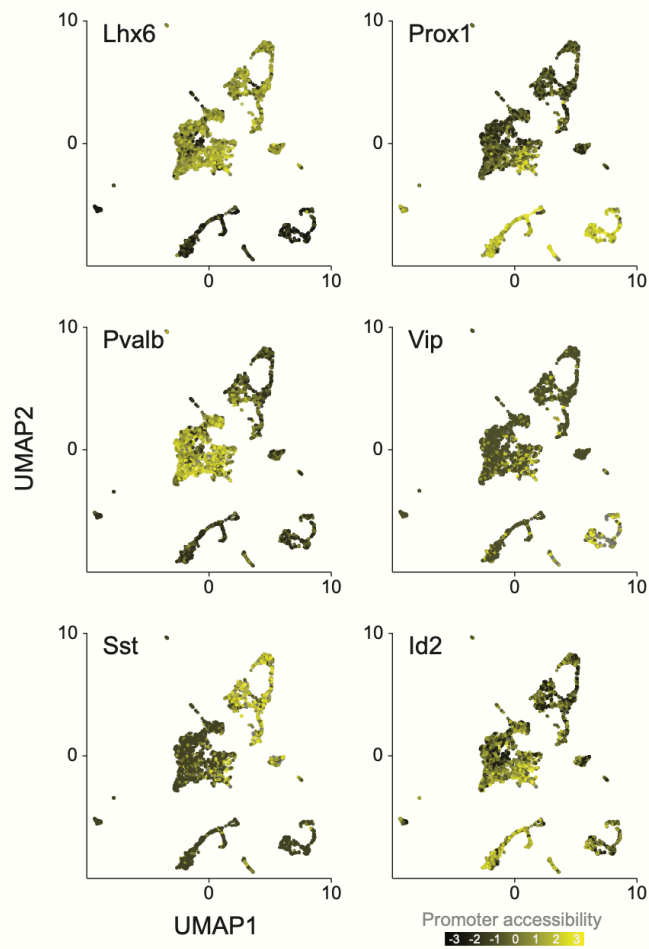


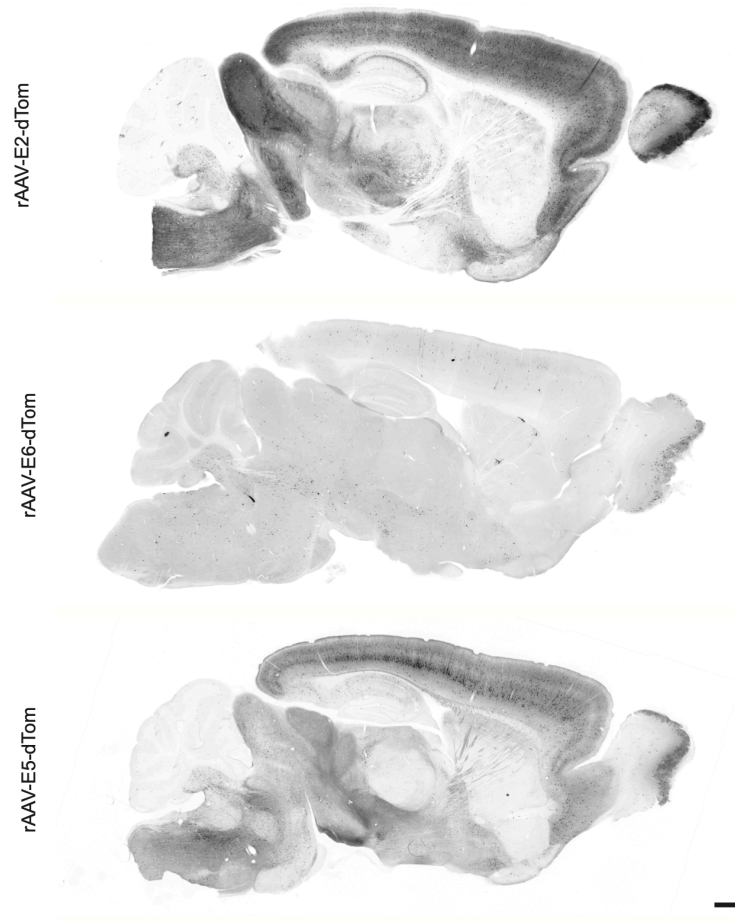
SUPPLEMENTARY FIGURES AND TABLES LEGENDS

Viral manipulation of functionally distinct neurons from mice to humans

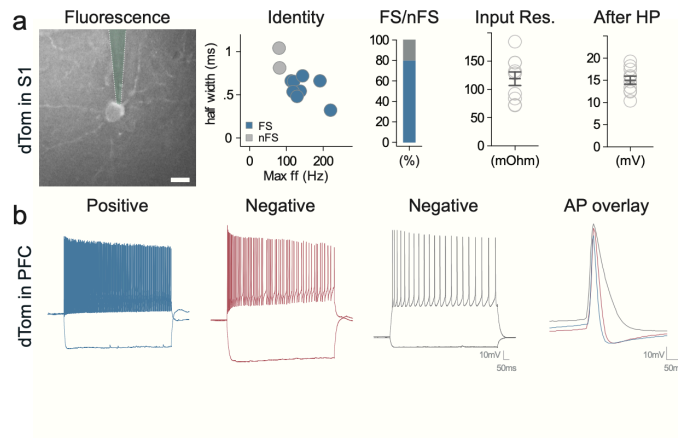
Vormstein-Schneider, Lin et al.



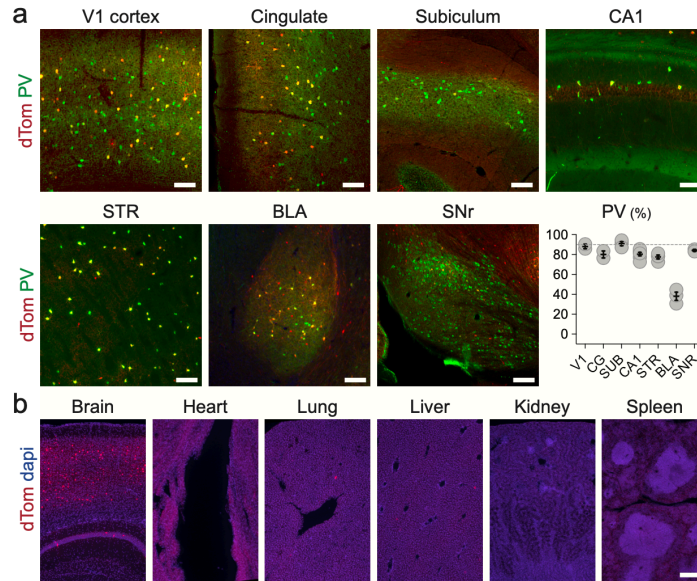
Supplementary Figure 1. UMAP plot of 3500 neuronal nuclei collected from 4 *Dlx6a*^{Cre::Sun1-GFP} mice colored promoter accessibility of the indicated canonical interneuron markers.



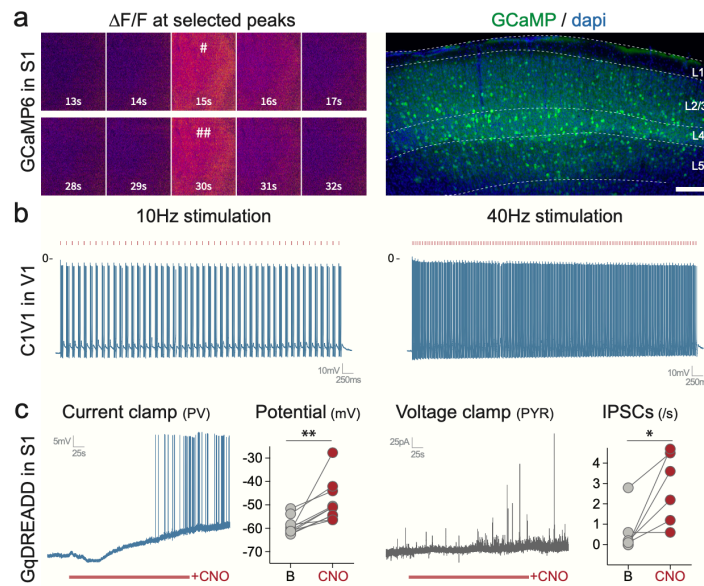
Supplementary Figure 2. Fluorescent images of sagittal sections from adult mice that were injected systemically with the indicated rAAV-E[x]-dTom and analyzed 3 weeks post-injection with IHC for the viral reporter. Scale bar represents 500um.



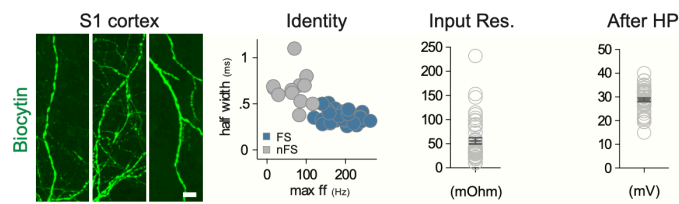
Supplementary Figure 3. Adult mice were injected systemically with rAAV-E2-dTomato. **(a)** Slice recording of the intrinsic properties of virally labeled neurons. The left panel shows a representative cell expressing the viral reporter. The green trace represents the recording pipet. The quantifications show the indicated parameters. The blue dots represent cells with stereotypical fast-spiking properties. **(b)** Representative slice recording traces of positive fast-spiking cell and negative. Scale bars represent 20um. On the graphs, dots represent individual measurements and the lines represent average +/- s.e.m.



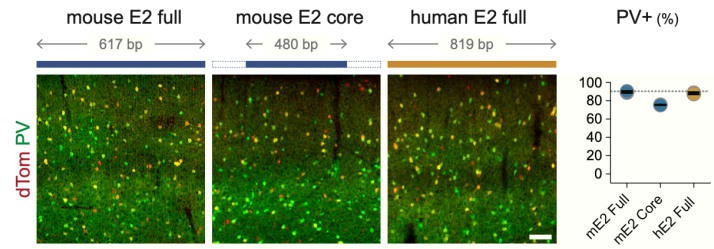
Supplementary Figure 4. Adult mice were injected systemically with rAAV-E2-dTomato and analyzed 3 weeks post-injection. **(a)** Coronal and sagittal sections were analyzed with IHC for the viral reporter and PV and the specificity to PV was reported across brain regions. **(b)** The native viral expression was analyzed from the indicated organs. Scale bars represent 100um (a) and 250um (b). On the graphs, dots represent individual measurements and the lines represent average \pm s.e.m. Values for specificity are listed in the supplementary table 2.



Supplementary Figure 5. Mice were injected systemically (**a** - P14 injection with rAAV-E2-GCaMP6f) and locally in the somatosensory cortex (**b** - rAAV-E2-C1V1-eYFP; **c** - rAAV-E2-GqDREADD). (**a**) Mice were analyzed 1-week post-injection. The left panel shows widefield images of two representative peaks shown by the pound sign in figure 3. The right panel shows a fluorescent image taken after GCaMP recordings. (**b**) Slice electrophysiology current clamp recording were performed 1-week post-injection. Cells expressing the viral reporter were targeted with either 10Hz or 40Hz laser stimulation (550nm) while the voltage was recorded over 3 seconds. (**c**) Slice electrophysiology current clamp recording were performed 1-week post-injection. The voltage was recorded before and after bath application of CNO. Scale bars represent 500um. The red bars represent laser stimulation. On the graphs, dots represent individual measurements.



Supplementary Figure 6. Human brain tissue obtained from surgical resection that was exposed to rAAV-E2-dTomato and maintained in culture for 7-14 days. **(a)** Representative image of the dendrites of virally labeled cells filled with Biocytin during the recording session. **(b)** Slice recording of the intrinsic properties of virally labeled neurons. The quantifications show the indicated parameters. The blue dots represent cells with stereotypical fast-spiking properties. Scale bars represent 100 μ m. On the graphs, dots represent individual measurements and the lines represent average \pm s.e.m.



Supplementary Figure 7. Adult mice were injected with the indicated modified rAAV-E2-dTomato construct and analyzed 3 weeks post-injection with IHC for the viral reporter and PV. The corresponding specificity is shown in the right panel. Scale bars represent 2 μ m. On the graphs, dots represent individual measurements and the lines represent average \pm s.e.m. Values for specificity are listed in the supplementary table 2.

RE	Gene	Target	Specificity	Position	Chr	Start	Stop	Size (bp)	scATAC PV	scATAC SST	scATAC VIP	scATAC ID2	bATAC Ex	Ms/Hm
E1	Scn1a	PV	22%	intergenic	chr2	66256056	66257335	1279	1	1	1	1	1	69%
E2	Scn1a	PV	90%	intronic	chr2	66364036	66364653	617	1	0	0	1	0	71%
E3	Scn1a	PV	57%	intronic	chr2	66383190	66384021	831	1	1	1	1	1	67%
E4	Scn1a	PV	14%	intronic	chr2	66387764	66388024	260	0	0	0	0	0	78%
E5	Scn1a	PYR	20%	intronic	chr2	66392447	66393109	662	1	1	1	1	1	72%
E6	Scn1a	VIP	88%	intronic	chr2	66401767	66402372	605	0	0	0	0	0	72%
E7	Scn1a	PV	33%	intronic	chr2	66407834	66410263	2429	1	1	1	1	1	74%
E8	Scn1a	PV	61%	intronic	chr2	66439814	66441457	1643	1	1	1	1	1	75%
E9	Scn1a	PV	47%	intergenic	chr2	66441748	66442268	520	1	0	0	0	1	72%
E10	Scn1a	PV	23%	intergenic	chr2	66450594	66451140	546	1	1	1	1	1	75%
E11	Pvalb	PV	90%	intronic	chr15	78204152	78204655	503	1	1	1	1	0	78%
E12	Pvalb	PV	59%	intronic	chr15	78204583	78204784	201	1	1	0	0	0	74%
E13	Pvalb	PV	67%	intronic	chr15	78205234	78205766	532	0	1	0	0	0	73%
E14	Acan	PV	94%	intergenic	chr7	79052127	79052622	495	1	0	0	0	0	72%
E15	Acan	PV	79%	intergenic	chr7	79053118	79053435	317	1	1	1	1	1	84%
E16	Acan	PV	58%	intronic	chr7	79056553	79057054	501	0	0	0	0	0	82%
E17	Acan	PV	54%	intronic	chr7	79079999	79080472	473	1	0	0	0	0	86%
E18	Tmem132c	PV	57%	intronic	chr5	127243448	127244121	673	1	1	0	0	0	70%
E19	Tmem132c	PV	57%	intronic	chr5	127257256	127257594	338	0	1	0	0	0	78%
E20	Tmem132c	PV	66%	intronic	chr5	127290515	127291016	501	1	0	0	0	0	77%
E21	Tmem132c	PV	71%	intronic	chr5	127300767	127301107	340	0	0	0	0	0	74%
E22	Tmem132c	PV	94%	intronic	chr5	127305150	127305592	442	1	0	0	0	0	75%
E23	Tmem132c	PV	64%	intronic	chr5	127323924	127324468	544	1	1	1	1	0	85%
E24	Tmem132c	PV	82%	intronic	chr5	127331966	127332522	556	1	1	1	1	0	74%
E25	Tmem132c	PV	73%	intronic	chr5	127355818	127356133	315	1	0	0	0	0	77%
E26	Lrcc38	PV	72%	intergenic	chr4	143348892	143349749	857	1	1	1	0	0	70%
E27	Lrcc38	PV	66%	intronic	chr4	143361408	143362362	954	1	0	1	0	0	71%
E28	Inpp5j	PV	83%	intergenic	chr11	3504821	3505244	423	1	1	1	1	1	77%
E29	Inpp5j	PV	94%	intergenic	chr11	3509025	3509652	627	1	1	0	0	0	74%
E30	Mef2c	PV	77%	intergenic	chr13	83503268	83504033	765	0	0	0	0	0	-
E31	Mef2c	PV	63%	intronic	chr13	83507235	83507457	222	0	0	0	0	0	68%
E32	Mef2c	PV	70%	intronic	chr13	83515122	83515409	287	0	0	0	0	0	70%
E33	Mef2c	PV	82%	intronic	chr13	83518268	83519179	911	1	1	1	1	1	-
E34	Pthlh	PV	48%	intronic	chr6	147263395	147263584	189	1	1	1	1	1	68%
E35	Pthlh	PV	86%	intergenic	chr6	147266874	147267390	516	0	0	0	0	0	69%

Supplementary Table 1. Table containing the specifications for all tested enhancers that includes their associated gene, target population, specificity for target population, location, presence of ATAC peaks, and conservation with the human sequence.

F	Quantification	n	mean	s.e.m	F	Quantification	n	mean	s.e.m	F	Quantification	n	mean	s.e.m
1e	E1_Reporter_layer1-6	3	17.1	4.7	1f	E2_Reporter / VIP_layer6	3	na	na	1f	E5_Density Gad1+_layer2/3	3	22.2	1.5
1e	E2_Reporter_layer1-6	3	78.7	11.4	1f	E5_Reporter / Gad1_layer1	3	91.7	8.3	1f	E5_Density Gad1+_layer4	3	12.2	0.5
1e	E3_Reporter_layer1-6	3	49.1	5.5	1f	E5_Reporter / Gad1_layer2/3	3	98.9	1.1	1f	E5_Density Gad1+_layer5	3	18.6	0.3
1e	E4_Reporter_layer1-6	3	16	2.6	1f	E5_Reporter / Gad1_layer4	3	95.7	0	1f	E5_Density Gad1+_layer6	3	8.4	1.9
1e	E5_Reporter_layer1-6	3	38.3	17	1f	E5_Reporter / Gad1_layer5	3	35	1.7	1f	E5_Density Gad1+_layer1	3	0.3	0.4
1e	E6_Reporter_layer1-6	3	8.1	0.2	1f	E5_Reporter / Gad1_layer6	3	94.7	5.3	1f	E5_Density Gad1+_layer2/3	3	0.3	0.4
1e	E7_Reporter_layer1-6	3	10.4	1.4	1f	E5_Reporter / PV_layer1	3	0	0	1f	E5_Density Gad1+_layer4	3	0.6	0
1e	E8_Reporter_layer1-6	3	41.9	9.2	1f	E5_Reporter / PV_layer2/3	3	36.3	7.7	1f	E5_Density Gad1+_layer5	3	34.7	3
1e	E9_Reporter_layer1-6	3	28.2	5.6	1f	E5_Reporter / PV_layer4	3	15.8	3.8	1f	E5_Density Gad1+_layer6	3	0.6	0.8
1e	E10_Reporter_layer1-6	3	22.3	7.2	1f	E5_Reporter / PV_layer5	3	17.8	4.5	1f	E6_Density Gad1+_layer1	3	0	0
1e	Dlx_Reporter_layer1-6	3	100.1	7.9	1f	E5_Reporter / PV_layer6	3	12.9	2.1	1f	E6_Density Gad1+_layer2/3	3	34.7	7.2
1e	E1_Reporter / Gad1_layer1-6	2	95.1	4.3	1f	E5_Reporter / SST_layer1	3	0	0	1f	E6_Density Gad1+_layer4	3	36.8	1.3
1e	E2_Reporter / Gad1_layer1-6	2	97.8	0	1f	E5_Reporter / SST_layer2/3	3	7.1	4.3	1f	E6_Density Gad1+_layer5	3	13.7	6.6
1e	E3_Reporter / Gad1_layer1-6	2	95	2.8	1f	E5_Reporter / SST_layer4	3	22.4	10.3	1f	E6_Density Gad1+_layer6	3	13.6	1
1e	E4_Reporter / Gad1_layer1-6	2	97.6	2.4	1f	E5_Reporter / SST_layer5	3	13.1	4.3	1f	E6_Density Gad1+_layer1	3	0	0
1e	E5_Reporter / Gad1_layer1-6	2	63.7	1.5	1f	E5_Reporter / SST_layer6	3	12.3	12.3	1f	E6_Density Gad1+_layer2/3	3	0	0
1e	E6_Reporter / Gad1_layer1-6	2	98.7	1.3	1f	E5_Reporter / VIP_layer1	3	na	na	1f	E6_Density Gad1+_layer4	3	0.6	0.9
1e	E7_Reporter / Gad1_layer1-6	2	89.5	4	1f	E5_Reporter / VIP_layer2/3	3	na	na	1f	E6_Density Gad1+_layer5	3	0	0
1e	E8_Reporter / Gad1_layer1-6	2	85.4	0.5	1f	E5_Reporter / VIP_layer4	3	na	na	1f	E6_Density Gad1+_layer6	3	0.6	0.9
1e	E9_Reporter / Gad1_layer1-6	2	98.6	1.4	1f	E5_Reporter / VIP_layer5	3	na	na	2b	E2_Reporter / PV_layer1-6	4	91.6	0.9
1e	E10_Reporter / Gad1_layer1-6	2	96.7	2.4	1f	E5_Reporter / VIP_layer6	3	na	na	2b	E2_Reporter / PV_layer1-6	8	90.8	1.1
1e	Dlx_Reporter / Gad1_layer1-6	4	93.4	1.3	1f	E6_Reporter / Gad1_layer1	3	0	0	2b	E2_PV / reporter_layer1-6	19	75.7	2.9
1e	E1_Reporter / PV_layer1-6	6	50.3	5.6	1f	E6_Reporter / Gad1_layer2/3	3	95.5	4.5	2c	E2_Reporter at .5_layer1-6	3	10	1.1
1e	E2_Reporter / PV_layer1-6	6	74	2.5	1f	E6_Reporter / Gad1_layer4	3	100	0	2c	E2_Reporter at 2_layer1-6	3	33	10.6
1e	E3_Reporter / PV_layer1-6	4	45.5	2.1	1f	E6_Reporter / Gad1_layer5	3	98.3	1.7	2c	E2_Reporter at 5_layer1-6	3	96.5	8.4
1e	E4_Reporter / PV_layer1-6	6	30.7	3.8	1f	E6_Reporter / Gad1_layer6	3	100	0	2c	E2_Reporter / PV at 5_layer1-6	3	86.4	0.5
1e	E5_Reporter / PV_layer1-6	6	22.8	2.4	1f	E6_Reporter / PV_layer1	3	0	0	2c	E2_Reporter / PV at 2_layer1-6	3	86.6	0.6
1e	E6_Reporter / PV_layer1-6	2	16	2	1f	E6_Reporter / PV_layer2/3	3	5.4	1.4	2c	E2_Reporter / PV at 5_layer1-6	3	91.3	0.8
1e	E7_Reporter / PV_layer1-6	6	50.8	2.1	1f	E6_Reporter / PV_layer4	3	3.4	0.6	2d	E2_Reporter / PV 1-15_layer1-6	4	56.7	2.3
1e	E8_Reporter / PV_layer1-6	4	47.5	3.4	1f	E6_Reporter / PV_layer5	3	2.3	0.6	2d	E2_Reporter / PV 7-15_layer1-6	5	67.2	1.5
1e	E9_Reporter / PV_layer1-6	6	52.8	6.3	1f	E6_Reporter / PV_layer6	3	1.8	0.3	2d	E2_Reporter / PV 10-15_layer1-6	3	81.7	1.1
1e	E10_Reporter / PV_layer1-6	4	29	2.7	1f	E6_Reporter / SST_layer1	3	0	0	2d	E2_Reporter / PV 4-7_layer1-6	2	60.9	1.9
1f	E2_Reporter / Gad1_layer1	3	0	0	1f	E6_Reporter / SST_layer2/3	3	0	0	2d	E2_Reporter / PV 7-10_layer1-6	5	78.1	1.8
1f	E2_Reporter / Gad1_layer2/3	3	94.7	0.9	1f	E6_Reporter / SST_layer4	3	7.5	4.6	3a	E2_Reporter / PV_layer1-6	4	85.3	0.6
1f	E2_Reporter / Gad1_layer4	3	100	0	1f	E6_Reporter / SST_layer5	3	5.9	2.6	3a	E2_PV / reporter_layer1-6	4	87.7	1.2
1f	E2_Reporter / Gad1_layer5	3	97.1	1	1f	E6_Reporter / SST_layer6	3	2.9	2.9	3b	E2_Delta_layer1-6	14	8.2	0.8
1f	E2_Reporter / Gad1_layer6	3	97.2	2.8	1f	E6_Reporter / VIP_layer1	3	0	0	4a	E2_Rat_layer1-6	1	93	na
1f	E2_Reporter / PV_layer1	3	0	0	1f	E6_Reporter / VIP_layer2/3	3	92.5	2.6	4a	E2_Marmoset_layer1-6	4	91.8	3.1
1f	E2_Reporter / PV_layer2/3	3	86.5	2.8	1f	E6_Reporter / VIP_layer4	3	76.3	8.8	4a	E2_Macaque_layer1-6	4	87.3	0.5
1f	E2_Reporter / PV_layer4	3	93.5	1.7	1f	E6_Reporter / VIP_layer5	3	76.7	3.8	4b	E2_Human_reporter_layerna	44	72.7	na
1f	E2_Reporter / PV_layer5	3	87.3	2.1	1f	E6_Reporter / VIP_layer6	3	96.2	3.8	4b	E2_Human_CIV1_layerna	10	na	na
1f	E2_Reporter / PV_layer6	3	87.3	2.1	1f	E2_Density Gad1+_layer1	3	0.3	0.5	5a	E11_Reporter / Gad1_layer1-6	2	94.7	1.3
1f	E2_Reporter / SST_layer1	3	0	0	1f	E2_Density Gad1+_layer2/3	3	12.5	1	5a	E11_Reporter / PV_layer1-6	3	91.3	1.6
1f	E2_Reporter / SST_layer2/3	3	0	0	1f	E2_Density Gad1+_layer4	3	30.9	3.1	5a	E14_Reporter / Gad1_layer1-6	2	92.5	2.7
1f	E2_Reporter / SST_layer4	3	6.1	0.8	1f	E2_Density Gad1+_layer5	3	35	1.4	5a	E14_Reporter / PV_layer1-6	3	93.6	1.1
1f	E2_Reporter / SST_layer5	3	3.3	1	1f	E2_Density Gad1+_layer6	3	18.8	4.8	5a	E22_Reporter / Gad1_layer1-6	2	97.6	2.4
1f	E2_Reporter / SST_layer6	3	7.6	1	1f	E2_Density Gad1+_layer1	3	0	0	5a	E22_Reporter / PV_layer1-6	3	92.9	2
1f	E2_Reporter / VIP_layer1	3	na	na	1f	E2_Density Gad1+_layer2/3	3	0.7	0.1	5a	E29_Reporter / Gad1_layer1-6	2	95.8	1.2
1f	E2_Reporter / VIP_layer2/3	3	na	na	1f	E2_Density Gad1+_layer4	3	0	0	5a	E29_Reporter / PV_layer1-6	2	94.3	1.3
1f	E2_Reporter / VIP_layer4	3	na	na	1f	E2_Density Gad1+_layer5	3	1.1	0.6	5b	E22_Reporter / Gad1_layer1-6	2	91.8	1.6
1f	E2_Reporter / VIP_layer5	3	na	na	1f	E2_Density Gad1+_layer6	3	0.7	0.9	5b	E22_Reporter / PV_layer1-6	6	81.3	1.6

Supplementary Table 2. Table containing the metadata associated with each of the quantification plot presented in this the figures of this manuscript.