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Supplemental Information

A Suite of Transgenic Driver and Reporter Mouse Lines with Enhanced Brain-Cell-Type Targeting and Functionality

Tanya L. Daigle, Linda Madisen, Travis A. Hage, Matthew T. Valley, Ulf Knoblich, Rylan S. Larsen, Marc M. Takeno, Lawrence Huang, Hong Gu, Rachael Larsen, Maya Mills, Alice Bosma-Moody, La' Akea Siverts, Miranda Walker, Lucas T. Graybuck, Zizhen Yao, Olivia Fong, Thuc Nghi Nguyen, Emma Garren, Garreck H. Lenz, Mariya Chavarha, Julie Pendergraft, James Harrington, Karla E. Hirokawa, Julie A. Harris, Philip R. Nicovich, Medea J. McGraw, Douglas R. Ollerenshaw, Kimberly A. Smith, Christopher A. Baker, Jonathan T. Ting, Susan M. Sunkin, Jérôme Lecoq, Michael Z. Lin, Edward S. Boyden, Gabe J. Murphy, Nuno M. da Costa, Jack Waters, Lu Li, Bosiljka Tasic, and Hongkui Zeng

Table S1. Driver lines generated by the Allen Institute for Brain Science. Related to **Figure 1**.

Line	JAX stock #	Transgenic type	Reference
A930038C07Rik-Tg1-Cre	017346	BAC random insertion	Harris et al., 2014
Adcyap1-F2A-Cre	030155	Knock-in at Stop codon	Harris et al., 2014
Avp-IRES2-Cre	023530	Knock-in at Stop codon	Harris et al., 2014
Camk2a-CreERT2	012362	Random insertion	Madisen et al., 2010
Cart-Tg1-Cre	009615	BAC random insertion	Harris et al., 2014
Ctgf-T2A-dgCre	028535	Knock-in at Stop codon	Tasic et al., 2016
Erbb4-F2A-CreERT2	012360	Knock-in at Stop codon	Madisen et al., 2010
Gnb4-IRES2-Cre	029587	Knock-in at Stop codon	Wang et al., 2017
Ndnf-IRES2-dgCre	028536	Knock-in at Stop codon	Tasic et al., 2016
Nr4a2-SA-IRES-Dre		Knock-in at 2nd intron?	Madisen et al., 2015
Ntng2-IRES2-Cre	029588	Knock-in at Stop codon	Wang et al., 2017
Nxph4-T2A-CreERT2	022861	Knock-in at Stop codon	Harris et al., 2014
Penk-F2A-CreERT2	022862	Knock-in at Stop codon	Harris et al., 2014
Pvalb-T2A-Cre	012358	Knock-in at Stop codon	Madisen et al., 2010
Pvalb-T2A-CreERT2	021189	Knock-in at Stop codon	Harris et al., 2014
Pvalb-T2A-dCre	022863	Knock-in at Stop codon	Harris et al., 2014
Pvalb-T2A-Dre	021190	Knock-in at Stop codon	Madisen et al., 2015
Pvalb-T2A-FlpE	021191	Knock-in at Stop codon	Madisen et al., 2015
Pvalb-T2A-FlpO	022730	Knock-in at Stop codon	Madisen et al., 2015
Rasgrf2-T2A-dCre	022864	Knock-in at Stop codon	Harris et al., 2014
Rorb-IRES2-Cre	023526	Knock-in at Stop codon	Harris et al., 2014
Rorb-T2A-tTA2	028537	Knock-in at Stop codon	Madisen et al., 2015
Scnn1a-Tg1-Cre	009111	BAC random insertion	Madisen et al., 2010
Scnn1a-Tg2-Cre	009112	BAC random insertion	Madisen et al., 2010
Scnn1a-Tg3-Cre	009613	BAC random insertion	Madisen et al., 2010
Slc17a7-IRES2-Cre	023527	Knock-in at Stop codon	Harris et al., 2014
Snap25-IRES2-Cre	023525	Knock-in at Stop codon	Harris et al., 2014
Sst-Cre		Knock-in at Start codon	Harris et al., 2014
Tac1-IRES2-Cre	021877	Knock-in at Stop codon	Harris et al., 2014
Tac2-IRES2-Cre	021878	Knock-in at Stop codon	Harris et al., 2014
Trib2-F2A-CreERT2	022865	Knock-in at Stop codon	Harris et al., 2014
Wfs1-Tg2-CreERT2	009614	BAC random insertion	Madisen et al., 2010
Wfs1-Tg3-CreERT2	009103	BAC random insertion	Madisen et al., 2010
Calb1-IRES2-Cre	028532	Knock-in at Stop codon	This paper
Calb1-T2A-dgCre	023531	Knock-in at Stop codon	This paper
Cart-IRES2-Cre	028533	Knock-in at Stop codon	This paper
Esr2-IRES2-Cre	030158	Knock-in at Stop codon	This paper
Fezf1-T2A-dCre	025110	Knock-in at Stop codon	This paper
Gnb4-IRES2-CreERT2	030159	Knock-in at Stop codon	This paper
Htr1a-IRES2-Cre	030160	Knock-in at Stop codon	This paper
Npr3-IRES2-Cre	031333	Knock-in at Stop codon	This paper
Npy-IRES2-FlpO	030211	Knock-in at Stop codon	This paper
Oxtr-T2A-Cre	031303	Knock-in at Stop codon	This paper
Pdyn-T2A-CreERT2	030197	Knock-in at Stop codon	This paper
Penk-IRES2-Cre-neo	025112	Knock-in at Stop codon	This paper
Plxnd1-IRES2-dgFlpO		Knock-in at Stop codon	This paper
Rasgrf2-T2A-dgFlpO	029589	Knock-in at Stop codon	This paper
Rorb-IRES2-FlpO	029590	Knock-in at Stop codon	This paper
Rorb-P2A-FlpO		Knock-in at Stop codon	This paper
Slc17a6-IRES2-FlpO	030212	Knock-in at Stop codon	This paper
Slc17a8-IRES2-Cre	028534	Knock-in at Stop codon	This paper
Slc32a1-IRES2-FlpO	031331	Knock-in at Stop codon	This paper
Slc32a1-T2A-FlpO	029591	Knock-in at Stop codon	This paper
Tacr1-T2A-Cre		Knock-in at Stop codon	This paper
Tnnt1-IRES2-CreERT2		Knock-in at Stop codon	This paper
Vipr2-IRES2-Cre	031332	Knock-in at Stop codon	This paper

Table S2. Reporter lines generated by the Allen Institute for Brain Science. Related to **Figures 2** and **3**.

Line	JAX stock #	Knock-in locus	Reference
Ai2(RCL-EYFP)	007920	ROSA26	Madisen et al., 2010
Ai3(RCL-EYFP)	007903	ROSA26	Madisen et al., 2010
Ai6(RCL-ZsGreen)	007906	ROSA26	Madisen et al., 2010
Ai9(RCL-tdT)	007909	ROSA26	Madisen et al., 2010
Ai14(RCL-tdT)	007914	ROSA26	Madisen et al., 2010
Ai27(RCL-ChR2H134R-tdT)	012567	ROSA26	Madisen et al., 2012
Ai32(RCL-ChR2H134R-EYFP)	012569, 024109	ROSA26	Madisen et al., 2012
Ai35(RCL-Arch-EGFP-ER2)	012735	ROSA26	Madisen et al., 2012
Ai38(RCL-GCaMP3)	014538	ROSA26	Zariwala et al., 2012
Ai39(RCL-eNpHR3.0-EYFP)	014539	ROSA26	Madisen et al., 2012
Ai57(RCFL-Jaws)		ROSA26	Madisen et al., 2015
Ai62(TITL-tdT)	022731	TIGRE	Madisen et al., 2015
Ai65(RCFL-tdT)	021875	ROSA26	Madisen et al., 2015
Ai66(RCRL-tdT)	021876	ROSA26	Madisen et al., 2015
Ai72(RCL-VSFPB)		ROSA26	Madisen et al., 2015
Ai78(TITL-VSFPB)	023528	TIGRE	Madisen et al., 2015
Ai79(TITL-Jaws)	023529	TIGRE	Madisen et al., 2015
Ai82(TITL-GFP)	023532	TIGRE	Madisen et al., 2015
Ai85(TITL-iGluSnFr)	026260	TIGRE	Madisen et al., 2015
Ai87(RCL-iGluSnFr)		ROSA26	Madisen et al., 2015
Ai92(TITL-YCX2.60)	026262	TIGRE	Madisen et al., 2015
Ai93(TITL-GCaMP6f)	024103	TIGRE	Madisen et al., 2015
Ai94(TITL-GCaMP6s)	024104	TIGRE	Madisen et al., 2015
Ai95(RCL-GCaMP6f)	024105	ROSA26	Madisen et al., 2015
Ai96(RCL-GCaMP6s)	024106	ROSA26	Madisen et al., 2015
Snap25-LSL-F2A-GFP	021879	Snap25	Madisen et al., 2015
Snap25-T2A-GCaMP6s	025111	Snap25	Madisen et al., 2015
TITL-RCaMP1.07	030217	TIGRE	Bethge et al., 2017
Ai31(RCL-Syp-EmGFP)		ROSA26	This paper
Ai34(RCL-Syp-tdT)	012570	ROSA26	This paper, see also Abraira et al., 2017
Ai40(RCL-ArchT-EGFP)	021188	ROSA26	This paper
Ai47(RCL-triGFP)		ROSA26	This paper, see also Steinecke et al., 2017
Ai63(TIT-tdT)		TIGRE	This paper
Ai65F(RCF-tdT)		ROSA26	This paper
Ai66R(RCR-tdT)		ROSA26	This paper
Ai75(RCL-nT)	025106	ROSA26	This paper
Ai80(RCFL-CatCh)	025109	ROSA26	This paper
Ai86(TITL-ArcLight)		TIGRE	This paper
Ai90(TITL-Chronos)	024100	TIGRE	This paper
Ai110(RCL-FnGF-nT)		ROSA26	This paper
Ai133(TITL-ssAPEX2tm)	030213	TIGRE	This paper
Ai134(TITL-ChR2-YFP)	031334	TIGRE	This paper
Ai136(TITL-ReaChR-YFP)	030216	TIGRE	This paper
Ai139(TIT2L-GFP-ICL-TPT)	030219	TIGRE	This paper
Ai140(TIT2L-GFP-ICL-tTA2)	030220	TIGRE	This paper
Ai148(TIT2L-GC6f-ICL-tTA2)	030328	TIGRE	This paper, see also Hsiang et al., 2017
Ai161(TIT2L-GFP-ICR-tTA2)	031561	TIGRE	This paper
Ai162(TIT2L-GC6s-ICL-tTA2)	031562	TIGRE	This paper
Ai163(TIT2L-GC6s-ICL-TPT)		TIGRE	This paper
Ai167(TIT2L-ChrimsonR-tdT-ICL-tTA2)		TIGRE	This paper
Ai168(TIT2L-oChIEF-P2A-tdT-ICL-tTA2)		TIGRE	This paper
Ai169(TIT2L-ASAP2s-ICL-tTA2)	031569	TIGRE	This paper
Ai170(TIT2L-ASAP2s-Kv-ICL-tTA2)	031570	TIGRE	This paper
Chrm2-tdT	030330	Chrm2	This paper

Acronyms: RCL, Rosa26 – CAG promoter – LoxP-STOP-LoxP. **RCFL**, Rosa26 – CAG promoter – FRT-STOP-FRT – LoxP-STOP-LoxP. **RCRL**, Rosa26 – CAG promoter – Rox-STOP-Rox – LoxP-STOP-LoxP. **RCF**, Rosa26 – CAG promoter – FRT-STOP-FRT. **RCR**, Rosa26 – CAG promoter – Rox-STOP-Rox. **LSL**, LoxP-STOP-LoxP. **TITL**, TIGRE – Insulators – TRE promoter – LoxP-STOP-LoxP. **TIT**, TIGRE – Insulators – TRE promoter. **TIT2L**, TIGRE – Insulators – TRE2 promoter – LoxP-STOP-LoxP. **ICL**, Insulators – CAG promoter – Lox2272-STOP2-Lox2272. **ICR**, Insulators – CAG promoter – Rox-STOP2-Rox. **FnGF**, FRT – nls-mNeonGreen – FRT. **GC6f**, GCaMP6f. **GC6s**, GCaMP6s. **nT**, nls-tdTomato. **Syp**, Synaptophysin. **tdT**, tdTomato. **TPT**, tdTomato-P2A-tTA2.

Table S3. Driver lines expressing trimethoprim (TMP)-inducible Cre or FlpO. Recombination patterns examined in adult mice (P56 or older) with drivers crossed to either a Cre reporter Ai14 or a Flp reporter Ai65F. Related to **Figure 1**.

Driver line	No TMP induction	With TMP induction in adult stage
Calb1-T2A-dgCre	Significant baseline level but not full recombination pattern	Full recombination pattern resembling that of the endogenous gene
Ctgf-T2A-dgCre	Very sparse baseline recombination	Full recombination pattern resembling that of the endogenous gene
Fezf1-T2A-dCre	Full recombination pattern resembling that of the endogenous gene, same as with TMP induction	Full recombination pattern resembling that of the endogenous gene, same as without TMP induction
Ndnf-IRES2-dgCre	Full recombination pattern resembling that of the endogenous gene, same as with TMP induction	Full recombination pattern resembling that of the endogenous gene, same as without TMP induction
Pvalb-T2A-dCre	Significant baseline level but not full recombination pattern	Full recombination pattern resembling that of the endogenous gene
Rasgrf2-T2A-dCre	Sparse baseline recombination	Full recombination pattern resembling that of the endogenous gene
Plxnd1-IRES2-dgFlpO	No recombination	Very sparse recombination pattern as a subset of that of the endogenous gene
Rasgrf2-T2A-dgFlpO	No recombination	Scattered recombination pattern as a subset of that of the endogenous gene

Table S4. Protein sequence of soma-enriched voltage sensor ASAP2s-Kv. Related to **Figure 4**.

The ASAP2s segment is labeled in green, with the circularly permuted GFP sequence underlined. The 65 amino acid segment from the C-terminus of the rat Kv2.1 potassium channel (orange) was fused to the C-terminus of ASAP2s via a flexible linker (blue). Black letters correspond to enzymatic restriction sites. Distinct elements of the protein are color-coded. This segment is sufficient to target a heterologous protein to neuronal soma and proximal dendrites and has been repeatedly used for soma targeting of opsins.

ASAP2s-Kv sequence
METTVRYEQGSELTKTSSSPTADEPTIKIDDGRDEGNEQDSCSNTIRRKISPFVMSFGFRVFGVVLIIVDIIVVIVDLAISEK KRGIREILEGVSLAIALFFLVDVLMRVFVEGFKNYFRSKLNTLDAVIVVGTLLINMTYSFSDLAAFNSHNVYITADKQKNGIK ANFTVRHNVEDGSVQLADHYQQNTPIGDGPVLLPDNHYLSTQTVLSKDPNEKRDHMVLLEFVTAAGITHGMDELYGGTGGSAS QGEELFTGVVPILVELDGDVNGHKFSVRGEGEGDATIGKLTLKFICTTGKLPVPWPTLVTTLTYGVQCFSRYPDHMKRHDFFK SAMPEGYVQERTISFKDDGKYKTRAVVKFEGDTLVNRIELKGTDFKEDGNILGHKLEYNTDQMPQMVTLLRVLRIVILIRIFQ LASQKKQLEVVTLKGSSGSSGSSTRQSQPILNTKEMAPQSKPPEELEMSSMPSPVAPLPARTEGVIDMRSMSSIDSFISCATD FPEATRF

Table S5. Problematic reporter and driver line crosses. Related to **Figure 7**.

Reporter	Driver	Genotype	Phenotype
Ai139	Gad2-IRES-Cre	Ai139/wt; Gad2-IRES-Cre/wt	Embryonic lethal
Ai140	Gad2-IRES-Cre	Ai140/wt; Gad2-IRES-Cre/wt	Embryonic lethal
Ai148	Gad2-IRES-Cre	Ai148/wt; Gad2-IRES-Cre/wt	Embryonic lethal
Ai136	Sim1-Cre_KJ18, ROSA26-ZtTA	Ai139/wt; Sim1-Cre_KJ18/wt; ROSA26-ZtTA/wt	Embryonic lethal
Ai140	Sim1-Cre_KJ18	Ai140/wt; Sim1-Cre_KJ18/wt	Embryonic lethal
Ai140	Emx1-IRES-Cre	Ai140/wt;Emx1-IRES-Cre/wt	Reduced body weight and brain size, thinned cortex, substantial neurodegeneration in hippocampal subfields, and high premature mortality rate; doxycycline treatment (to suppress GFP expression) did not reverse phenotype
Ai148	Emx1-IRES-Cre	Ai148/wt; Emx1-IRES-Cre/wt	Reduced body weight and brain size, thinned cortex, substantial neurodegeneration in hippocampal subfields, and high premature mortality rate; doxycycline treatment (to suppress GCaMP6f expression) did not reverse phenotype
Ai148	Camk2a-Cre	Ai148/wt; Camk2a-Cre/wt	Reduced brain size and some neurodegeneration in hippocampal subfields
Ai148	Slc17a7-IRES2-Cre	Ai148/wt; Slc17a7-IRES2-Cre/wt	Reduced brain size and some neurodegeneration in hippocampal subfields
Ai148	Sst-IRES-Cre	Ai148/wt; Sst-IRES-Cre/wt	Ulcerative dermatitis (most commonly in anogenital region, lower jaw, and sternum), with occasional rectal prolapse and/or seizure, seen in ~30% mice with an average onset at ~P100
Ai168	Pvalb-IRES-Cre	Ai168/wt; Pvalb-IRES-Cre/wt	Reduced body weight, head tilt and atrophy of hind limbs; phenotype can be ameliorated by doxycycline treatment
Ai75	Snap25-IRES2-Cre	Ai75/wt; Snap25-IRES2-Cre/wt	Premature death (around 4 weeks of age)

Table S6. All observations of normal and aberrant cortical activity in cortical pan-excitatory GCaMP6 expressing lines. Related to **Figure 7**.

Animals with aberrant activity are highlighted (gray), observations with aberrant activity are highlighted in red, with the corresponding sex and age of animals at the time of each observation. We found no relationship between these events and the age of the animal.

Genotype	Mouse ID#	Sex	Age at observation (postnatal days)
Slc17a7-IRES2-Cre;Ai162	292915	F	52
Slc17a7-IRES2-Cre;Ai162	292917	F	52
Slc17a7-IRES2-Cre;Ai162	297312	M	110
Slc17a7-IRES2-Cre;Ai162	297310	M	110
Slc17a7-IRES2-Cre;Ai162	304572	F	170
Slc17a7-IRES2-Cre;Ai162	315689	F	120
Slc17a7-IRES2-Cre;Ai162	321607	F	97, 191
Slc17a7-IRES2-Cre;Ai148	343025	M	77
Slc17a7-IRES2-Cre;Ai148	343027	F	77, 99
Slc17a7-IRES2-Cre;Ai148	329284	M	67
Slc17a7-IRES2-Cre;Ai148	329286	M	67
Slc17a7-IRES2-Cre;Ai148	347103	M	57, 79
Slc17a7-IRES2-Cre;Ai148	347105	F	71
Slc17a7-IRES2-Cre;Ai148	347893	M	67, 75
Slc17a7-IRES2-Cre;Camk2a-tTa;Ai93	303474	F	69, 118
Slc17a7-IRES2-Cre;Camk2a-tTa;Ai93	302981	M	60, 68, 111
Slc17a7-IRES2-Cre;Camk2a-tTa;Ai93	301333	F	67, 118
Slc17a7-IRES2-Cre;Camk2a-tTa;Ai93	306069	F	67, 96
Slc17a7-IRES2-Cre;Camk2a-tTa;Ai93	301329	M	67, 118