Sgcb_Q11F)

Table S3

Expression of *Sgce* in one-month-old gene-trap mice. Primers 1 (85F/85R), all isoforms. Primers 2 (98F/98R), long isoforms. Primers 3 (E9F/E11bR), brain-specific isoform. Primers 4 (E9F/β-gal_R2), *Sgce*/*lacZ* fusion transcript. QRT-PCR values are referenced to wild-type (*Sgce*$^{+/+}$) cerebral cortex and presented as means ± SEM (n = 3 mice/genotype). *Sgce*$^{m+/pGt}$, *Sgce*$^{mGt/p+}$, and *Sgce*$^{mGt/pGt}$ indicate paternal heterozygotes, maternal heterozygotes, and homozygotes, respectively.

Genotype	**Cerebral cortex**					**Cerebellum**				
	Primers 1	Primers 2	Primers 3	Primers 4		Primers 1	Primers 2	Primers 3	Primers 4	
				Random	Oligo(dT)				Random	Oligo(dT)
Sgce$^{+/+}$	1.00 ± 0.05	1.00 ± 0.09	1.00 ± 0.06	0.00 ± 0.00	0.00 ± 0.00	1.86 ± 0.09	1.21 ± 0.08	0.94 ± 0.05	0.00 ± 0.00	0.00 ± 0.00
Sgce$^{m+/pGt}$	0.31 ± 0.02	0.00 ± 0.00	0.00 ± 0.00	0.18 ± 0.03	0.09 ± 0.01	0.57 ± 0.04	0.00 ± 0.00	0.00 ± 0.00	0.30 ± 0.08	0.16 ± 0.03
Sgce$^{mGt/p+}$	0.99 ± 0.03	0.98 ± 0.03	0.94 ± 0.02	0.00 ± 0.00	0.00 ± 0.00	1.83 ± 0.08	1.18 ± 0.06	0.97 ± 0.04	0.00 ± 0.00	0.00 ± 0.00
Sgce$^{mGt/pGt}$	0.29 ± 0.03	0.00 ± 0.00	0.00 ± 0.00	0.15 ± 0.03	0.08 ± 0.01	0.54 ± 0.03	0.00 ± 0.00	0.00 ± 0.00	0.28 ± 0.06	0.15 ± 0.03

Table S4
Rating scale for abnormal movements

Abnormal Movement	Scoring
Face - All Abnormal Movements	0, 1, 2, 3, or 4
Face Tonus	0 or 1
Face Clonus	0 or 1
Face Tremor	0 or 1
Neck - All Abnormal Movements	0, 1, 2, 3, or 4
Neck Tremor	0 or 1
Neck Twisting	0 or 1
Neck Bobbing	0 or 1
Neck Wagging	0 or 1
Neck Sustained Extension	0 or 1
Neck Sustained Flexion	0 or 1
Trunk - All abnormal movements	0, 1, 2, 3, or 4
Trunk Tremor	0 or 1
Trunk Twisting	0 or 1
Trunk Sustained Extension	0 or 1
Trunk Sustained Flexion	0 or 1
Forelimb - All Abnormal Movements	0, 1, 2, 3, or 4
Forelimb Tremor	0 or 1
Forelimb Twisting	0 or 1
Forelimb Clonus	0 or 1
Forelimb Sustained Extension	0 or 1
Forelimb Sustained Flexion	0 or 1
Hindlimb - All Abnormal Movements	0, 1, 2, 3, or 4
Hindlimb Tremor	0 or 1
Hindlimb Twisting	0 or 1
Hindlimb Clonus	0 or 1
Hindlimb Sustained Extension	0 or 1
Hindlimb Sustained Flexion	0 or 1

Definitions: wagging - head moving repeatedly from side to side, bobbing - head moving repeatedly up and down, clonus - repeated rhythmic abnormal movements, tonus - sustained abnormal movement/posture involving muscle contractions (i.e., a hindimb extended caudally because the animal was too weak to pull it back would not be considered tonus)

Table S5

Spectral counts and protein coverage for sarcoglycan (SG) peptides in immunoaffinity purifications of ε-SG from whole brain of wild-type and *Sgce*$^{m+/pGt}$ mice. Complexes containing ε-SG were captured using esg3788 (all ε-SG isoforms) and esg2-1358 (ε-SG “brain-specific”) antibodies. Eluted proteins were analyzed via mass spectrometry. Spectral counts for each SG and the percent of the SG protein covered by peptides identified in the mass spectrometry analysis are provided for each immunoaffinity purification (IAP).

Protein	UniProt accession number	esg3788 IAP				esg2-1358 IAP			
		Wild-type		*Sgce*$^{m+/pGt}$		Wild-type		*Sgce*$^{m+/pGt}$	
		Spectral count	Protein coverage	Spectral count	Protein coverage	Spectral count	Protein coverage	Spectral count	Protein coverage
ε-SG	O70258	9	16.16%	1	2.54%	2	5.08%	0	0.00%
β-SG	P82349	17	30.31%	2	11.56%	8	23.44%	0	0.00%
δ-SG	P82347	13	33.22%	5	26.56%	8	26.99%	0	0.00%
ζ-SG	Q8BX51	8	29.90%	2	8.72%	10	39.23%	0	0.00%

Table S6

Biogenic monoamines in 3-month old wild-type (WT) and *Sgce*$^{m+/pGt}$ mice. Values are means (ng/mg protein) ± SEM. DOPAC, 3,4-dihydroxyphenylacetic acid; DA, dopamine; 5-HIAA, 5-hydroxyindoleacetic acid; HVA, homovanillic acid; 5-HT, 5-hydroxytryptophan; 3-MT, 3-methoxytyramine. There were no significant effects of genotype.

Gender, Genotypes (numbers)	**Noradrenaline**	**DOPAC**	**DA**	**5-HIAA**	**HVA**	**5-HT**	**3-MT**
M, WT (n=3)	0.98±0.11	16.37±0.57	115.30±8.45	5.31±0.25	14.74±0.35	7.46±0.65	11.70±0.63
M, *Sgce*$^{m+/pGt}$ (n=3)	1.32±0.49	15.95±2.97	121.81±3.34	7.84±2.52	18.96±3.24	8.94±1.56	11.94±1.39
F, WT (n=3)	0.87±0.15	16.22±1.18	134.47±6.63	6.75±0.38	17.94±0.22	8.40±0.60	12.48±1.55
F, *Sgce*$^{m+/pGt}$ (n=3)	2.63±1.15	12.96±2.34	102.36±23.14	6.69±0.39	12.73±2.47	11.23±2.41	9.66±1.70

Table S7

Expression of genes that contribute to the dystrophin-glycoprotein complex. *Raw expression value in cerebellum as reported by BioGPS (biogps.org, maximum value chosen if multiple probesets existed). **Qualitative assessment of Allen Brain Atlas in situ hybridization images.

Gene Symbol	**Description**	**Average intensity values**		**Fold change**	***p* value**	**BioGPS**	**Allen Brain Atlas***
		Wild-type	***Sgce*$^{m+/pGt}$**			**Level***	**Cerebellum**
Agrin	Agrin proteoglycan	266.8±7.9	261.8±4.8	-1.02	0.603	267.8	All neurons
Alg14	Asparagine-linked glycosylation 14 homolog (yeast)	428.2±13.0	440.9±8.1	1.03	0.428	126.3	All neurons
Alg2	Asparagine-linked glycosylation 2 homolog (yeast, alpha-1,3-mannosyltransferase)	852.2±10.7	883.6± 8.1	1.04	0.041	1225.1	All neurons
Ank2	Ankyrin 2, brain	3438.3±34.6	3336.2±36.1	-1.03	0.068	11768.5	High in Purkinje cells
Arhgef9	CDC42 guanine nucleotide exchange factor (GEF) 9	1620.0±10.5	1548.4±27.0	-1.04	0.033	371.5	High in Purkinje cells
B3Galnt2	UDP-GalNAc:betaGlcNAc beta 1,3-galactosaminyltransferase, polypeptide 2	311.9± 5.1	315.0±11.1	1.01	0.806	138.6	High in Purkinje cells
B3Gnt1	UDP-GlcNAc:betaGal beta-1,3-N-acetylglucosaminyltransferase 1	450.3±6.1	435.7±7.1	-1.03	0.148	801.7	High in Purkinje cells
Bgn	Biglycan	85.8± 2.6	82.2± 3.7	-1.04	0.441	74.0	All neurons
Calm1	Predicted gene 7743; calmodulin 3; calmodulin 2; calmodulin 1; predicted gene 7308	2760.5±47.9	2766.7±40.3	1.00	0.923	76182.8	High in Purkinje cells
Cav3	Caveolin 3	54.0±1.1	62.3±3.6	1.15	0.055	4.6	All neurons
Csk	c-src tyrosine kinase	199.6±2.9	199.0±5.6	-1.00	0.920	52.9	All neurons
Dag1	Dystroglycan 1	719.8±10.2	756.4±14.0	1.05	0.061	785.8	High in Purkinje cells
Dmd	Dystrophin, muscular dystrophy	335.3±7.5	331.3±6.4	-1.01	0.694	155.8	High in Purkinje cells
Drp2	Dystrophin related protein 2	313.8±4.2	310.9±8.8	-1.01	0.773	52.9	All neurons
Dtna	Dystrobrevin alpha	1772.4±30.0	1703.4±23.6	-1.04	0.100	1650.2	High in Purkinje cells
Dtnb	Dystrobrevin, beta	594.8±10.7	578.5±11.0	-1.03	0.314	90.1	High in Purkinje cells
Dtnbp1	Dystrobrevin binding protein 1	259.7±4.7	261.0±5.2	1.01	0.854	308.6	All neurons
Fkrp	Fukutin related protein	237.4±5.9	240.9±6.3	1.01	0.694	158.8	High in Purkinje cells
Fktn	Fukutin	325.8±9.7	297.1±13.1	-1.10	0.108	610.8	High in Purkinje cells
Fyn	Fyn proto-oncogene	541.6±9.0	518.8±10.8	-1.04	0.136	1180.7	High in Purkinje cells
Gne	Glucosamine	392.4±8.9	376.0±5.1	-1.04	0.141	97.6	All neurons
Grb2	Growth factor receptor bound protein 2; predicted gene 12791	544.7±13.6	531.4±6.7	-1.03	0.398	706.4	High in Purkinje cells
Hspg2	Perlecan (heparan sulfate proteoglycan 2)	161.8±2.5	161.4±4.6	1.00	0.946	37.2	All neurons
Ispd	RIKEN cDNA 4930579E17 gene	70.3±5.0	69.5±3.3	-1.01	0.890	5.8	All neurons
Lama2	Laminin, alpha 2	227.3±4.8	239.5±7.4	1.05	0.194	38.8	All neurons
Large	Like-glycosyltransferase	1444.4±16.1	1396.8±15.4	-1.03	0.059	982.3	High in Purkinje cells
Mapk12	Mitogen-activated protein kinase 12	1056.8±23.1	990.1±38.8	-1.07	0.171	360.8	All neurons
Nck1	Non-catalytic region of tyrosine kinase adaptor protein 1	540.0±8.4	525.9±5.8	-1.03	0.200	564.7	All neurons
Nl2	Neuroligin 2	1199.2±18.6	1213.4±20.4	1.01	0.620	713.1	High in Purkinje cells
Nos3	Nitric oxide synthase 3, endothelial cell	156.2±5.1	160.1±3.5	1.02	0.542	28.7	All neurons

Gene Symbol	**Description**	**Average Intensity Values**		**Fold Changes**	**p-value**	**BioGPS**	**Allen Brain Atlas**
		Wild Type	**Knockout**			**Level**	**Presence in Cerebellum**
Plec	Plectin 1	190.8±2.9	193.7±2.5	1.02	0.467	341.3	High in purkinje cells
Pomgnt1	Protein O-linked mannose beta1,2-N-acetylglucosaminyltransferase	251.6±3.2	250.2±4.4	-1.01	0.795	305.5	High in purkinje cells
Pomgnt2	Protein O-linked mannose beta 1,4-N-acetylglucosaminyltransferase 2	183.9±4.4	188.6±6.3	1.03	0.552	115.2	All cells
Pomt1	Protein-O-mannosyltransferase 1	215.6±6.7	219.8±4.9	1.02	0.629	83.6	High in purkinje cells
Pomt2	Protein-O-mannosyltransferase 2	518.1±7.7	514.2±4.8	-1.01	0.678	22.0	High in purkinje cells
Rapsn	Receptor-associated protein of the synapse	74.7±1.9	73.1±4.3	-1.02	0.733	4.6	High in purkinje cells
Sgca	Sarcoglycan, alpha (dystrophin-associated glycoprotein)	99.4±2.0	103.4±2.2	1.04	0.216	4.6	All cells
Sgcb	Sarcoglycan, beta (dystrophin-associated glycoprotein)	531.5±15.3	503.2±14.5	-1.06	0.209	545.5	High in purkinje cells
Sgcd	Sarcoglycan, delta (dystrophin-associated glycoprotein)	87.8±2.5	85.0±4.1	-1.03	0.581	4.6	All cells
Sgce	Sarcoglycan, epsilon	627.4±7.0	300.5±13.3	-2.09	9.13E-10	387.6	All cells
Sgcg	Sarcoglycan, gamma (dystrophin-associated glycoprotein)	63.2±1.7	62.3±2.2	-1.01	0.760	4.6	All cells
Sgcz	Sarcoglycan zeta	84.7±3.6	77.0±2.9	-1.10	0.135	no data	All cells
Shc1	Predicted gene 5500; src homology 2 domain-containing transforming protein C1	144.5±2.0	149.3±3.5	1.03	0.269	24.6	All cells
Slc35A3	Solute carrier family 35 (UDP-N-acetylglucosamine (UDP-GlcNAc) transporter), member 3	139.1±2.1	136.7±2.3	-1.02	0.298	245.2	All cells
Snap25	Synaptosomal-associated protein 25	10901.0±122.0	10903.3±144.1	1.00	0.991	57901.7	High in purkinje cells
Snta1	Syntrophin, acidic 1	172.1±4.1	174.1±4.2	1.01	0.732	38.3	All cells
Sntb1	Syntrophin, basic 1	68.0±2.4	62.2±3.6	-1.09	0.215	7.2	All cells
Sntb2	Syntrophin, basic 2	264.1±5.0	271.1±9.3	1.03	0.519	39.4	All cells
Sntg1	Syntrophin, gamma 1	102.3±1.5	100.2±4.3	-1.02	0.650	4.6	High in purkinje cells
Sntg2	Syntrophin, gamma 2	58.9±1.3	59.0±2.0	1.00	0.981	5.6	All cells
Src	Rous sarcoma oncogene	333.9±5.6	349.5±5.3	1.05	0.071	54.0	No data
Sspn	Sarcospan	62.3±1.9	60.5±2.5	-1.03	0.564	42.9	All cells
Stx1A	Syntaxin 1A (brain)	66.3±3.5	77.0±4.2	1.16	0.082	19.9	All cells
Syne1	Synaptic nuclear envelope 1	4266.7±52.6	4213.7±82.6	-1.01	0.517	8329.7	High in purkinje cells
Tmem5	Sransmembrane protein 5	202.5±4.0	187.1±5.2	-1.08	0.041	226.0	High in purkinje cells
Utrn	Utrophin	503.0±8.8	492.9±6.1	-1.02	0.368	467.8	High in purkinje cells

Table S8

Enriched KEGG pathways

Regulated	Pathway	No. of Genes	Enrichment[a]	Raw *p*[b]	Adj *p* value[c]
Up-Regulated					
1.10 Fold Change	Systemic lupus erythematosus	9	5.05	7.85E-05	5.30E-03
	Ribosome	7	5.13	4.00E-04	8.90E-03
	Osteoclast differentiation	8	4.80	3.00E-04	8.90E-03
	Primary bile acid biosynthesis	3	13.92	1.20E-03	2.01E-02
	Circadian rhythm - mammal	3	9.49	3.70E-03	4.13E-02
	RIG-I-like receptor signaling pathway	5	5.04	3.20E-03	4.13E-02
	Cytosolic DNA-sensing pathway	4	5.06	8.00E-03	7.66E-02
	Toll-like receptor signaling pathway	5	3.45	1.54E-02	1.23E-01
	Adipocytokine signaling pathway	4	4.09	1.66E-02	1.23E-01
	Apoptosis	4	3.35	3.18E-02	2.13E-01
1.15 Fold Change	Vitamin digestion and absorption	2	14.44	8.40E-03	4.51E-02
	Osteoclast differentiation	4	5.97	4.60E-03	4.51E-02
	Antigen processing and presentation	3	6.93	9.40E-03	4.51E-02
	Systemic lupus erythematosus	4	5.59	5.80E-03	4.51E-02
	Primary bile acid biosynthesis	2	23.10	3.30E-03	4.51E-02
	Ribosome	3	5.47	1.77E-02	7.08E-02
	Toll-like receptor signaling pathway	3	5.15	2.08E-02	7.13E-02
	Lysosome	3	4.23	3.45E-02	1.00E-01
	mTOR signaling pathway	2	6.54	3.76E-02	1.00E-01
	Hepatitis C	3	3.79	4.51E-02	1.08E-01
1.20 Fold Change	mTOR signaling pathway	2	14.63	8.30E-03	2.90E-02
	Osteoclast differentiation	3	10.03	3.40E-03	2.90E-02
	Jak-STAT signaling pathway	3	7.75	6.90E-03	2.90E-02
	Hepatitis C	3	8.49	5.40E-03	2.90E-02
	ErbB signaling pathway	2	8.91	2.13E-02	5.96E-02
	Toll-like receptor signaling pathway	2	7.68	2.81E-02	6.28E-02
	MAPK signaling pathway	3	4.37	3.14E-02	6.28E-02
	Systemic lupus erythematosus	2	6.25	4.08E-02	6.35E-02
	Lysosome	2	6.30	4.02E-02	6.35E-02
	Protein processing in endoplasmic	2	4.67	6.85E-02	9.59E-02
Down-Regulated					
1.10 Fold Change	B cell receptor signaling pathway	3	3.96	4.04E-02	2.52E-01
	T cell receptor signaling pathway	4	3.65	2.44E-02	2.52E-01
	African trypanosomiasis	2	6.30	3.99E-02	2.52E-01
	Mucin type O-Glycan biosynthesis	2	7.82	2.68E-02	2.52E-01
	Axon guidance	3	2.29	1.44E-01	5.18E-01
	Focal adhesion	4	1.96	1.48E-01	5.18E-01
	Long-term potentiation	2	2.92	1.50E-01	5.18E-01
	Insulin signaling pathway	3	2.14	1.65E-01	5.18E-01
	Apoptosis	2	2.35	2.08E-01	5.50E-01
	Small cell lung cancer	2	2.27	2.20E-01	5.50E-01
1.15 Fold Change	Toll-like receptor signaling pathway	2	6.72	3.59E-02	1.07E-01
	Jak-STAT signaling pathway	2	4.52	7.25E-02	1.08E-01
	Metabolic pathways	2	0.58	1.00E-00	1.00E-00
1.20 Fold Change	None				

[a] Enrichment relative to number of reference genes in the genome based on the hypergeometric test. [b] Hypergeometric test based. [c] Benjamini & Hochberg multiple test correction.

Table S9

IPA top up- and down-regulated biological functions and canonical pathways

	Top Biological Functions	***P* value**[a]	**No. of Molecules**
	Up-Regulated		
	Molecular and Cellular Functions		
	Cell Cycle	2.28E-02 – 2.22E-07	10
	Cellular Development	2.31E-02 – 2.22E-07	32
	Cell Death and Survival	2.04E-02 – 1.22E-05	27
	DNA Replication, Recombination, and Repair	2.15E-02 – 9.98E-05	10
	Cell-To-Cell Signaling and Interaction	2.42E-02 – 1.11E-04	18
	Physiological System Development and Function		
	Embryonic Development	2.26E-02 – 1.22E-05	23
	Hematological System Development and Function	2.31E-02 – 1.11E-04	28
	Humoral Immune Response	1.96E-02 – 1.11E-04	8
	Connective Tissue Development and Function	1.93E-02 – 1.70E-04	28
	Skeletal and Muscular System Development and Function	2.37E-02 – 1.70E-04	18
	Top Canonical Pathways	***P* value**[b]	**Overlap**[c]
	Regulation of eIF4 and p70S6K Signaling	1.35E-03	3.8%
	mTOR Signaling	4.21E-03	2.9%
	Glucocorticoid Receptor Signaling	5.07E-03	2.3%
	IL-17A Signaling in Gastric Cells	7.90E-03	9.1%
	EIF2 Signaling	1.54E-02	2.6%
ID	**Associated Network Functions**		**Score**[d]
1	Cell Cycle, Cellular Development, Cell Death and Survival		39
2	Cell Cycle, Organ Morphology, Reproductive System Development and Function		23
3	Embryonic Development, Organismal Development, Nervous System Development and Function		23
4	Humoral Immune Response, Protein Synthesis, Connective Tissue Development and Function		15
5	Cancer, Cell Death and Survival, Organismal Injury and Abnormalities		15
	Down-Regulated		
	Molecular and Cellular Functions		
	Protein Synthesis	2.33E-02 – 6.77E-04	4
	Cellular Development	4.85E-02 – 1.11E-03	13
	Amino Acid Metabolism	2.06E-02 – 2.60E-03	2
	Cell Death and Survival	4.82E-02 – 2.60E-03	7
	Cell Morphology	4.08E-02 – 2.60E-03	7
	Physiological System Development and Function		
	Connective Tissue Development and Function	4.57E-02 – 2.79E-05	7
	Organ Morphology	4.57E-02 – 2.79E-05	9
	Skeletal and Muscular System Development and Function	4.57E-02 – 2.79E-05	5
	Tissue Development	4.85E-02 – 2.79E-05	11
	Tissue Morphology	4.82E-02 – 2.79E-05	8
	Top Canonical Pathways	***P* value**[b]	**Overlap**[c]
	Basal Cell Carcinoma Signaling	7.60E-04	4.3%
	Zymosterol Biosynthesis	1.55E-02	16.7%
	Mouse Embryonic Stem Cell Pluripotency	2.48E-02	2.1%
	Type I Diabetes Mellitus Signaling	2.63E-02	2.1%
	Cholesterol Biosynthesis I	3.32E-02	7.7%
ID	**Associated Network Functions**		**Score**[d]
1	Cell Cycle, Embryonic Development, Organ Development		24
2	Infectious Diseases, Respiratory Disease, Cell Death and Survival		22
3	Cancer, Organismal Injury and Abnormalities, Reproductive System Disease		15
4	Cell Cycle, Cell Death and Survival, Reproductive System Development and Function		2
5	Lipid Metabolism, Small Molecule Biochemistry, Vitamin and Mineral Metabolism		2

[a] Fischer's exact test was used to calculate a p-value determining the probability that each biological function assigned to that data set is due to chance alone. [b] Fischer's exact test was used to calculate a p-value determining the probability that each canonical pathway assigned to that data set is due to chance alone. [c] Number of genes in a pathway that were found in our significant gene list compared to the total number of genes in that pathway. [d] Network score is the negative log of the p-value for the likelihood that network molecules would be found together by chance alone. A higher score indicates a greater statistical significance that molecules depicted in the network are interconnected.

Table S10

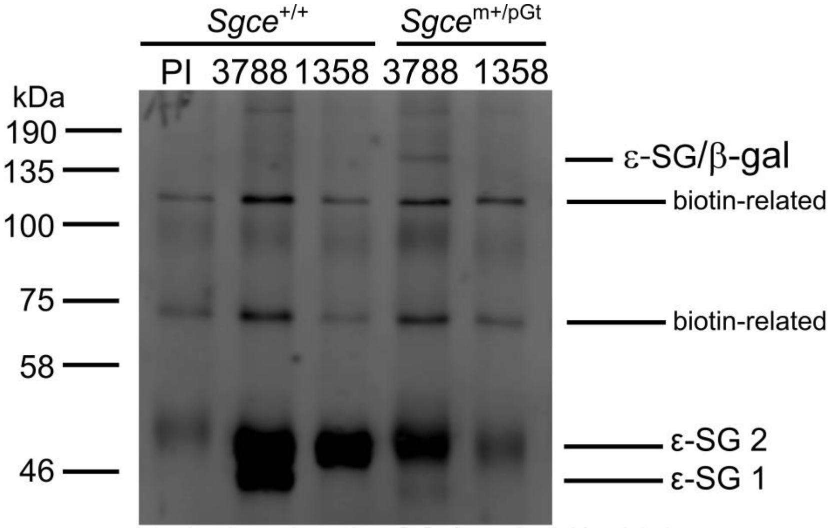
Top upstream regulators

Upstream Regulators		***p* value of overlap**
For Significantly Up-regulated Genes		
Ifnar1	Interferon (alpha, beta and omega) receptor 1	2.43E-08
Crem	CAMP responsive element modulator	7.11E-08
Creb1	CAMP responsive element binding protein 1	2.98E-07
Ptger4	Prostaglandin E teceptor 4 (subtype EP4)	9.78E-07
Stat1	Signal transducer and activator Of Transcription 1	2.35E-06
For Significantly Down-regulated Gene		
Tnfrsf4	Tumor necrosis factor receptor superfamily, member 4	8.49E-04
Nfe2l1	Nuclear factor, erythroid 2-like 1	1.20E-03
Kap	Kidney androgen regulated protein	2.72E-03
Smarca4	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily A, member 4	4.31E-03
Ppard	Peroxisome proliferator-activated receptor delta	4.98E-03

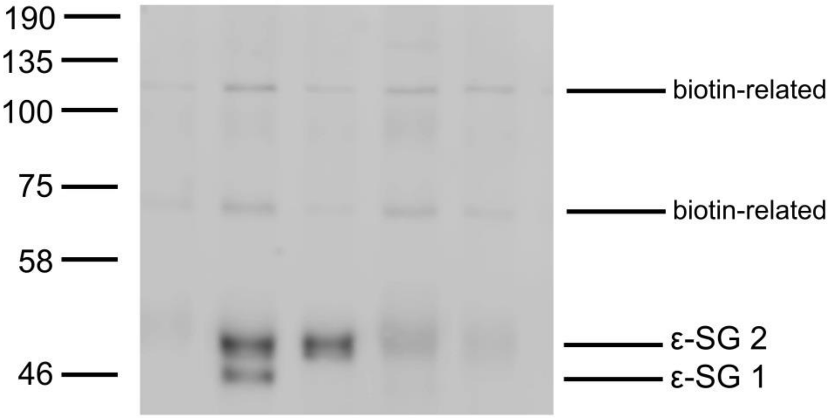
The overlap *p* value calls likely upstream regulators based on significant overlap between dataset genes and known targets regulated by a transcription regulator. The overlap *p* value is calculated using Fisher’s Exact Test.

```
481     ACTCTATAGGCTTCAGCTGGTGATATTGTTGAGTCAAAACTAGAGCCTGGACCACTGATATCCTGTCTTTAACAAATTGG   560

481     TGAGATATCCGAAGTCGACCACTATAACAACTCAGTTTTGATCTCGGACCTGGTGACTATAGGACAGAAATTGTTTAACC   560

        RsaI             AluI                     BfaI                EcoRV      MseI


                                                                   Human Adenovirus Type 3/5 SA

561     ACTAATCGATACCGTCGACTCGAGGCTAGAACTAGTGGATCCCCCGGGCTGCAGATCTGTAGGGCGCAGTAGTCCAGGGT   640

561     TGATTAGCTATGGCAGCTGAGCTCCGATCTTGATCACCTAGGGGGCCCGACGTCTAGACATCCCGCGTCATCAGGTCCCA   640

                      SalI         BfaI   BfaI    DpnI   SmaI     PstI          HhaI

                            XhoI         SpeI   BamHI   MspI      BglII

                                              BstYI            BstYI

                                              Sau3AI           Sau3AI

                                                                DpnI


                                                splice site (686)      AdiPCR1F

                                                     ↓ S  R  L  R  T  N  S  S  R  S  F

641     TTCCTTGATGATGTCATACTTATCCTGTCCCTTTTTTTTCCACAGCTCGCGGTTGAGGACAAACTCTTCGCGGTCTTTCC   720

641     AAGGAACTACTACAGTATGAATAGGACAGGGAAAAAAAAGGTGTCGAGCGCCAACTCCTGTTTGAGAAGCGCCAGAAAGG   720
AdiPCR1R                                     AluI


        AdiPCR1nestF                             β-galactosidase

        Q  W  G  S  T  V  S  I  S  L  M  I  C  D  M  A  D  P  V  V  L  Q  R  R  D  W  E

721     AGTGGGGATCGACGGTATCGATAAGCTTGATGATCTGTGACATGGCGGATCCCGTCGTTTTACAACGTCGTGACTGGGAA   800

721     TCACCCCTAGCTGCCATAGCTATTCGAACTACTAGACACTGTACCGCCTAGGGCAGCAAAATGTTGCAGCACTGACCCTT   800

              Sau3AI            HindIII    DpnI        NlaIII

                 DpnI              AluI   Sau3AI            BamHI

                                                        BstYI

                                                        Sau3AI

                                                          DpnI


         N  P  G  V  T  Q  L  N  R  L  A  A  H  P  P  F  A  S  W  R  N  S  E  E  A  R  T

801     AACCCTGGCGTTACCCAACTTAATCGCCTTGCAGCACATCCCCCTTTCGCCAGCTGGCGTAATAGCGAAGAGGCCCGCAC   880

801     TTGGGACCGCAATGGGTTGAATTAGCGGAACGTCGTGTAGGGGGAAAGCGGTCGACCGCATTATCGCTTCTCCGGGCGTG   880

                            MseI                              AluI                 HaeIII
```

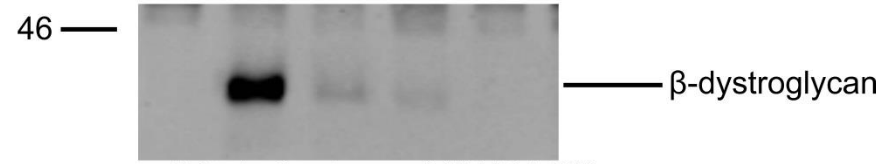
Fig. S1. Splice site for chimeric ε-SG/β-gal fusion protein based on known sequence of the Gep-SD5 vector.



biotinylated anti-ε-SG (esg3790) - high exposure



biotinylated anti-ε-SG (esg3790)



anti-β-dystroglycan (MANDAG2)

Fig. S2. Western blots of immunoaffinity purifications (IAPs) of ε-SG-containing complexes from WT C57BL/6J and *Sgce*$^{m+/pGt}$ mice. The left three lanes contain proteins isolated from WT brain tissue whereas the right two lanes contain protein from *Sgce*$^{m+/pGt}$ brain tissue. Lanes are labelled with the antibody used to isolate proteins: PI, preimmune IgG; 3788, esg3788 anti-ε-SG; 1358, esg2-1358 anti-ε-SG brain-specific isoform. The biotinylated anti-ε-SG antibody detects both the major isoform (lower band, ε-SG 1) and brain-specific isoform (upper bands, ε-SG 2) of ε-SG in IAPs using the esg3788 anti-ε-SG antibody, and only the brain-specific isoform in IAPs using the esg2-1358 anti-ε-SG brain-specific isoform antibody. Western blot using the anti-β-dystroglycan antibody MANDAG2 showing co-purifications of β-dystroglycan in the esg3788 and esg-1358 IAPs from WT tissue. β-dystroglycan is severely reduced in the esg3788 IAP from *Sgce*$^{m+/pGt}$ brain tissue and absent in the esg-1358 IAP. With high exposure, a putative chimeric ε-SG/β-gal band is seen at ~159 kDa.

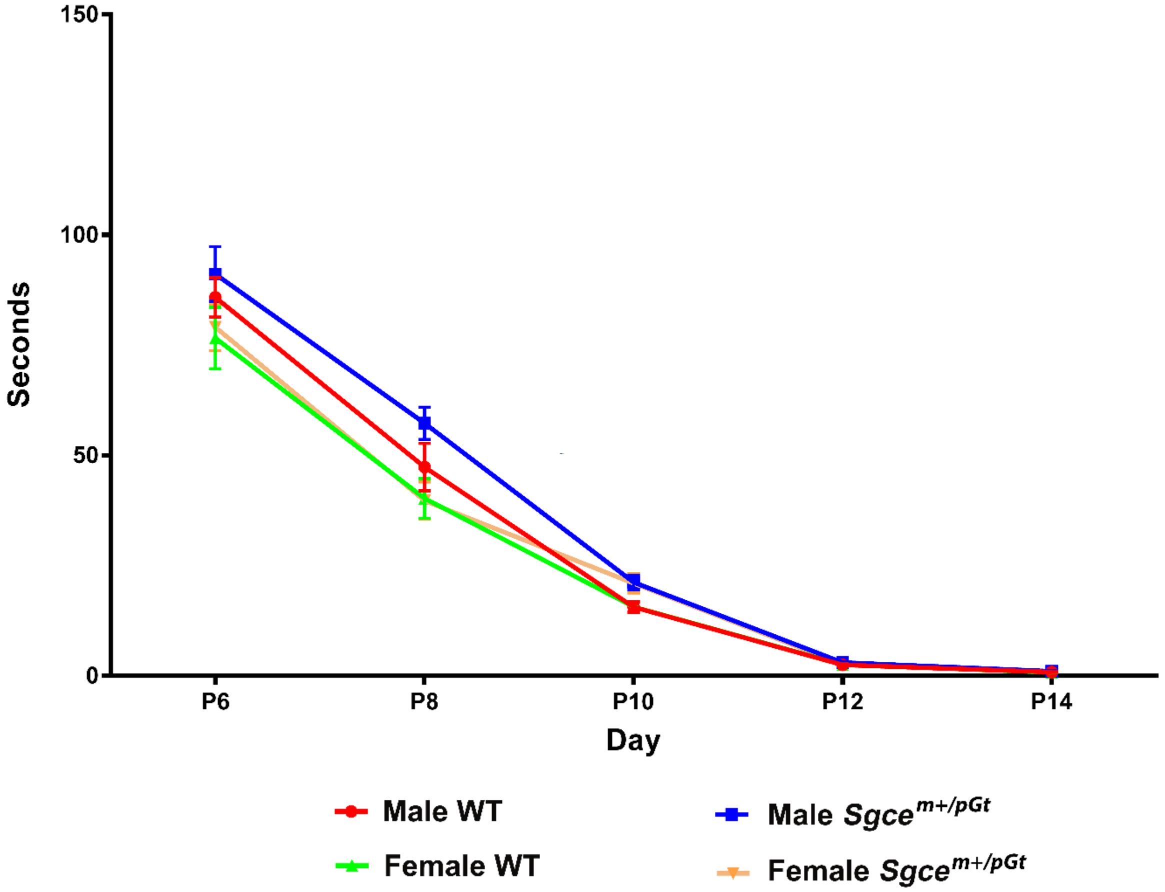


Fig. S3. Righting reflex for *Sgce*$^{m+/pGt}$ mice (n= 15 for both males and females) and wild-type (WT) littermates (n = 18 males and 16 females).

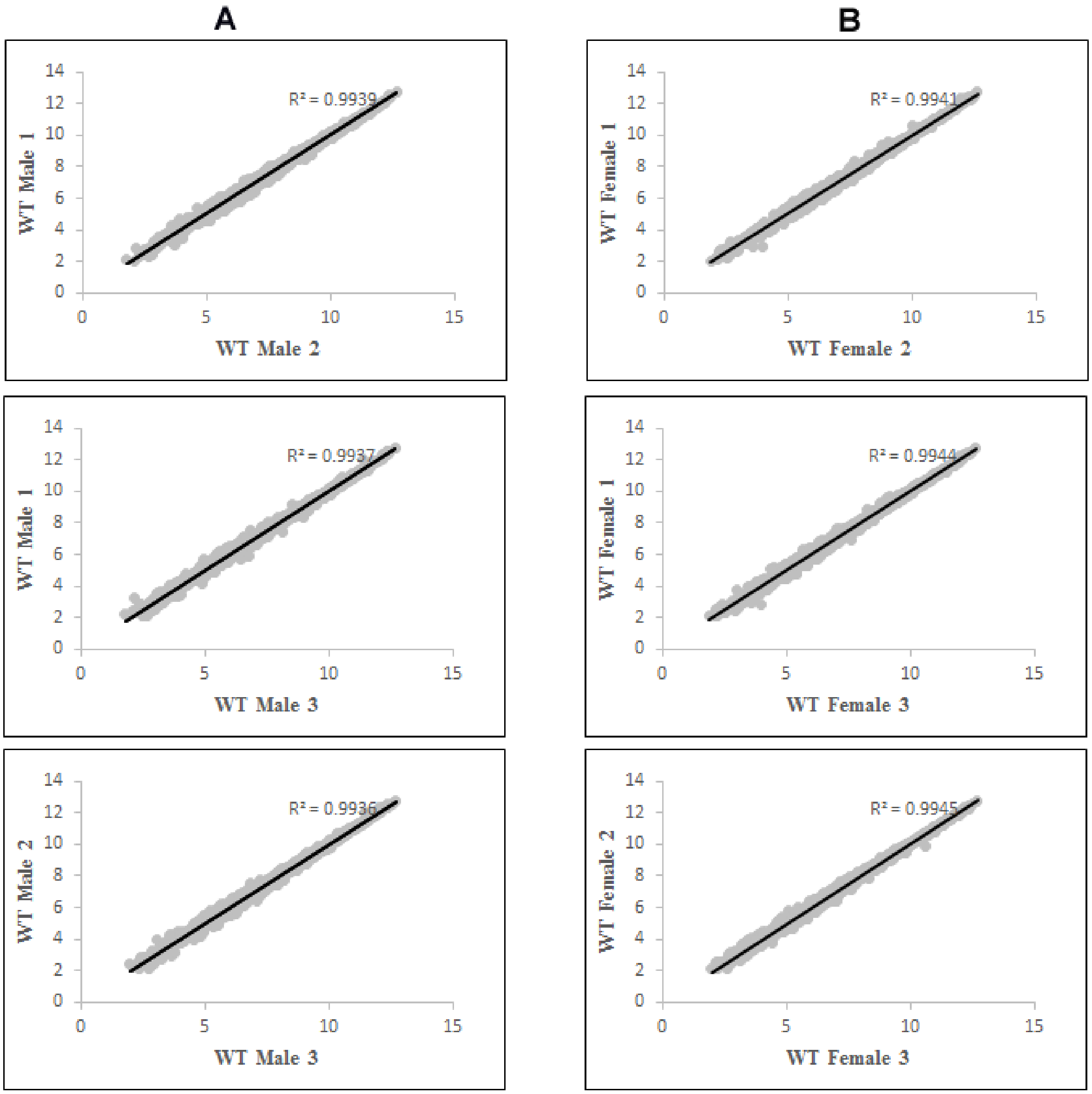


Fig. S4. Scatter plots of filtered and normalized expression values for 3 male (A) and 3 female (B) WT mouse gene-expression microarrays.

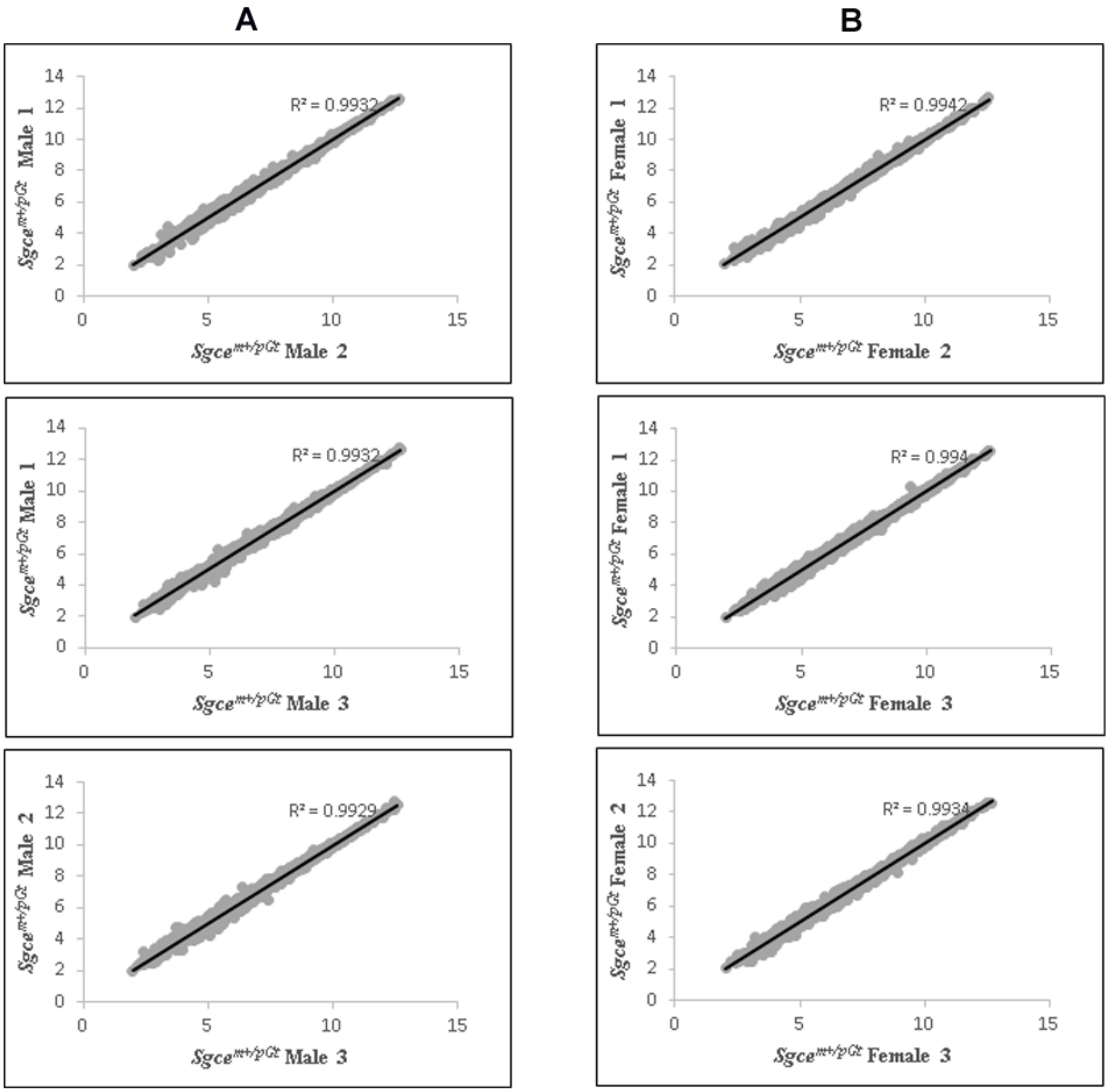


Fig. S5. Scatter plots of filtered and normalized expression values for 3 male (A) and 3 female (B) *Sgce*$^{m+/pGt}$ mouse gene-expression microarrays.

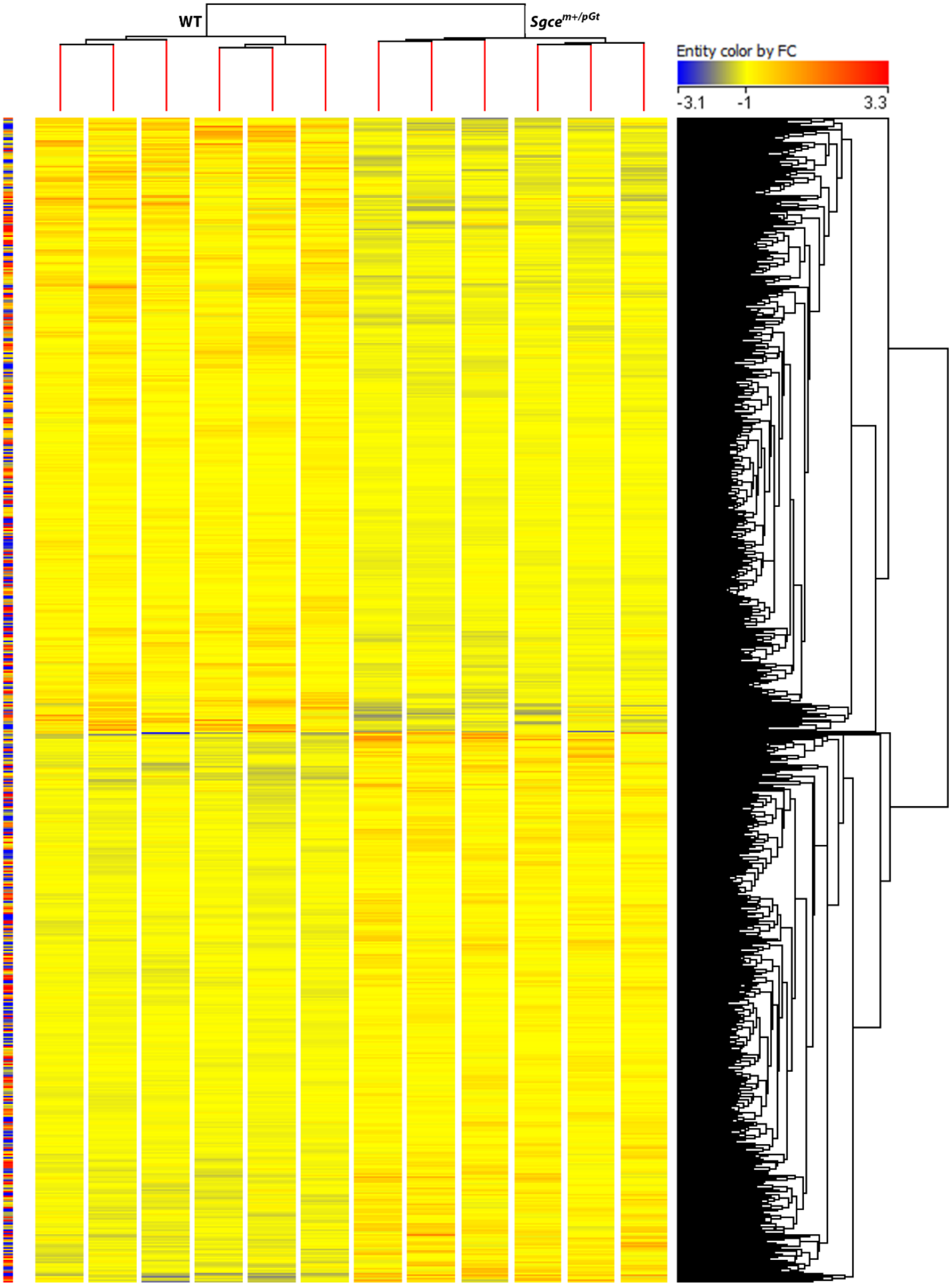


Fig. S6. Heat map for whole-genome gene expression analysis of *Sgce*$^{m+/pGt}$ and WT (*Sgce*$^{+/+}$) mouse cerebellum (*Sgce*$^{m+/pGt}$, 3 male and 3 female mice; *Sgce*$^{+/+}$, 3 male and 3 female WT littermates).

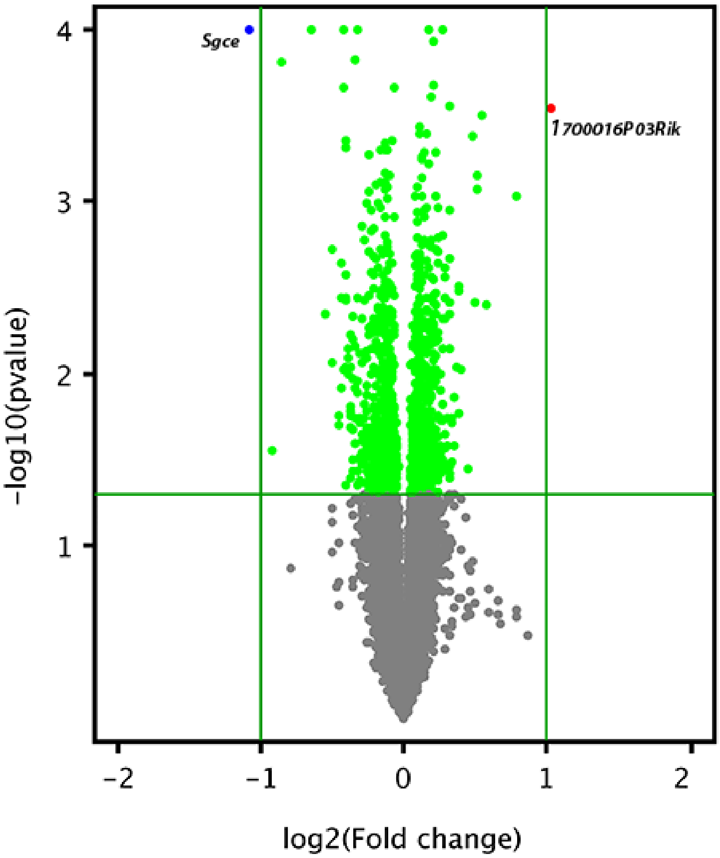


Fig. S7. A volcano plot for whole-genome gene expression analysis of *Sgce* gene-trap mouse cerebellum (*Sgce*$^{m+/pGt}$, 3 male and 3 female mice; *Sgce*$^{+/+}$, 3 male and 3 female littermates). The plot displays mean fold differences for each probe set in *Sgce*$^{+/+}$ and *Sgce*$^{m+/pGt}$ samples as a function of *p* value. Genes showing differential expression with *p* values < 0.05 are depicted with green dots. Other genes are represented with gray dots. Red dots represent genes with > 2X up-regulation ($p < 0.05$) and blue dots represent genes with > 2X down-regulation ($p < 0.05$).

Video S1
“Tiptoe” walking in a female P16 *Sgce*$^{m+/pGt}$ mouse

Video S2
Sustained hindlimb flexion posturing in response to hindlimb displacement in a male P14 *Sgce*$^{m+/pGt}$ mouse