**SUPPLEMENTARY INFORMATION**

# Hominoid SVA-lncRNA *AK057321* targets human-specific SVA retrotransposons in *SCN8A* and *CDK5RAP2* to initiate neuronal maturation

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**Supplementary Tables 1-20**

**Supplementary Table 1**. SVA-lncRNA *AK057321* shRNA target sequences and cloning primers.

**Supplementary Table 2**. Construction primers used to modify lentiCRISPRv2 hygro (Addgene #98291) to express in tandem sgRNAs with Cas9 and either mcherry or blue fluorescent protein.

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**Supplementary Table 6**. Primers used to generate Tet-inducible *CDK5RAP2* cDNA.

**Supplementary Table 7.** Primers used to clone *CHAF1B* SVA into pGL3 luciferase vector.

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**Supplementary Table 11**. Table of BAC clone numbers used in this study.

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**Supplementary Table 15**. Primers used to clone zeocin resistance gene.

**Supplementary Table 16**. Table of IDT primers and probes used in gene expression studies.

**Supplementary Table 17**. Table of Eurofin primers used in gene expression studies.

**Supplementary Table 18**. Primers used for relative quantitative PCR (rqPCR) for *AK057321* expression analysis in Supplementary Fig. 12.

**Supplementary Table 19**. Thermocycler conditions for reverse transcriptase and polymerase chain reactions.

**Supplementary Table 20**. Genomic IDT primers and probes used in SVA-lncRNA *AK057321* binding studies.

**Supplementary Data 1-6 (excel spreadsheets)**

**Supplementary Data 1.** Duplication of SVA-lncRNA *AK057321* in rare cases of autism spectrum disorder.

**Supplementary Data 2.** Source data for main manuscript Figure graphs.

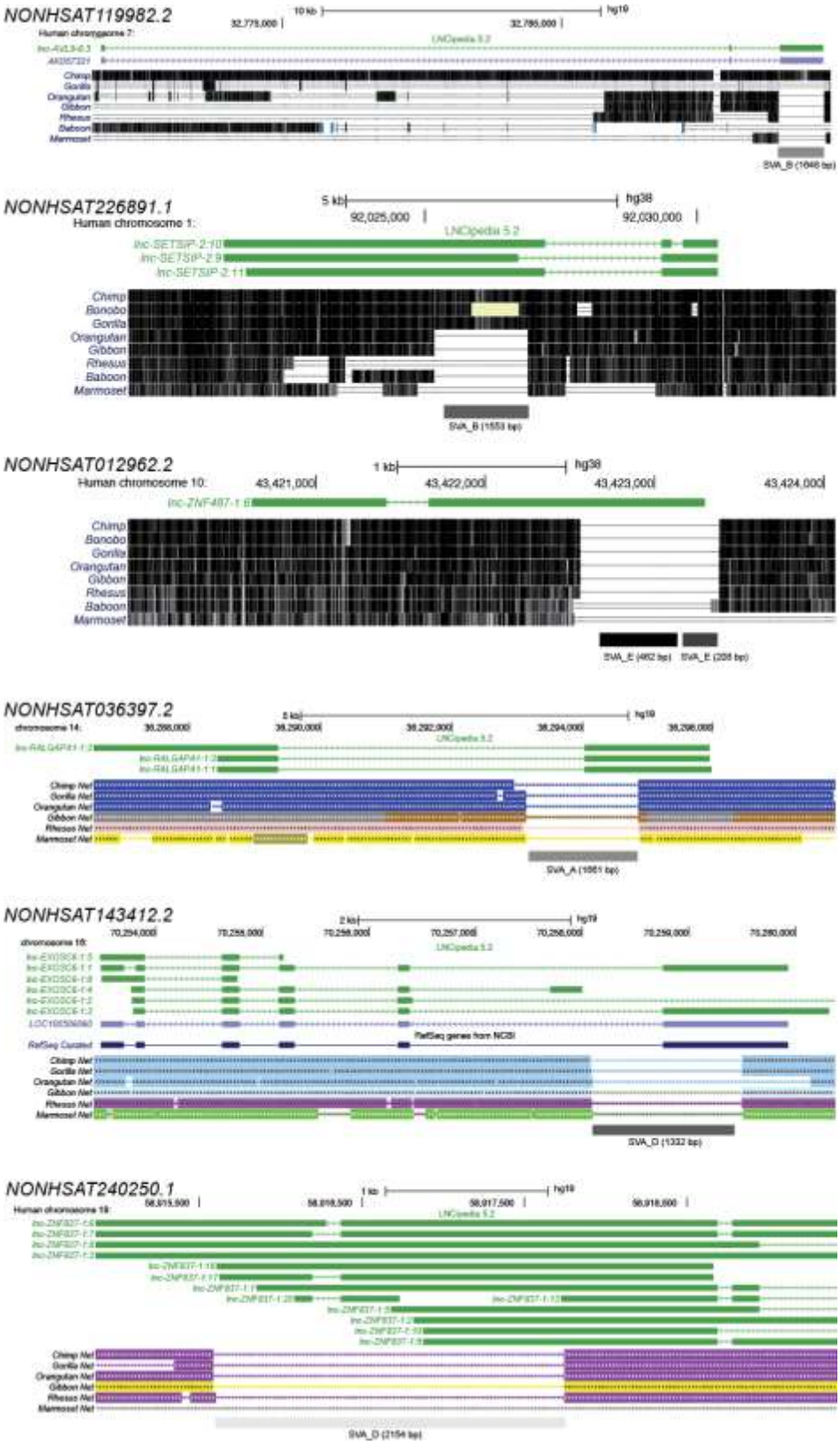
**Supplementary Data 3.** Source data for supplementary manuscript Figure graphs.

**Supplementary Data 4.** Human genes containing intronic SVAs.

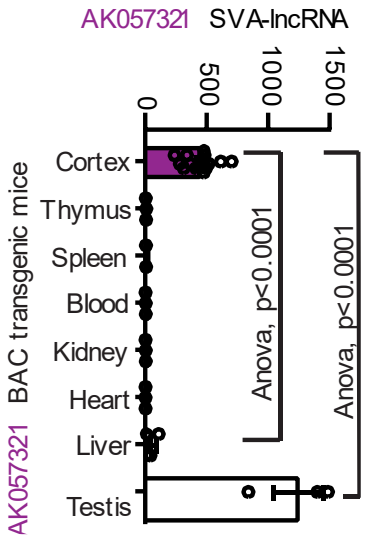
**Supplementary Data 5.** Gene ontology disease enrichment of human genes with intragenic SVAs.

**Supplementary Data 6.** Gene ontology term enrichment of human genes with intragenic SVAs.

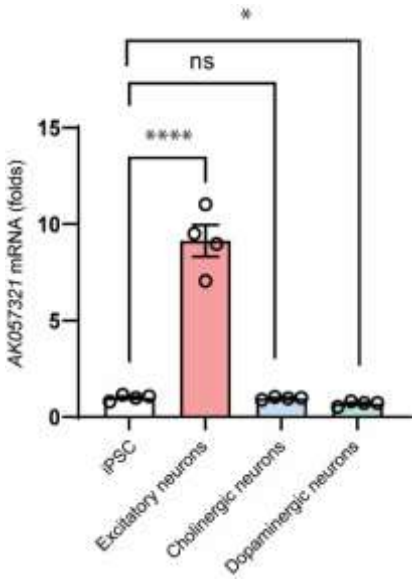
**Supplementary Figures 1-21**



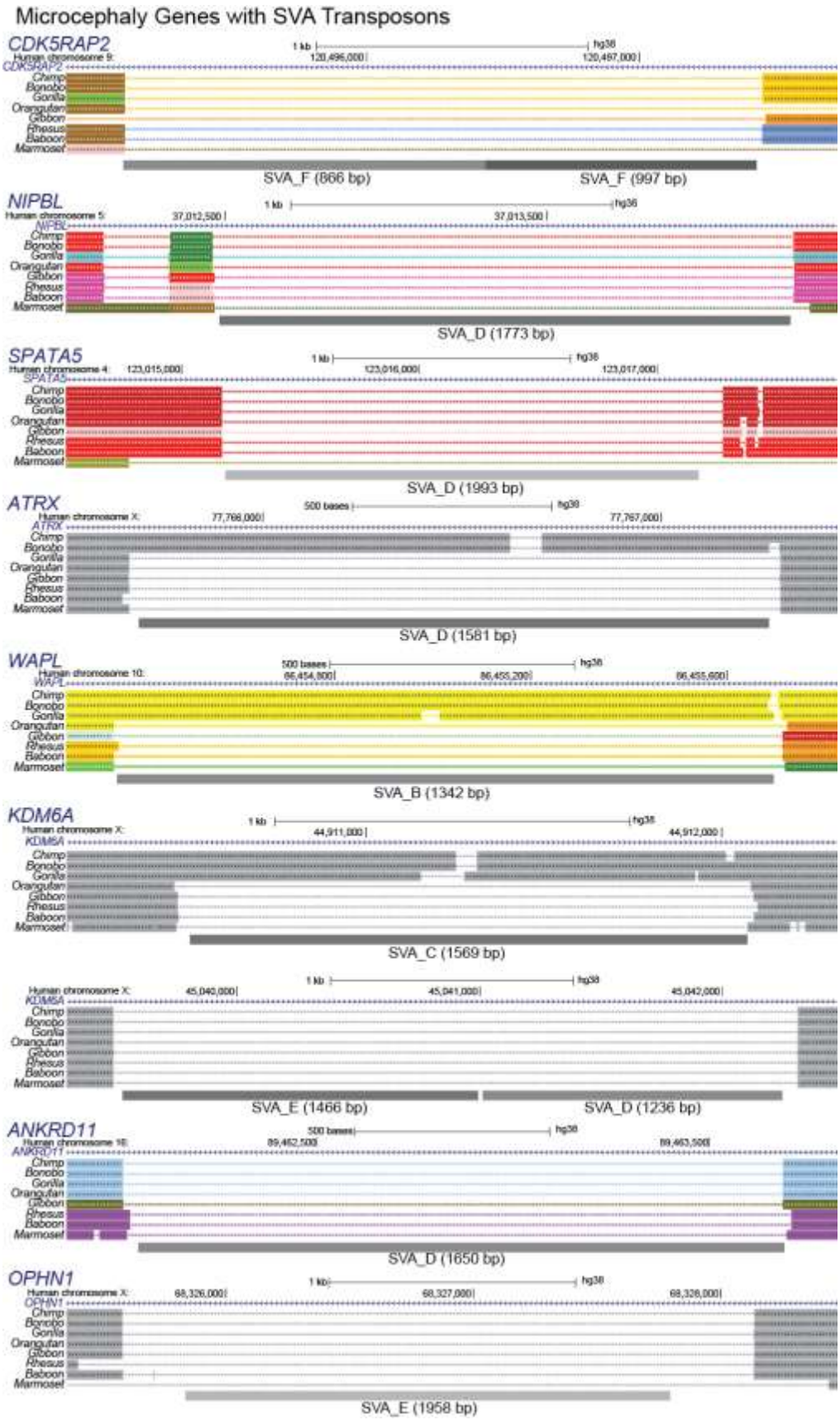

**Supplementary Fig. 1:** Example long non-coding RNAs which contain SVA transposon including SVA-lncRNA *AK057321* (NONSAT119982.2) (UCSC genome browser, GRCh38/gh38).



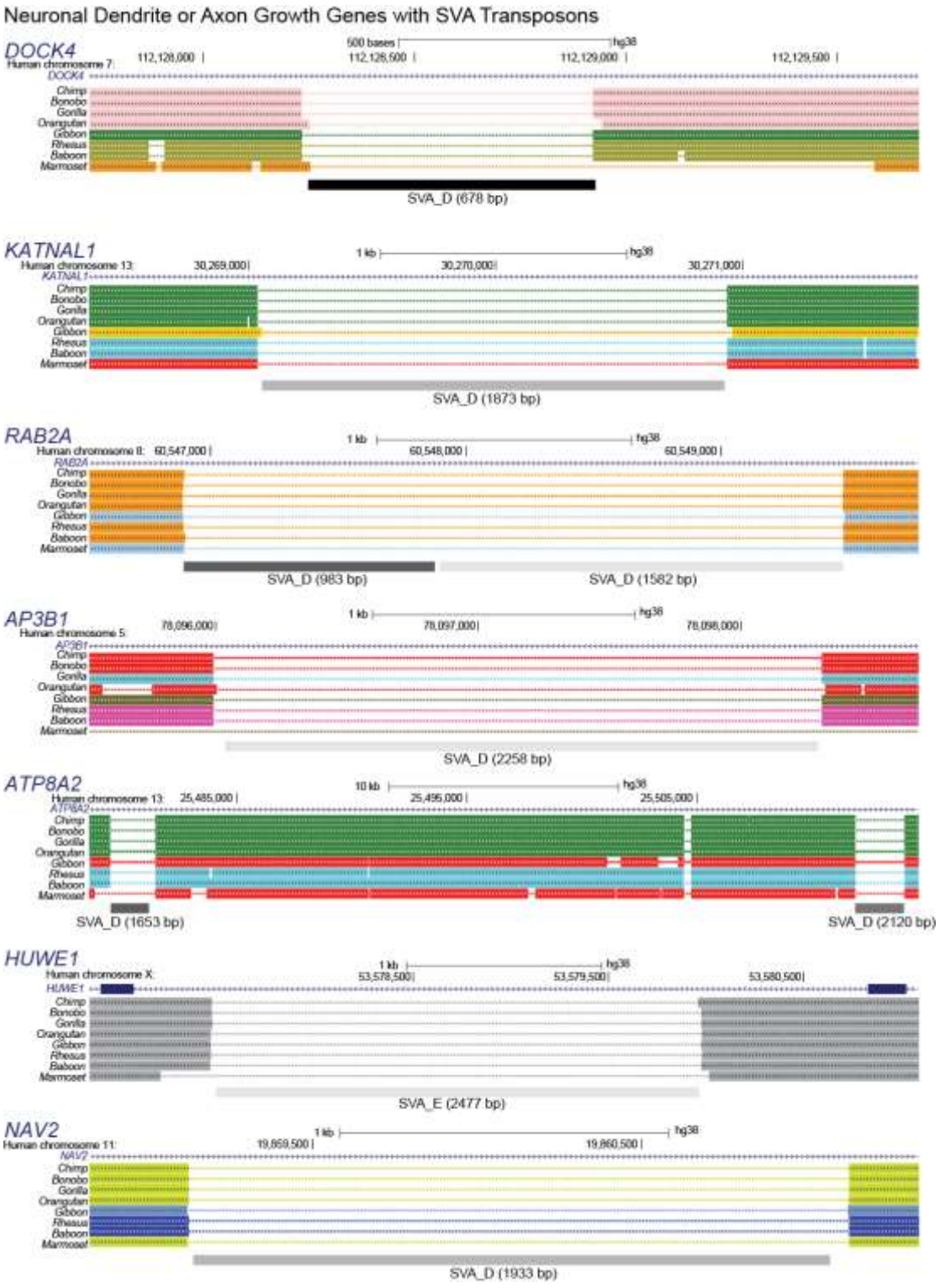

**Supplementary Fig. 2:** Expression of full-length SVA-lncRNA *AK057321* human gene in a transgenic mouse compared to wild-type mice (*GAPDH*, reference; n=14 biologicals for cortex and 1 for other tissue, measured in triplicate). One-way ANOVA ($F_{6,24}$=26.14, p<0.0001; excluding testis) and ($F_{7,26}$ =34.72, p<0.0001 with all tissues). Data represent the mean ± SEM.



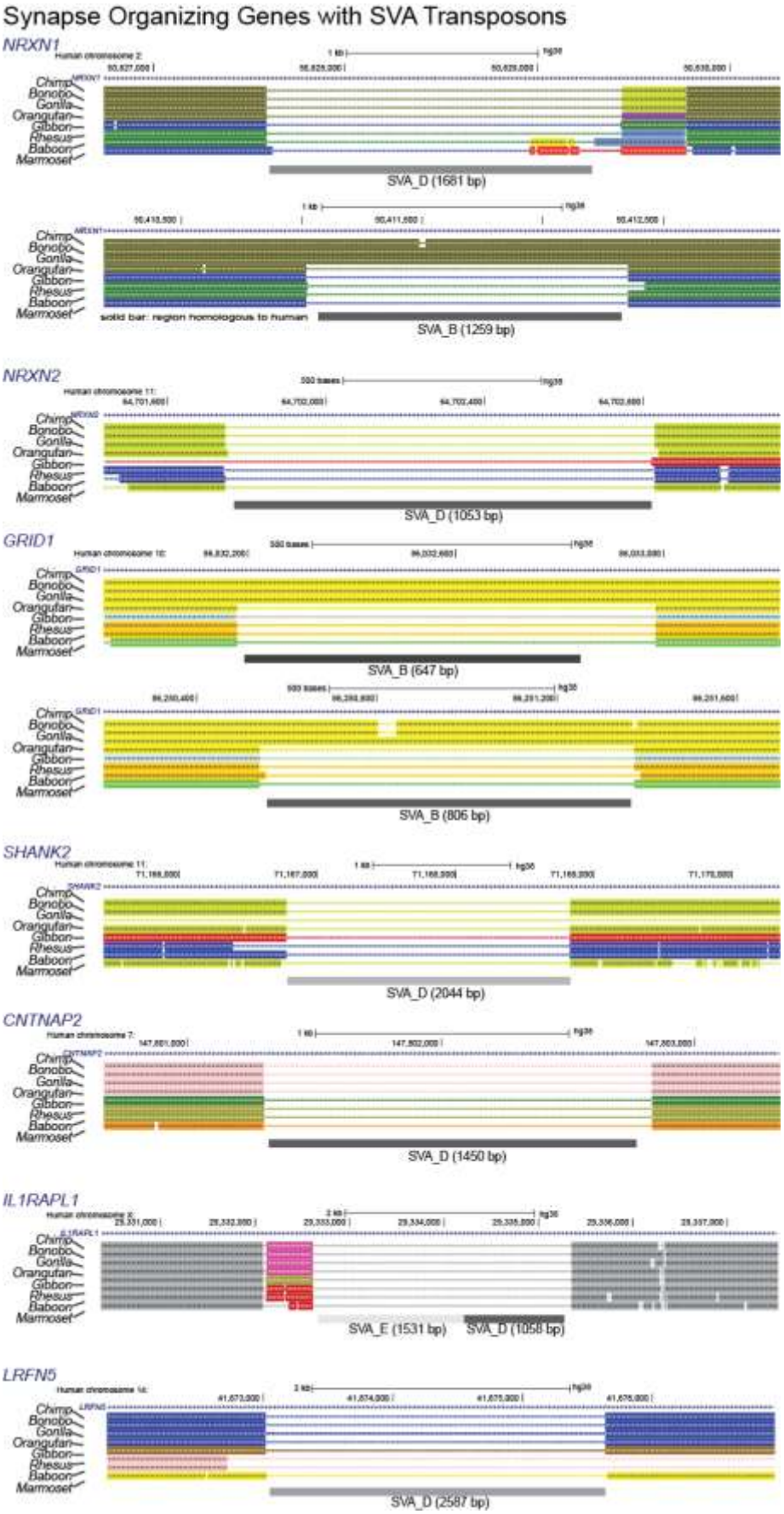

**Supplementary Fig. 3:** SVA-lncRNA *AK057321* mRNA increases as iPSC cells are differentiated into excitatory (glutamatergic), but not cholinergic or dopaminergic neurons. RNA from each cell type was obtained from Elixirgen Scientific and gene expression was determined by RT-qPCR with *GAPDH* as the internal reference gene. Unpaired Student's t test. Data represent the mean ± SEM.**** p<0.0001, *** p<0.001, ** p<0.01, * p<0.05 and ns p>0.05 versus control.



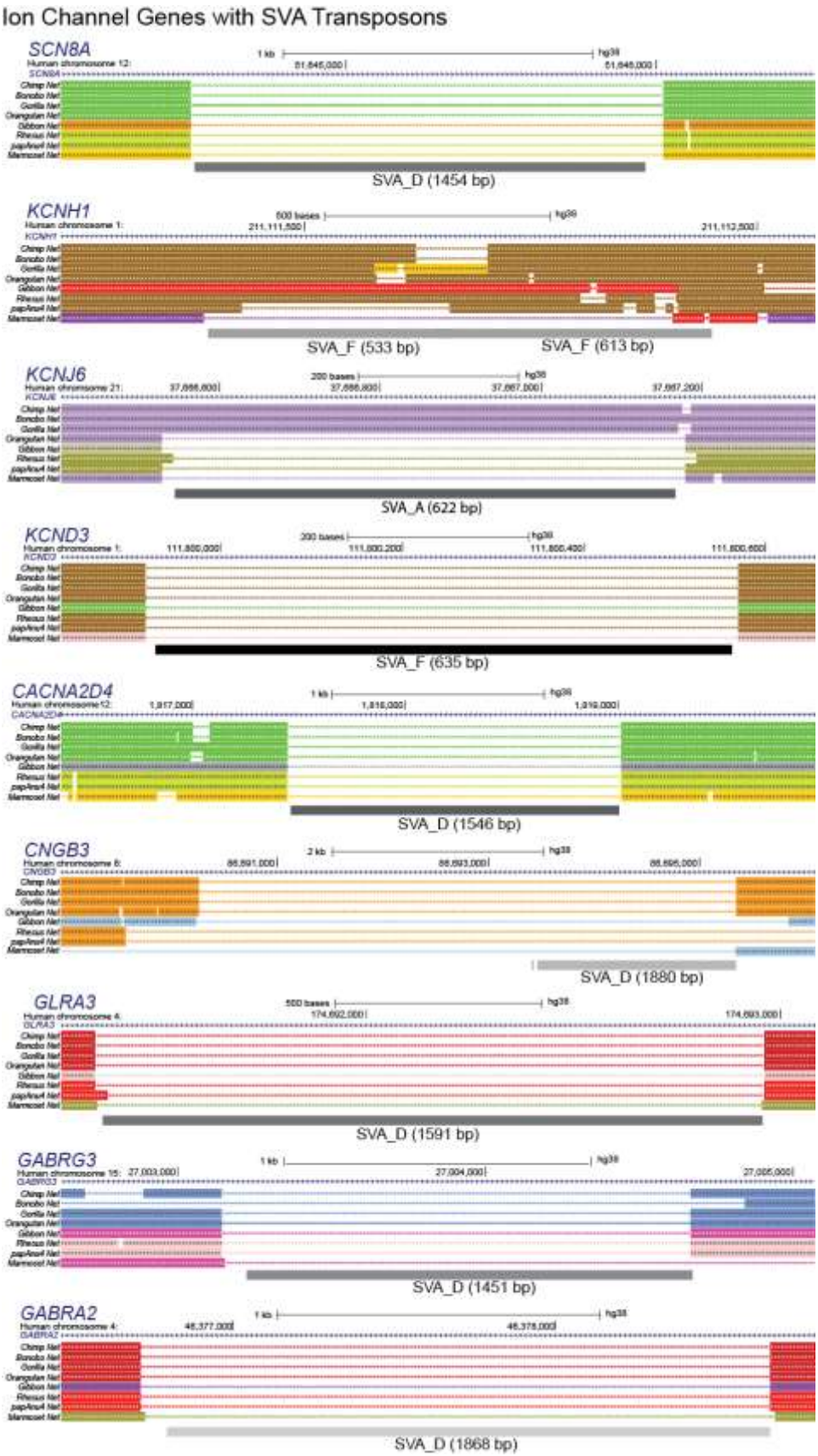

**Supplementary Fig. 4:** Example microcephaly genes with intronic SVAs (UCSC genome browser, GRCh38/gh38).




**Supplementary Fig. 5:** Example neuronal dendrite and axon growth genes with intronic SVAs (UCSC genome browser, GRCh38/gh38).




**Supplementary Fig. 6.** Example synapse organizing genes within intronic SVAs (UCSC genome browser, GRCh38/gh38).

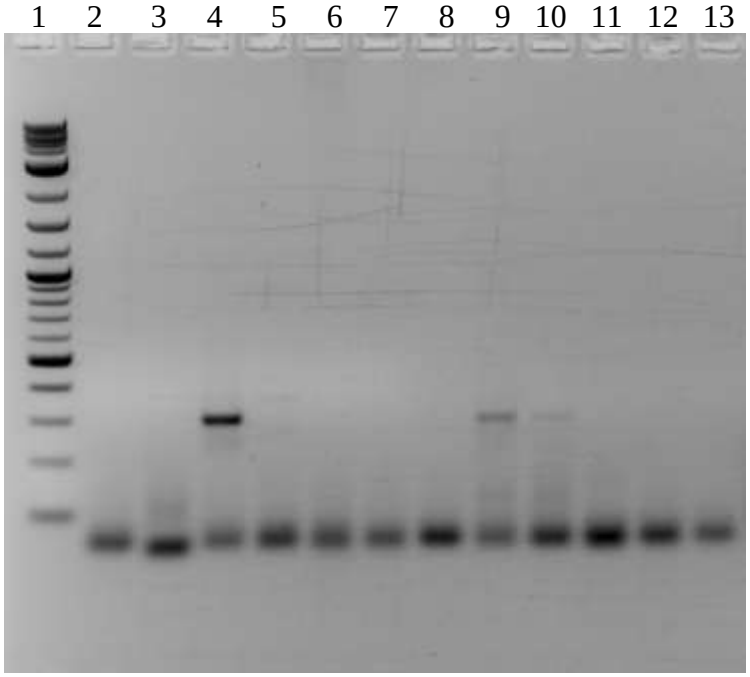



**Supplementary Fig. 7:** Example ion channel genes that contain SVA transposons (UCSC genome browser, GRCh38/gh38).

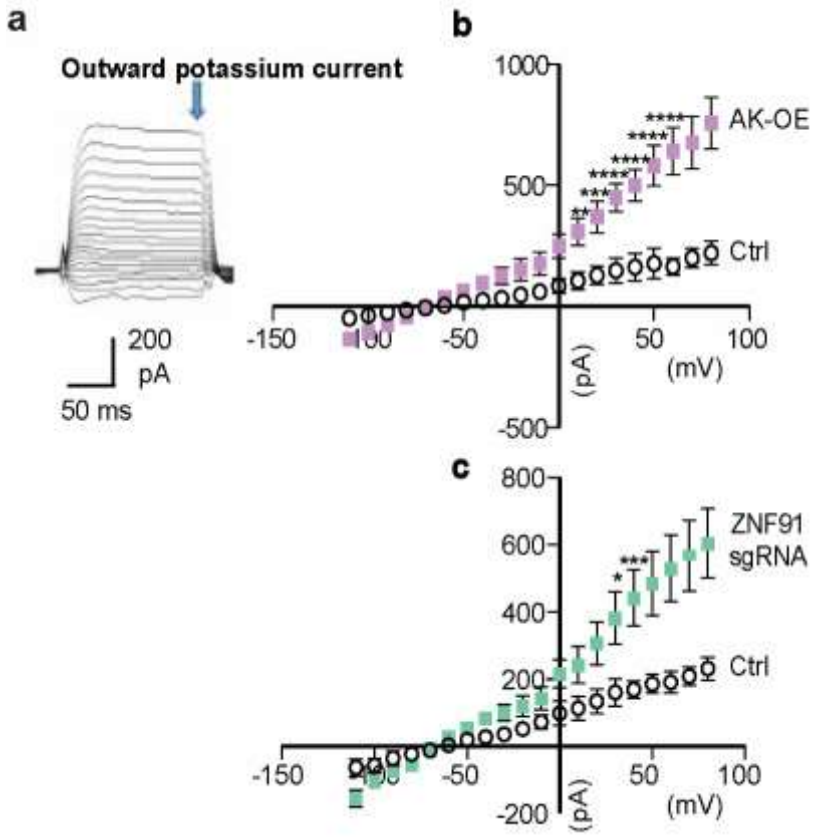
**a**

| Lane | Expected size | PCR primers | Cas9/sgRNA transfection |
|---|---|---|---|
| 1 | DNA ladder | NEB 1kb Plus DNA ladder | NA |
| 2 | 2870 bp | *AK057321* del SVA F1 & R1 | Cas9/sgRNA control |
| 3 | 309 bp | *AK057321* del SVA F1 & R1 | Set 1 guides |
| 4 | 302 bp | *AK057321* del SVA F1 & R1 | Set 2 guides |
| 5 | 365 bp | *AK057321* del SVA F1 & R1 | Set 3 guides |
| 6 | 2870 bp | *AK057321* del SVA F1 & R1 | Ntera-2 no transfection |
| 7 | none | *AK057321* del SVA F1 & R1 | None – water control |
| 8 | 2870 bp | *AK057321* del SVA F1 & R1 | 1:10 Cas9/sgRNA control gDNA |
| 9 | 309 bp | *AK057321* del SVA F1 & R1 | 1:10 dilution Set 1 guide gDNA |
| 10 | 302 bp | *AK057321* del SVA F1 & R1 | 1:10 dilution Set 2 guide gDNA |
| 11 | 364 bp | *AK057321* del SVA F1 & R1 | 1: 10 dilution Set 3 guide gDNA |
| 12 | 2870 bp | *AK057321* del SVA F1 & R1 | 1:10 dilution Ntera-2 gDNA |
| 13 | none | *AK057321* del SVA F1 & R1 | None – water control |

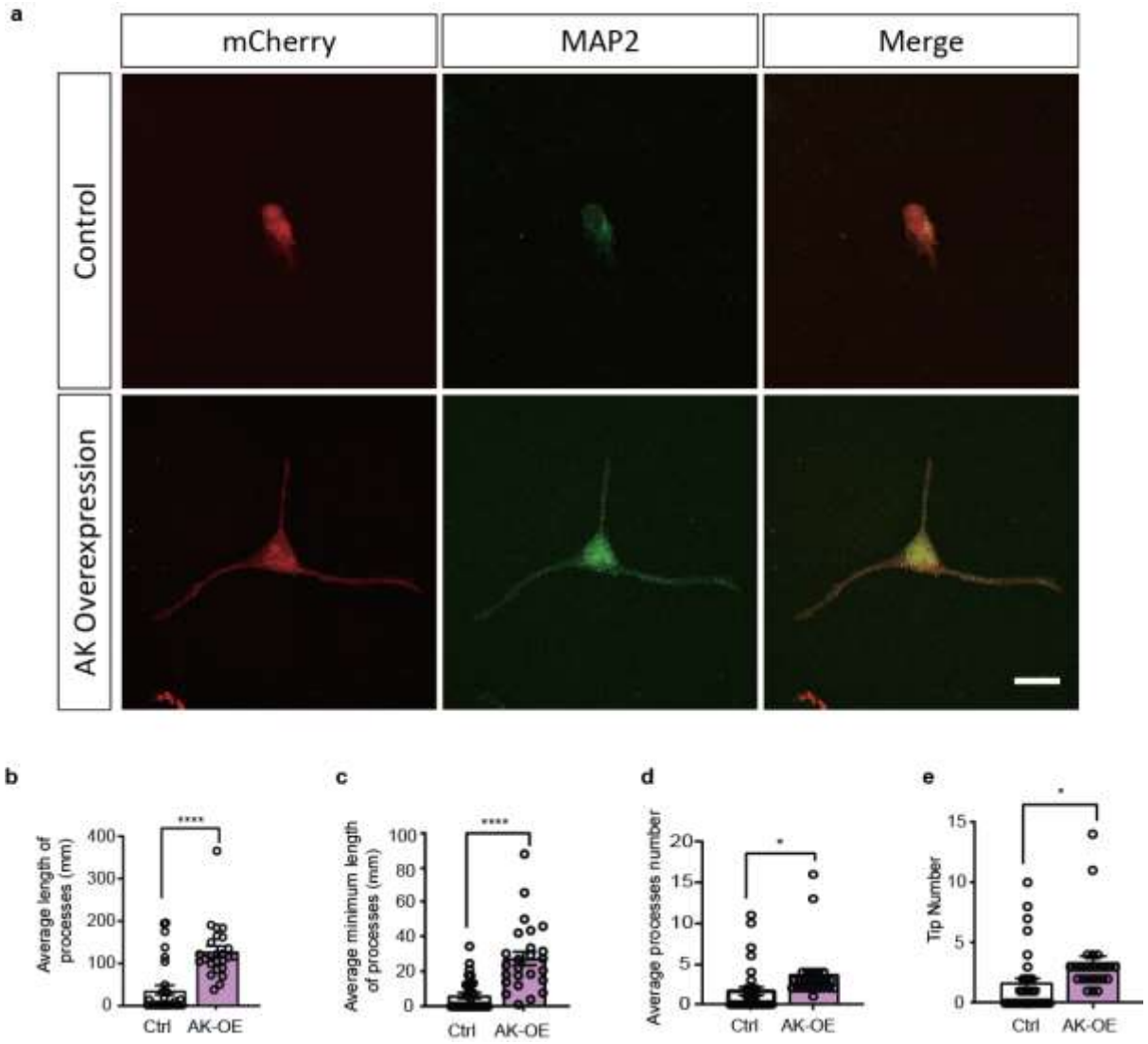
**b**




**Supplementary Fig. 8:** Complete gel image for **Fig. 1h**, deletion of the SVA_B within SVA-lncRNA *AK057321*. **a**, Table for the genomic samples and primers used to detect deletion of the SVA within *AK057321* for the uncropped gel image in **b** that was used to generate **Fig. 1h**. All sgRNA combinations and sequences are in Supplementary Table 3 and the genomic PCR primer sequences are listed in Supplementary Table 4. Set 2 guides showed evidence of deletion of the SVA based on the expected band size of 302 bp, lanes 4 and 10. Note that set 1 guides also showed a band of the expected size 309 bp in lane 9. The undeleted PCR band (i.e. band spanning the SVA) was not visualized in lanes 2, 6, 8 and 12 because of the short PCR extension time.




**Supplementary Fig. 9:** Outward Potassium currents are larger in SVA-lncRNA *AK057321* overexpressing (AK-OE) and *ZNF91* sgRNA treatment groups measured during depolarizing voltage steps. **a**, Current responses to voltage steps in different treatment groups. **b** and **c**, Total Ik currents were significantly larger in *AK057321* OE (n=6) and *ZNF91* sgRNA (n=6) groups than that in the control group**.** Two-way ANOVA with Bonferroni post hoc tests. Data represent the mean ± SEM. **** $p<0.0001$, ** $p<0.01$.

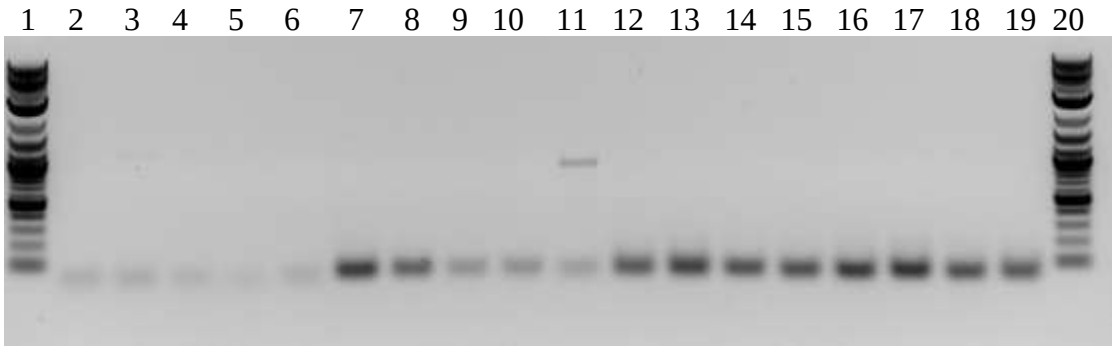



**Supplementary Fig. 10:** Additional quantification of neuronal morphology of NTera-2 cells with or without SVA-lncRNA *AK057321* overexpression (AK-OE). **a**, NTera-2 cells transfected with control or AK overexpression plasmids (containing mCherry reporter, red fluorescence), and 13 days after plating, the cells were fixed, permeabilization and stained with MAP2 antibody (green immunofluorescence). Scale bar is 20 microns. **b**, Quantification of average mean length of processes from NTera-2 cells with or without *AK057321* OE. **c**, Quantification of average minimum length of processes. **d**, Quantification of average process number. **e**, Quantification of tip number. All graphs are presented as Mean ± SEM. Control, N = 31, AK-OE, N = 25. Unpaired two-tailed Student's t test. Data represent the mean ± SEM.**** $p<0.0001$, *** $p<0.001$, ** $p<0.01$, * $p<0.05$ versus control.

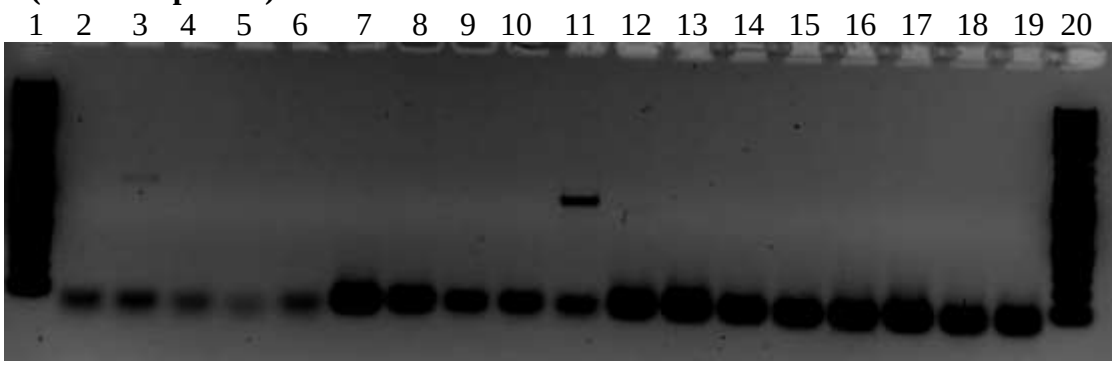
**a**

| Lane | Expected size | PCR primers | Cas9/sgRNA transfection |
|---|---|---|---|
| 1 | DNA ladder | NEB 1kb Plus DNA ladder | NA |
| 2 | 1255 bp | *CDK5RAP2* del SVA F1 and R1 | Set 1 guides |
| 3 | 1230 bp | *CDK5RAP2* del SVA F1 and R1 | Set 2 guides |
| 4 | 1188 bp | *CDK5RAP2* del SVA F1 and R1 | Set 3 guides |
| 5 | 1757 bp | *CDK5RAP2* del SVA F1 and R1 | Set 4 guides |
| 6 | 1787 bp | *CDK5RAP2* del SVA F1 and R1 | Set 5 guides |
| 7 | none | *CDK5RAP2* del SVA F1 and R1 | None – water control |
| 8 | 4372 bp | *CDK5RAP2* del SVA F2 and R1 | Ntera-2 no transfection |
| 9 | 4372 bp | *CDK5RAP2* del SVA F2 and R1 | Cas9/sgRNA control |
| 10 | 993 bp | *CDK5RAP2* del SVA F2 and R1 | Set 1 guides |
| 11 | 968 bp | *CDK5RAP2* del SVA F2 and R1 | Set 2 guides |
| 12 | 926 bp | *CDK5RAP2* del SVA F2 and R1 | Set 3 guides |
| 13 | 1495 bp | *CDK5RAP2* del SVA F2 and R1 | Set 4 guides |
| 14 | 1525 bp | *CDK5RAP2* del SVA F2 and R1 | Set 5 guides |
| 15 | none | *CDK5RAP2* del SVA F2 and R1 | None – water control |
| 16 | 4677 bp | *CDK5RAP2* del SVA F3 and R1 | Ntera-2 no transfection |
| 17 | 4677 bp | *CDK5RAP2* del SVA F3 and R1 | Cas9/sgRNA control |
| 18 | 1298 bp | *CDK5RAP2* del SVA F3 and R1 | Set 1 guides |
| 19 | 1273 bp | *CDK5RAP2* del SVA F3 and R1 | Set 2 guides |
| 20 | DNA ladder | NEB 1kb Plus DNA ladder | NA |
| 21 | DNA ladder | NEB 1kb Plus DNA ladder | NA |
| 22 | 1231 bp | *CDK5RAP2* del SVA F3 and R1 | Set 3 guides |
| 23 | 1800 bp | *CDK5RAP2* del SVA F3 and R1 | Set 4 guides |
| 24 | 1830 bp | *CDK5RAP2* del SVA F3 and R1 | Set 5 guides |
| 25 | none | *CDK5RAP2* del SVA F3 and R1 | None – water control |
| 26 | 4461 bp | *CDK5RAP2* del SVA F4 and R2 | Ntera-2 no transfection |
| 27 | 4461 bp | *CDK5RAP2* del SVA F4 and R2 | Cas9/sgRNA control |
| 28 | 1152 bp | *CDK5RAP2* del SVA F4 and R2 | Set 1 guides |
| 29 | 1057 bp | *CDK5RAP2* del SVA F4 and R2 | Set 2 guides |
| 30 | 1015 bp | *CDK5RAP2* del SVA F4 and R2 | Set 3 guides |
| 31 | 1584 bp | *CDK5RAP2* del SVA F4 and R2 | Set 4 guides |
| 32 | 1614 bp | *CDK5RAP2* del SVA F4 and R2 | Set 5 guides |
| 33 | none | *CDK5RAP2* del SVA F4 and R2 | None – water control |
| 34 | 4531 bp | *CDK5RAP2* del SVA F5 and R2 | Ntera-2 no transfection |
| 35 | 4531 bp | *CDK5RAP2* del SVA F5 and R2 | Cas9/sgRNA control |
| 36 | 1126 bp | *CDK5RAP2* del SVA F5 and R2 | Set 1 guides |
| 37 | 1127 bp | *CDK5RAP2* del SVA F5 and R2 | Set 2 guides |
| 38 | 1085 bp | *CDK5RAP2* del SVA F5 and R2 | Set 3 guides |
| 39 | 1654 bp | *CDK5RAP2* del SVA F5 and R2 | Set 4 guides |
| 40 | DNA ladder | NEB 1kb Plus DNA ladder | NA |

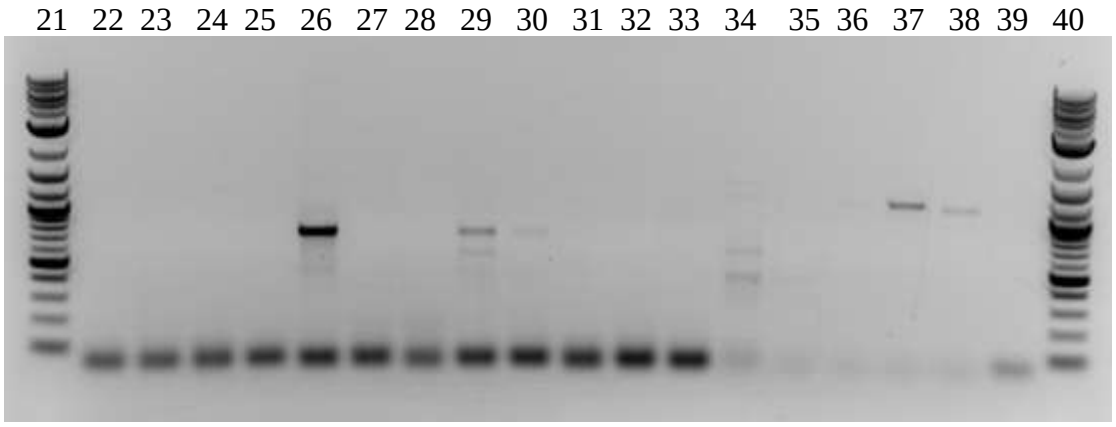
**b**



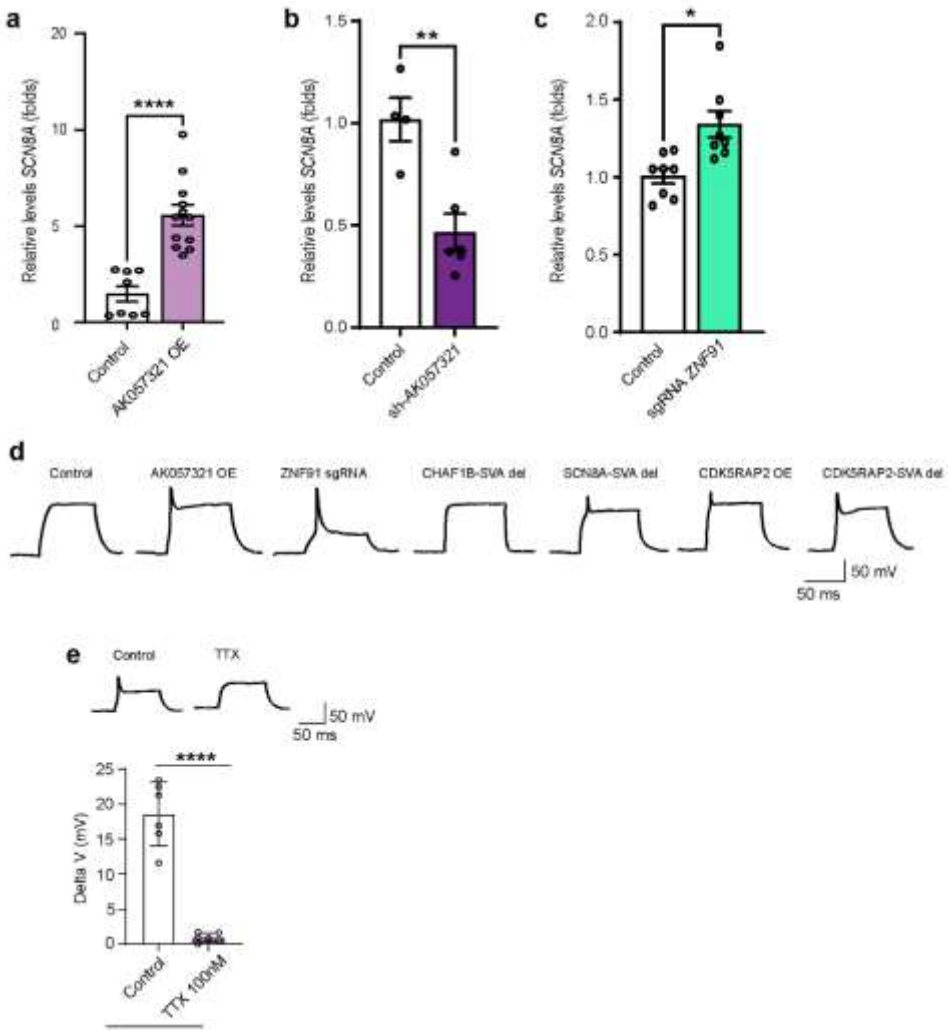

**b (darker exposure)**




**c**




**Supplementary Fig. 11:** Complete gel image for deletion of the SVA_F within *CDK5RAP2*. **a**, Table to explain each lane shown in the uncropped and unedited DNA agarose gel images shown in **b** and **c**. Note that panel **b** is the parent image that was used to generate **Fig. 3b**, and panel **c** is additional data. All sgRNA combinations and sequences are in Supplementary Table 3 and all genomic PCR primer sequences are listed in Supplementary Table 4. Set 2 guides showed evidence of deletion of the SVA based on the expected band sizes obtained with different primer sets (i.e., lane 11, lane 37, and a weak band in lane 3). Note that set 3 guides also showed a band of the proper size in lane 38. Lanes 26, 27 and 30 had bands of incorrect sizes, and this screening primer combination of *CDK5RAP2* del SVA F4 and R2 was not used further. The undeleted PCR band (i.e., with the SVA is not visualized in lanes 8, 9, 16, 17, 26, 27, 34 and 35 because of the high GC content within the tandem SVA_F and because the PCR extension time was too short for bands over 2 Kb.

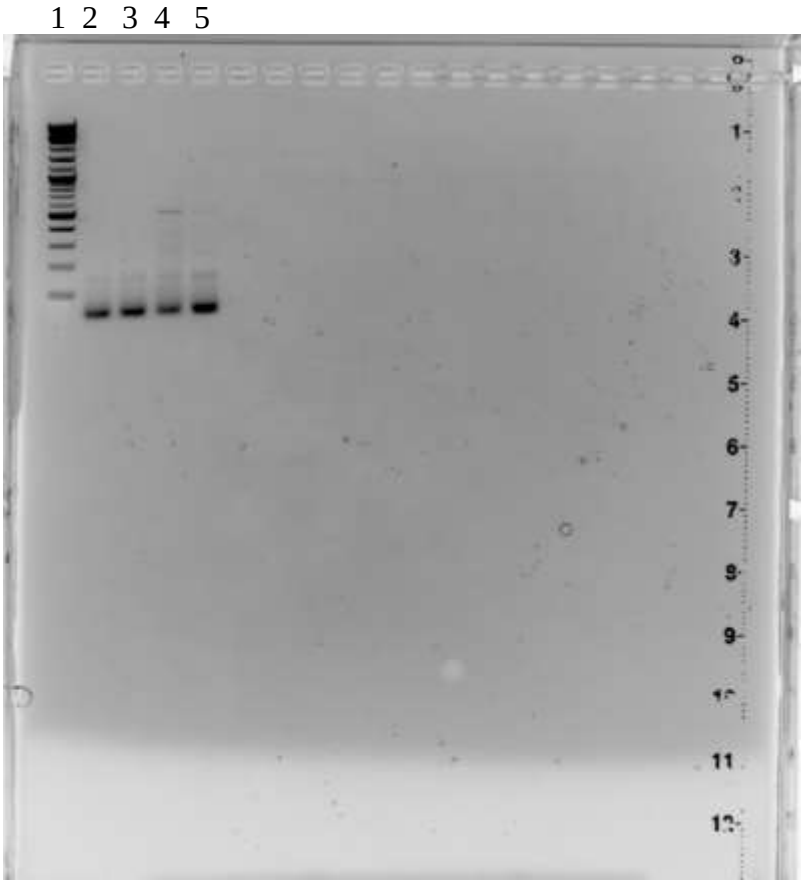



**Supplementary Fig. 12:** Effects of SVA-lncRNA *AK057321* and other interventions on *SCN8A* expression and tetrodotoxin-inhibited sodium spikes. **a**, RT-qPCR quantification of *SCN8A* mRNA in NTera-2 cells transfected to increased SVA-lncRNA *AK057321* expression (OE) or control plasmid with *GAPDH* as the internal reference gene. **b**, RT-qPCR quantification of *SCN8A* mRNA in NTera-2 cells transfected with either sh-*AK057321* or sh-scramble with *GAPDH* as the internal reference gene. **c**, RT-qPCR quantification of *SCN8A* mRNA in NTera-2 cells transfected with sgRNA/Cas9 *ZNF91* vs. control with *GAPDH* as the internal reference gene. Unpaired Student's two-tailed t test for individual gene comparisons to control in **a**-**c**. **d**, Example sodium spikes evoked in the *AK057321* OE, *ZNF91* sgRNA, *SCN8A*-SVA del, *CDK5RAP2* OE and *CDK5RAP2*-SVA del groups. 300 pA or larger current steps failed to induce sodium spikes in control and *CHAF1B*-SVA del groups. **e**, Evoked sodium spikes were blocked by 100 nM tetrodotoxin (TTX, n=7 in each group), .**** $p<0.0001$, *** $p<0.001$, ** $p<0.01$, * $p<0.05$, NS $P>0.05$, versus control, paired Student's t test. Data represent the mean ± SEM (**a**-**c**, **e**).

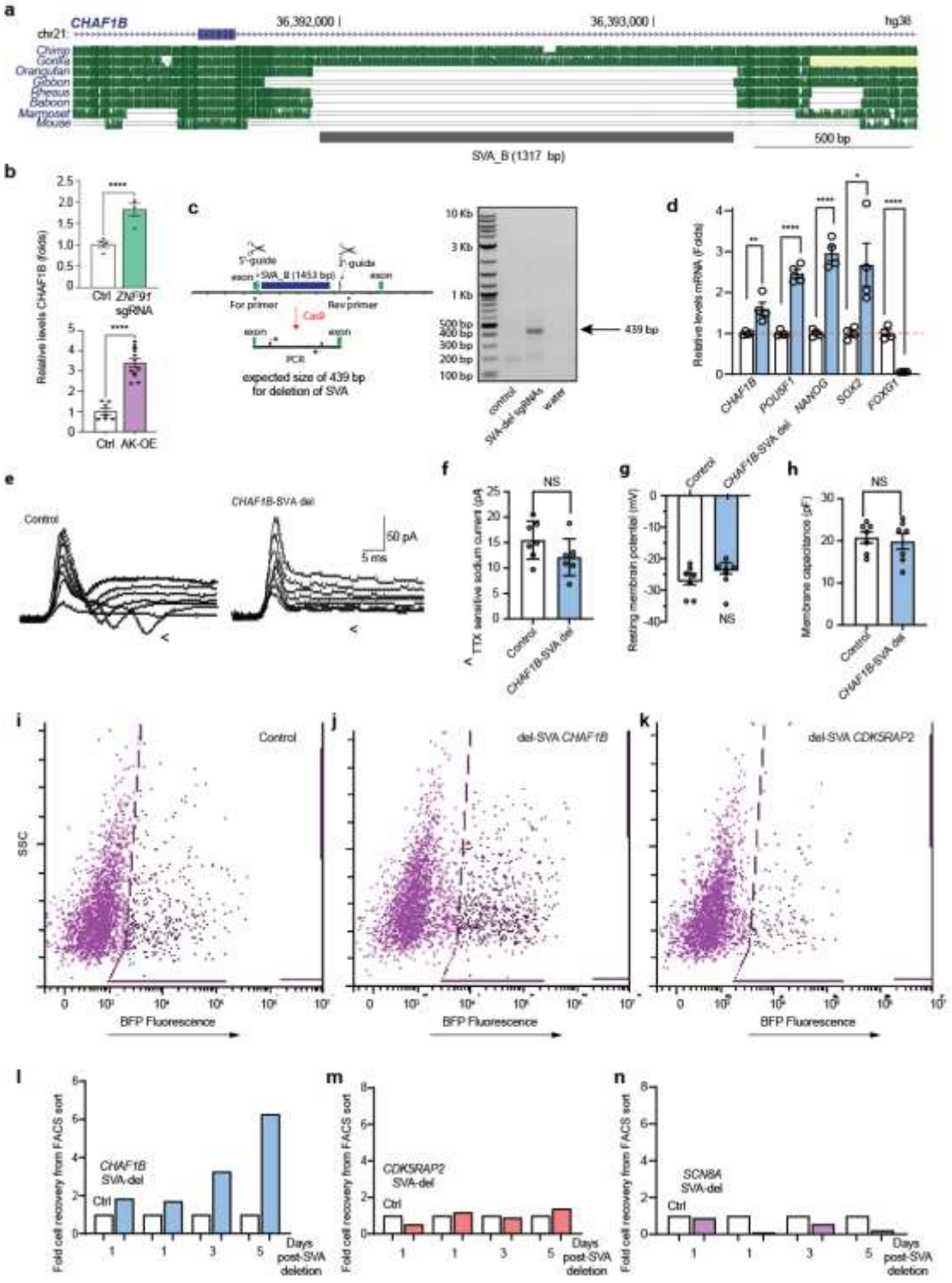
**a**

| Lane | Expected size | PCR primers | Cas9/sgRNA transfection |
|---|---|---|---|
| 1 | DNA ladder | NEB 1kb Plus DNA ladder | NA |
| 2 | 2423 bp | *SCN8A* del SVA F1 and R1 | Cas9/sgRNA control |
| 3 | 2423 bp | *SCN8A* del SVA F1 and R1 | *CHAF1B* sgRNA set 1 |
| 4 | 515 bp | *SCN8A* del SVA F1 and R1 | *SCN8A* sgRNA set 1 |
| 5 | none | *SCN8A* del SVA F1 and R1 | water |

**b**




**Supplementary Fig. 13:** Complete gel image for deletion of the intronic SVA_D within *SCN8A*. Uncropped and unedited DNA agarose gel image used to generate **Fig. 4a** showing the expected PCR product size of 515 bp is produced with Cas9/sgRNAs used to delete the intronic SVA within the *SCN8A* gene. **a**, Table of the genomic samples and primers used in the PCRs to detect the deletion of the SVA within *SCN8A* shown in **b**. The sgRNA combination and sequences are in Supplementary Table 3 and the genomic PCR primer sequences are listed in Supplementary Table 4. *SCN8A* guides showed evidence of deletion of the SVA, lane 4. Note that neither the Cas9/sgRNA control nor the *CHAF1B* sgRNA set 1 (additional control) showed deletion. The undeleted PCR band (i.e., band spanning the SVA) was not visualized in lanes 2 and 3 because PCRs were optimized with a short PCR extension time.



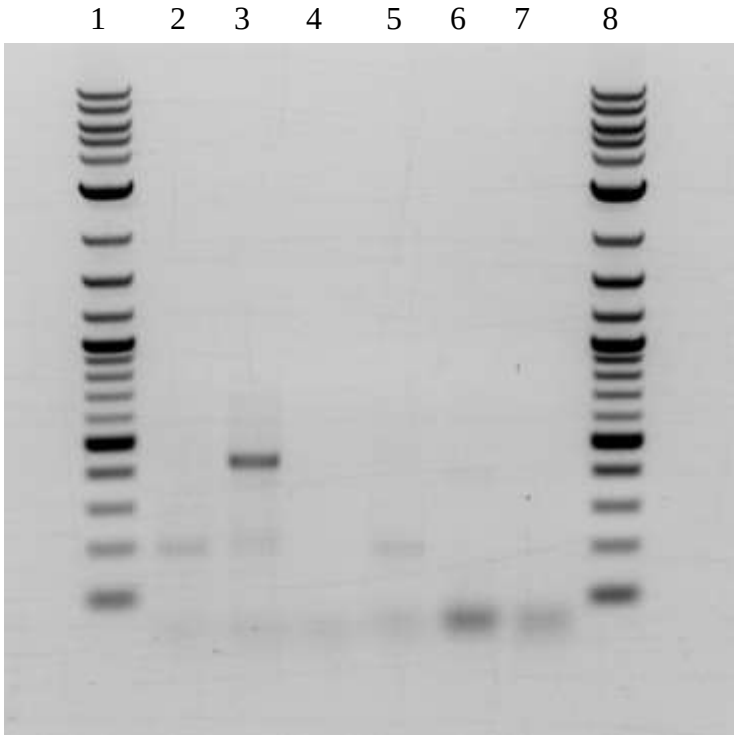

**Supplementary Fig. 14:** Deleting the SVA in *CHAF1B* increases stemness gene transcripts and overall cell number recovery. **a**, Schematic showing SVA_B located within the *CHAF1B* gene (UCSC genome browser, GRCh38/gh38). **b**, RT-qPCR of *CHAF1B* in NTera-2 cells transfected with SVA-lncRNA *AK057321* (AK-OE) vs. control plasmid or ZNF91 sgRNA/Cas9 vs. control, with *GAPDH* as the internal reference gene. Unpaired Student's two-tailed t test for individual gene comparisons to control. **c**, Strategy for Crispr/Cas9 deletion of the SVA_B within *CHAF1B* employed with DNA agarose gel image showing expected SVA-deletion PCR product size of 439 bp with sgRNAs cloned in tandem. **d**,

NTera-2 cells transfected with *CHAF1B* SVA-deletion sgRNAs were sorted and analyzed for gene expression by RT-qPCR with *GAPDH* as the internal reference gene. **e**, Representative sodium current traces in *CHAF1B*-SVA del group in response to step depolarization. **f**, TTX sensitive current in *CHAF1B*-SVA deleted (n=7) is not significantly different than controls (n=7). Unpaired Student's t test. **g**, Resting membrane potential (RMP) in *CHAF1B*-SVA deleted (n=7) and control (n=7) are not significantly different. Unpaired Student's t test. **h,** Capacitance in *CHAF1B*-SVA deleted (n=7) and control (n=7) are not significant different. Unpaired Student's t test. Data represent the mean ± SEM. **i-k**, Representative FACS sorting profiles for del-SVA *CHAF1B* (**j**), del-SVA *CDK5RAP2* (**k**) and control (**i**) sorted cells. The gating strategy for all sorting was based solely on fluorescence encoded in each transfected vector (x-axis), including control. **l-n**, Cell number recovery from each indicated sort from 4 independent experiments expressed as folds increase as compared to control = 1-fold. Note that days post transfection for each sort are indicated. Data represent the mean ± SEM.**** $p<0.0001$, *** $p<0.001$, ** $p<0.01$, * $p<0.05$, NS $P>0.05$, versus control.

**a**

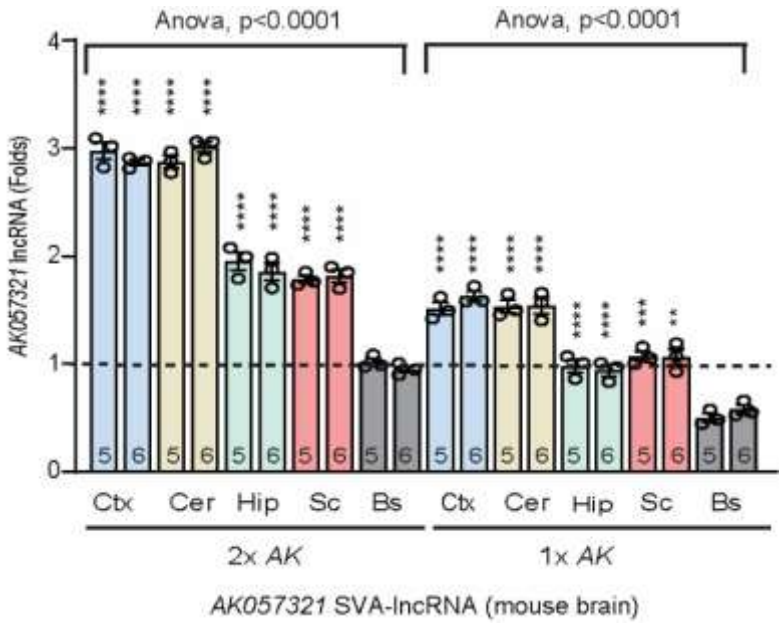
| Lane | Expected size | PCR primers | Cas9/sgRNA transfection |
|---|---|---|---|
| 1 | DNA ladder | NEB 1kb Plus DNA ladder | NA |
| 2 | 2014 bp | *CHAF1B* del SVA F1 and R1 | Cas9/sgRNA control |
| 3 | 439 bp | *CHAF1B* del SVA F1 and R1 | *CHAF1B* sgRNA set 1 |
| 4 | none | *CHAF1B* del SVA F1 and R1 | water |
| 5 | NA | NA | NA |
| 6 | NA | NA | NA |
| 7 | NA | NA | NA |
| 8 | DNA ladder | NEB 1kb Plus DNA ladder | NA |

**b**

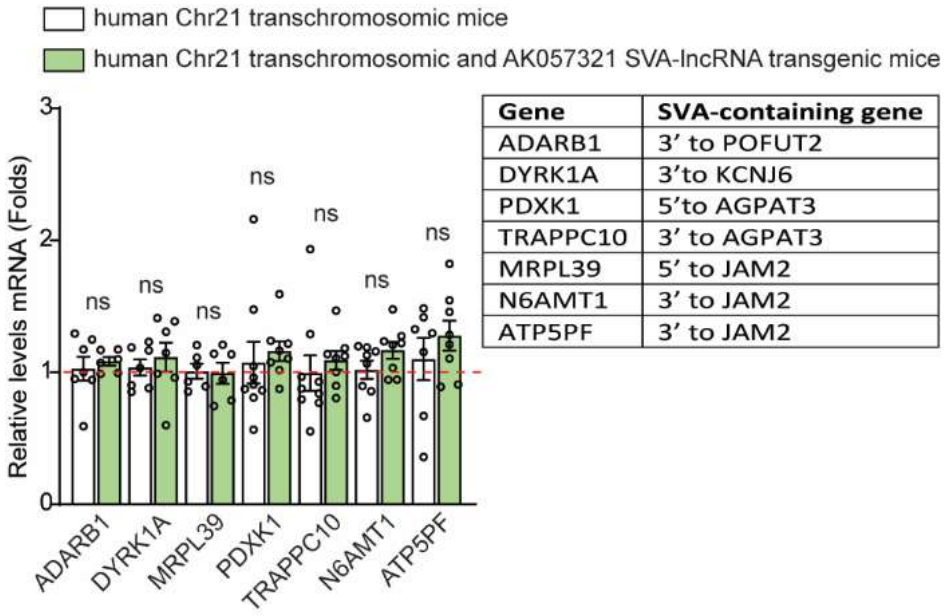



**Supplementary Fig. 15:** Complete gel image for deletion of the intronic SVA_B within

*CHAF1B*. Uncropped and unedited DNA agarose gel image used to generate Supplementary Fig. 15c, a DNA agarose gel image showing the expected PCR product size of 439 bp is produced with Cas9/sgRNAs designed to delete the intronic SVA within the *CHAF1B* gene. The sgRNA sequence combination is in the Supplementary Table 3 and the genomic PCR primer sequences are listed in Supplementary Table 4. *CHAF1B* guides showed evidence of deletion of the SVA, lane 4. The undeleted PCR band (i.e., band spanning the SVA) was not visualized in lane 2 because PCRs were optimized for a short PCR extension time. Lanes 5-7 are from PCRs designed to detect the deletion of a different intragenic SVA.

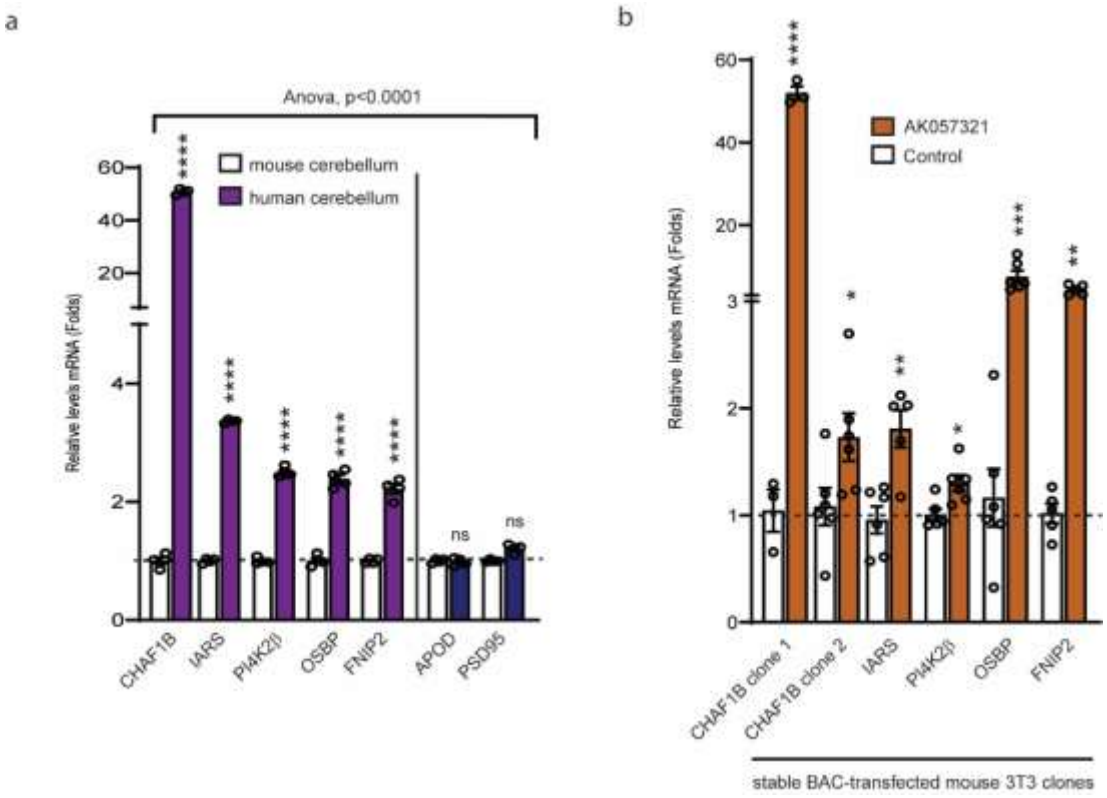



**Supplementary Fig. 16:** SVA-lncRNA *AK057321* expression is enriched in cortex and cerebellum relative to brainstem when expressed as a transgene in mouse in two independent transgenic mouse lines, 5 and 6. **a**, In 2x *AK057321* (homozygous) and 1x *AK057321* (heterozygous) mice, *AK057321* expression is increased more in cortex (Ctx), cerebellum (Cer), hippocampus (Hip) subcortex (Sc) compared to brainstem (Bs). One-way ANOVA ($F_{9,20}$=179.27, p<0.0001) in 2x *AK057321* (homozygous) mice with Bonferroni post hoc tests for each region compared to Bs. One-way ANOVA ($F_{9,20}$=51.29, p<0.0001) in 1x *AK057321* (heterozygous) with Bonferroni post hoc tests for each region compared to Bs. Note that in 2x *AK057321* (homozygous) compared to 1x *AK057321* (heterozygous) mice, *AK057321* expression is nearly doubled in expression within each region; one-way ANOVA ($F_{19,40}$=186.3, p<0.0001). Data represent the mean ± SEM. **** p<0.0001, *** p<0.001, ** p<0.01 versus Bs.

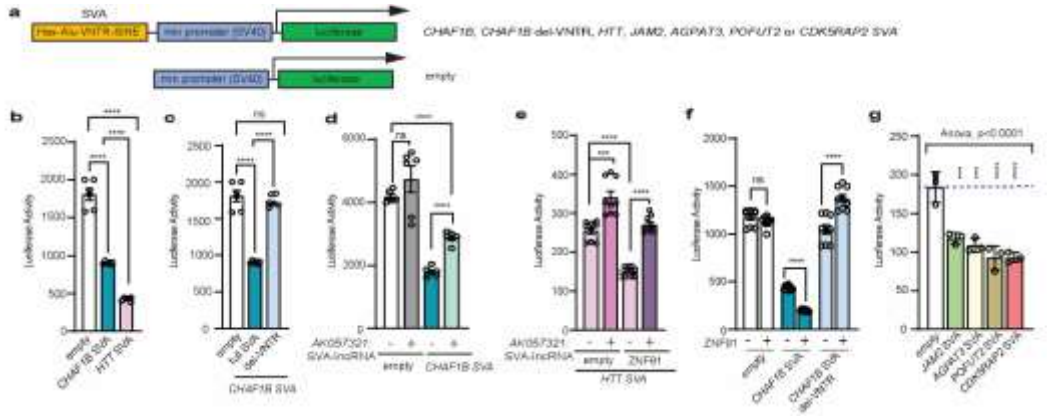



| Gene | SVA-containing gene |
|---|---|
| ADARB1 | 3' to POFUT2 |
| DYRK1A | 3'to KCNJ6 |
| PDXK1 | 5'to AGPAT3 |
| TRAPPC10 | 3' to AGPAT3 |
| MRPL39 | 5' to JAM2 |
| N6AMT1 | 3' to JAM2 |
| ATP5PF | 3' to JAM2 |

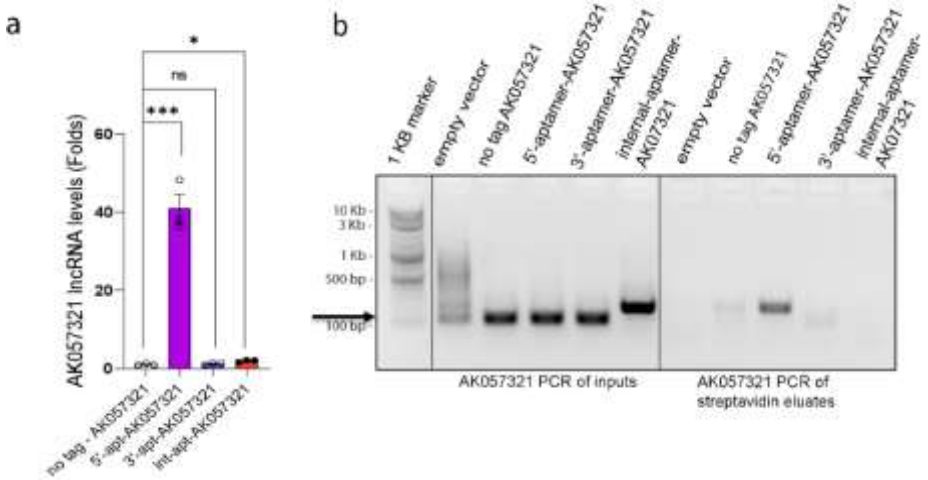
**Supplementary Fig. 17:** *AK057321* fails to regulated human chromosome 21 genes lacking SVAs. **a**, RT-qPCR expression levels of human genes nearby to the human genes with intragenic SVAs from mouse cortex of human Chr21 transchomosomic/1x *AK057321* transgenic mice compared to human Chr21 transchromosomic mice. B2M used as the internal reference gene. Unpaired Student's t test. Data represent the mean ± SEM. ns $p>0.05$. **b**, Table indicates the SVA-containing gene closest to the neighboring gene analyzed.




**Supplementary Fig. 18:** Multiple human genes with intronic SVAs are up-regulated in human relative to mouse cerebellum and are upregulated by SVA-lncRNA *AK057321* in mouse 3T3 fibroblast stably expressing these human genes (bacterial artificial chromosome, BAC vector). **a**, RNA was isolated from mouse or human cerebellum, and RT-qPCR was performed for each indicated gene. Two control genes that encode apolipoprotein D (APOD), a white matter restricted protein and postsynaptic density protein 95, a grey matter enriched synaptic protein, each display minimal differences between mouse and human cerebellum. Note that neither of the control genes has an SVA insert. One-way ANOVA ($F_{13,42}$=7.134, p<0.0001) with Bonferroni post hoc tests. **b**, Individual 3T3 clones stably transfected with the indicated BAC DNA were infected with either *AK057321* SVA-lncRNA or control virus followed by harvest, RNA extraction and RT-qPCR with Gapdh as the internal reference gene. Unpaired Student's t test. Data represent the mean ± SEM. **** p<0.0001, *** p<0.001, ** p<0.01, * p<0.05, ns p>0.05.



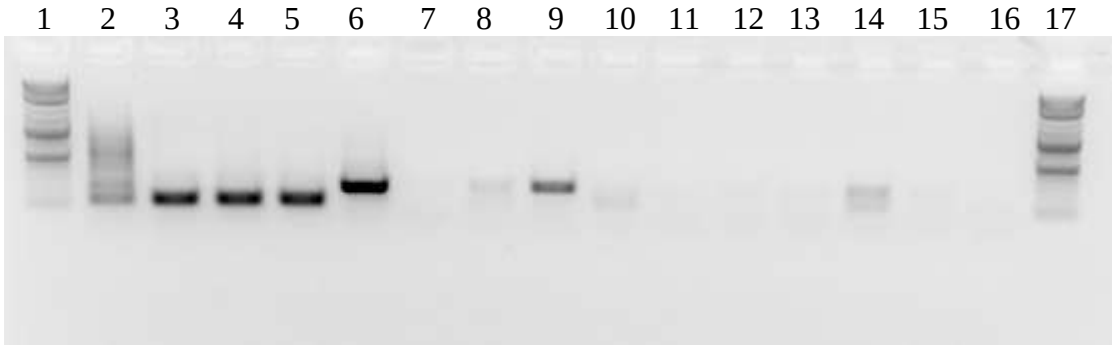
**Supplementary Fig. 19:** Transcriptional repression by intronic SVA transposons and ZNF91 transcription factor is reversed fully by VNTR repeat deletion (in *CHAF1B* SVA) and partially by SVA-lncRNA *AK057321*. **a**, Schematics representing structure of minimal luciferase reporter with or without added SVA transposon sequences. **b,** Luciferase activity using the *CHAF1B* SVA, *HTT* SVA reporter or empty reporter plasmid. **c**, Luciferase activity using the *CHAF1B* SVA, *CHAF1B del-VNTR* or empty reporter plasmid. **d**, Luciferase activity with the *CHAF1B* SVA or empty reporter plasmid and co-transfected with either *AK057321* SVA-lncRNA or control plasmid. **e**, Luciferase activity of the *HTT* SVA reporter plasmid co-transfected with *AK057321* SVA-lncRNA with and without *ZNF91*. **f,** Luciferase activity of the *CHAF1B* SVA, *CHAF1B SVA del-VNTR* or empty reporter plasmid co-transfected with and without *ZNF91*. **g**, Luciferase activity of other intronic SVAs, *JAM2*, *AGPAT3*, *POFUT2* and *CDK5RAP2* compared to the empty vector reporter. One-way ANOVA ($F_{4,10}$ =26.71, p<0.0001) versus empty vector reporter with Bonferroni post hoc tests. (**b-f**) Unpaired Student's t test. Data represent the mean ± SEM. **** p<0.0001, *** p<0.001, ** p<0.01, * p<0.05, ns p>0.05.



**Supplementary Fig. 20:** 5'-apatamer-tagged SVA-lncRNA *AK057321* binds to streptavidin beads. A dual-apatamer tag with affinity for streptavidin was inserted at three different locations in *AK057321*. HEK293T cells were transfected with each version and compared to un-tagged *AK057321*, followed by cell lysis, precipitation on streptavidin beads, elution by heating, and analysis for associated *AK057321* by RT-qPCR (**a**) and by RT followed by PCR and analysis of product(s) on a DNA agarose gel (**b**). Unpaired Student's t test. Data represent the mean ± SEM. *** p<0.001, * p<0.05, ns p>0.05.

**a**

| Lane | Expected size | PCR primers | Input/pulldown |
|---|---|---|---|
| 1 | DNA ladder | NEB 1 kb Plus DNA ladder | NA |
| 2 | 110 bp | *AK057321* FWD 1 & REV 1 | empty vector |
| 3 | 110 bp | *AK057321* FWD 1 & REV 1 | *AK057321* – no tag |
| 4 | 110 bp | *AK057321* FWD 1 & REV 1 | *AK057321* - 5’ aptamer tag |
| 5 | 110 bp | *AK057321* FWD 1 & REV 1 | *AK057321* - 3’ aptamer tag |
| 6 | 211 bp | *AK057321* FWD 1 & REV 1 | *AK057321* - internal aptamer tag |
| 7 | 110 bp | *AK057321* FWD 1 & REV 1 | empty vector |
| 8 | 110 bp | *AK057321* FWD 1 & REV 1 | *AK057321* – no tag |
| 9 | 110 bp | *AK057321* FWD 1 & REV 1 | *AK057321* - 5’ aptamer tag |
| 10 | 110 bp | *AK057321* FWD 1 & REV 1 | *AK057321* - 3’ aptamer tag |
| 11 | 211 bp | *AK057321* FWD 1 & REV 1 | *AK057321* - internal aptamer tag |
| 12 | 110 bp | *AK057321* FWD 1 & REV 1 | empty vector |
| 13 | 110 bp | *AK057321* FWD 1 & REV 1 | *AK057321* – no tag |
| 14 | 110 bp | *AK057321* FWD 1 & REV 1 | *AK057321* - 5’ aptamer tag |
| 15 | 110 bp | *AK057321* FWD 1 & REV 1 | *AK057321* - 3’ aptamer tag |
| 16 | 211 bp | *AK057321* FWD 1 & REV 1 | *AK057321* - internal aptamer tag |
| 17 | DNA ladder | NEB 1 kb Plus DNA ladder | NA |




**Supplementary Fig. 21:** Complete gel image for 5'-apatamer-tagged SVA-lncRNA *AK057321* binds to streptavidin beads. **a**, Table indicating the primers used and samples analyzed in each lane of the uncropped and unedited DNA agarose gel image PCR bands shown in **b** that was used to generate Supplementary Fig. 21b. Primer sequences are listed in Supplementary Tables 5 and 16. PCR reactions are on lanes 1-6 are from the inputs prior to pulldowns, lanes 7-11 were pulldowns with streptavidin beads that were eluted with heat and lanes 12-16 are pulldowns with streptavidin beads that were eluted with biotin. Note that the internal aptamer tag results in a larger PCR band (lane 6) because the tag (extra 101 bp) is located within the PCR region spanned by the forward and reverse primers.

**Supplementary Tables 1-20**

**Supplementary Table 1**. SVA-lncRNA *AK057321* shRNA target sequences and cloning primers.

| **Oligo name** | **Oligo Sequence (5' – 3')** |
|---|---|
| shRNA-1S | GACTATATCATCATGTACA |
| shRNA-1A | TGTACATGATGATATAGTC |
| shRNA-2S | CATCAAGATGCAGTCTCCC |
| shRNA-2A | GGGAGACTGCATCTTGATG |
| UbC Fwd | ttattatatcttgtggaaaggacgaggatccggaagaattcgagcggccgcgaATTAACCCGTGTCGGCTC |
| UbC Rev | tcgtggcgccagaGTCTAACAAAAAAGCCAAAAACG |
| P2A Fwd | ttggctttttgttagacTCTGGCGCCACGAATTTC |
| P2A Rev | ctggtcaacttggccatTCTAGACACCATAGGACCAG |
| Zeocin Fwd | tatggtgtctagaATGGCCAAGTTGACCAGTG |
| Zeocin Rev | cctcccctgaaccTCAGTCCTGCTCCTCGGC |
| T2A Fwd | gccgaggagcaggactgaGGTTCAGGGGAGGGAAGAG |
| T2A Rev | tcgcccttgctcaccatggtggcgaccggtTCTAGAGGTCATGGGTCC |

**Supplementary Table 2**. Construction primers used to modify lentiCRISPRv2 hygro (Addgene #98291) to express in tandem sgRNAs with Cas9 and either mcherry or blue fluorescent protein.

| **Oligo name** | **Oligo Sequence (5' – 3')** |
|---|---|
| mcherry for hygro Fwd | ccgaaaaagcctgaactcaccgcgacgtctgtcCCGGTCGCCACCATGGTG |
| mcherry for hygro Rev | atccagaggttgattgtcgacttaacgcgtCTAGTTACTTGTACAGCTCGTCCATGC |
| long guide Fwd | tccagtttggttaattaaggtaccTTCGGGTTTATTACAGGGACAGC |
| long guide Rev | taggccctcctcgagGATGTGCGCTCTGCCCAC |
| short guide Fwd | cagagcgcacatcctcgagGAGGGCCTATTTCCCATG |
| short guide Rev | aattcccactcctttcaagacctagcTCCTTTCAAGACCTAGCTAG |
| T2A Fwd | ggctgtgtagaagtacttcgccgaacgcgtGGTTCAGGGGAGGGAAGAG |
| T2A Rev | tccttaatcagctcgctTCTAGAGGTCATGGGTCC |
| BFP Fwd | catgacctctagaAGCGAGCTGATTAAGGAG |
| BFP Rev | atccagaggttgtcgacttaacgcgtTTAATTAAGCTTGTGCCC |

**Supplementary Table 3**. sgRNA sequences used to delete SVAs.

| **Gene with SVA** | **Oligo name** | **Oligo Sequence (5' – 3')** | **In tandem cloning** |
|---|---|---|---|
| *AK057321* | *AK057321* sgRNA 1 left | GACAGCAATTTAGCAGTATCTGG | Set 1 |
| *AK057321* | *AK057321* sgRNA 1 right | GCTTTGGATACCTCGTAGGTGGG | Set 1 |
| *AK057321* | *AK057321* sgRNA 1 left | GACAGCAATTTAGCAGTATCTGG | Set 2 |

| | | | |
|---|---|---|---|
| *AK057321* | *AK057321* sgRNA 2 right | GGTCATCGTGCCCACCTACGAGG | Set 2 |
| *AK057321* | *AK057321* sgRNA 1 left | GACAGCAATTTAGCAGTATCTGG | Set 3 |
| *AK057321* | *AK057321* sgRNA 3 right | ATGAGCTTGAATAGTTATCTTGG | Set 3 |
| *CDK5RAP2* | *CDK5RAP2* sgRNA 1 left | GGCTTAGATTATGGTGCATCAGG | Set 1 |
| *CDK5RAP2* | *CDK5RAP2* sgRNA 1 right | GAGCTCCCAATGGCCAAGTCTGG | Set 1 |
| *CDK5RAP2* | *CDK5RAP2* sgRNA 2 left | CCACGAGGGGTTTTATGCCCTGG | Set 2 |
| *CDK5RAP2* | *CDK5RAP2* sgRNA 2 right | TGTTCAGATTGACCCAGACTTGG | Set 2 |
| *CDK5RAP2* | *CDK5RAP2* sgRNA 3 left | GGATTTTATGCCTTGAGCCCTGG | Set 3 |
| *CDK5RAP2* | *CDK5RAP2* sgRNA 3 right | CAATTTGAAGGAGCTCCCAATGG | Set 3 |
| *CDK5RAP2* | *CDK5RAP2* sgRNA 4 left | TGAGGTTAGTGCTAGTCACTTGG | Set 4 |
| *CDK5RAP2* | *CDK5RAP2* sgRNA 4 right | ACCTGCAACAGTTATTACTGTGG | Set 4 |
| *CDK5RAP2* | *CDK5RAP2* sgRNA 5 left | TTCAAAGTATGACGAGAAGCAGG | Set 5 |
| *CDK5RAP2* | *CDK5RAP2* sgRNA 5 right | GTTGTATTATGTCTACCATGAGG | Set 5 |
| *SCN8A* | *SCN8A* sgRNA 1 left | GGGATCTTAGAAGGGATGCAGGG | Set 1 |
| *SCN8A* | *SCN8A* sgRNA 1 right | AGTCTACAGGATGCCACTAATGG | Set 1 |
| *SCN8A* | *SCN8A* gRNA 2 left | GCTGATCACAAGAAGTAGTGTGG | Set 2 |
| *SCN8A* | *SCN8A* gRNA 2 right | TCAGGAACACATTAGTCTACAGG | Set 2 |
| *CHAF1B* | *CHAF1B* gRNA left | ACTTCTAAATTAGACCAGCCTGG | Set 1 |
| *CHAF1B* | *CHAF1B* gRNA right | TTTACGATGAGTGCATTAAATGG | Set 1 |
| *CHAF1B* | *CHAF1B* gRNA left | ACTTCTAAATTAGACCAGCCTGG | Set 2 |
| *CHAF1B* | *CHAF1B* gRNA right | GTAAACAGAGATCACTGCCATGG | Set 2 |

**Supplementary Table 4.** Genomic PCR primers used to screen for SVA deletions.

| **Oligo name** | **Oligo Sequence (5' – 3')** |
|---|---|
| *AK057321* del SVA F1 | TCACAGGGTCTGACAATTCAAA |
| *AK057321* del SVA R1 | GTGTGTATCCTTATAGTTGAGCAG |
| *CDK5RAP2* del SVA F 1 | TGACCTTGACTGGTTTGAAGAG |
| *CDK5RAP2* del SVA F 2 | CAGGTGGTGAGAATATGGGAAA |
| *CDK5RAP2* del SVA F 3 | AGTCTTGGCTAATCTGGAACAG |
| *CDK5RAP2* del SVA F 4 | GTCGGAGTCAAAGGAATGAGAA |
| *CDK5RAP2* del SVA F 5 | GGCTTGTCTGGTGTTTCTCT |
| *CDK5RAP2* del SVA R 1 | GAGGGAGAACCTGCTTACTTATT |
| *CDK5RAP2* del SVA R 2 | GCCTGTCATCTCAGCACTTT |
| *SCN8A* del SVA F 1 | GTTGTGTTAAGGGTCAACTGAATAG |
| *SCN8A* del SVA R 1 | GTATTGTCTGTGGCTGCTTCT |
| *CHAF1B* del SVA F 1 | AATCGCTTGAACCCAGGAG |
| *CHAF1B* del SVA R 1 | CTGCAGATGCTGTCATCCTAT |

**Supplementary Table 5**. A sephadex and a streptavidin dual aptamer tag.

| **Dual Aptamer Tag Oligo Sequence (5' – 3')** |
|---|
| TCCGAGTAATTTACGTTTTGATACGGTTGCGGAACCGACCAGAATCATGCAA GTGCGTAAGATAGTCGCGGGCCGGG |

**Supplementary Table 6.** Primers used to generate Tet-inducible *CDK5RAP2* cDNA.

| **Oligo name** | **Oligo Sequence (5' – 3')** |
|---|---|
| TetO FWD | ATCTCGAGTTTACCACTCCCTATCAGTGATAGA |
| TetO REV | GAGCTCTGCTTATATAGGCCTCCCACCGTAC |
| *CDK5RAP2* TetO HiFi For | gccttttgctggccttttgctcacatgtATCTCGAGTTTACCACTC |
| *CDK5RAP2* TetO HiFi Rev | cgagatctgagtccggtagcgctGAGCTCTGCTTATATAGG |

**Supplementary Table 7.** Primers used to clone *CHAF1B* SVA into pGL3 luciferase vector.

| **Primer name** | **Primer oligo sequence (5'-3')** |
|---|---|
| CHAF1B SVA FWD | CCTCTCCCTCTCCCTCTC |
| CHAF1B SVA REV | AGTATTTATTGATCATTCTTGGGTGTTTC |
| CHAF1B SVA FWD HiFi NEB assembly | atttctctatcgataggtaccCCTCTCCCTCTCCCTCTC |
| CHAF1B SVA REV HiFi NEB assembly | tcgcagatctcgagcccgggctagcAGTATTTATTGATCATTCTTGGGTGTTTC |

**Supplementary Table 8.** Primers used to generate *CHAF1B* SVA minusVNTR sequence into pGL3 luciferase vector.

| **Primer name** | **Primer oligo sequence (5'-3')** |
|---|---|
| *CHAF1B* Part A SVA FWD | CCTCTCCCTCTCCCTCTC |
| *CHAF1B* Part A SVA REV | TTTGGGAGGCCAAGGCAG |
| *CHAF1B* Part B FWD | TGGGAGGTGTACCCAACAG |
| *CHAF1B* Part B REV | AGTATTTATTGATCATTCTTGGGTGTTTC |
| *CHAF1B* Part A SVA FWD HiFi NEB assembly | atttctctatcgataggtaccCCTCTCCCTCTCCCTCTC |
| *CHAF1B* Part A SVA REV HiFi NEB assembly | acacctcccaTTTGGGAGGCCAAGGCAG |
| *CHAF1B* Part B FWD HiFi NEB assembly | gcctcccaaaTGGGAGGTGTACCCAACAG |
| *CHAF1B* Part B REV HiFi NEB assembly | tcgcagatctcgagcccgggctagcAGTATTTATTGATCATTCTTGGGTGTTTC |

**Supplementary Table 9.** Primers used to clone *HTT* SVA into pGL3 luciferase vector.

| **Primer name** | **Primer oligo sequence (5'-3')** |
|---|---|
| HTT SVA FWD | GCAGAATAATGCTCCCCTCT |
| HTT SVA REV | GGCAGCAGCATATACCGAGT |
| HTT SVA screen FWD | GCCAATTGTGCAGTTCCTTT |
| HTT SVA screen REV | GATACTCGCAGCCAACCATT |

**Supplementary Table 10.** Primers used to clone *JAM2*, *AGPAT3*, *POFUT2* and *CDK5RAP2* SVAs into pGL3 luciferase vector.

| **Primer name** | **Primer oligo sequence (5'-3')** |
|---|---|
| *JAM2* SVA FWD | CAGCCTTGTCAACACCTTTATTT |
| *JAM2* SVA REV | TTTGTGGAGGAACACGATCTC |
| *AGPAT3* SVA FWD | AACATCAGCACAGACCAAGAA |
| *AGPAT3* SVA REV | GCTTTCTGCCTTTCAGACTTTG |
| *POFUT2* SVA FWD | GGATCCTCCAGTAAGGACAGATA |
| *POFUT2* SVA REV | CCACAGATGCCGTCAGAAA |
| *CDK5RAP2* SVA FWD | CCGGGAGGATGGAGTTCA |

| | |
|---|---|
| *CDK5RAP2* SVA REV | TTTGGAGGTGCGTAATGTCAG |
| *JAM2* HiFi SVA FWD | ATTTCTCTATCGATAGGTACCCAGCCTTGTCAACACCTTTATTTC |
| *JAM2* HiFi SVA REV | TCGCAGATCTCGAGCCCGGGCTAGCTTTGTGGAGGAACACGATC |
| *AGPAT3* HiFi SVA FWD | ATTTCTCTATCGATAGGTACCAACATCAGCACAGACCAAG |
| *AGPAT3* HiFi SVA REV | TCGCAGATCTCGAGCCCGGGCTAGCGCTTTCTGCCTTTCAGAC |
| *POFUT2* HiFi SVA FWD | ATTTCTCTATCGATAGGTACCGGATCCTCCAGTAAGGAC |
| *POFUT2* HiFi SVA REV | TCGCAGATCTCGAGCCCGGGCTAGCCCACAGATGCCGTCAGAAAG |
| *CDK5RAP2* HiFi SVA FWD | ATTTCTCTATCGATAGGTACCCCGGGAGGATGGAGTTCAG |
| *CDK5RAP2* HiFi SVA REV | TCGCAGATCTCGAGCCCGGGCTAGCTTTGGAGGTGCGTAATGTCAG |
| *JAM2* HiFi SVA FWD | ATTTCTCTATCGATAGGTACCCAGCCTTGTCAACACCTTTATTTC |

**Supplementary Table 11**. Table of BAC clone numbers used in this study.

| **Gene** | **Clone ID** |
|---|---|
| *CHAF1B* | RP11-108J14 |
| *IARS* | CTD-2055I8 |
| *PI4K2β* | RP11-23L20 |
| *OSBP* | CTD-2303H12 |
| *FNIP2* | RP11-28O10 |

**Supplementary Table 12**. Table of primers used in BAC recombineering.

| **Primer name** | **Oligo primer sequence (5'-3')** |
|---|---|
| NeomycinR FWD | CTGAAGAGGAGTTTACGTCCAG |
| NeomycinR REV | ATTAAGGGTTCCGCAAGCTC |
| 5' homology arm to pBACe3.6 (RP11) | CGCATTAAAGCTTATCGATGATAAGCTGTCAAACATGAGAATTGATCCGG |
| Forward primer for neo insertion cassette (RP11) | CGCATTAAAGCTTATCGATGATAAGCTGTCAAACATGAGAATTGATCCGG*CTGAAGAGGAGTTTACGTCCAG* |

| | |
|---|---|
| 3’ homology arm to pBACe3.6 (RP11) | CTGCATCCGATGCAAGTGTGTCGCTGTCGACGGTGACCCTATAGTCGAGG |
| Reverse primer for neo insertion cassette (RP11) | CTGCATCCGATGCAAGTGTGTCGCTGTCGACGGTGACCCTATAGTCGAGG*ATTAAGGGTTCCGCAAGCTC* |
| 5’ homology arm to pBeloBAC11 (CTD) | TTCCTTTCTCTGTTTTTGTCCGTGGAATGAACAATGGAAGTCCGAGCTCA |
| Forward primer for neo insertion cassette (CTD) | TTCCTTTCTCTGTTTTTGTCCGTGGAATGAACAATGGAAGTCCGAGCTCA*CTGAAGAGGAGTTTACGTCCAG* |
| 3’ homology arm to pBeloBAC11 (CTD) | TACAATCTGCTCTGATGCCGCATAGTTAAGCCAGCCCCGACACCCGCCAA |
| Reverse primer for neo insertion cassette (CTD) | TACAATCTGCTCTGATGCCGCATAGTTAAGCCAGCCCCGACACCCGCCAAATTAAGGGTTCCGCAAGCTC |

**Supplementary Table 13**. Table of BAC screening primers.

| **Primer name** | **Primer oligo sequence (5’-3’)** |
|---|---|
| RP11-neo-Seq-for | CGATGAGCGCATTGTTAGATTTC |
| RP11-neo-Seq-rev | GGTTATGTGGACAAAATACCTGGTT |
| CTD-neo-Seq-for | GACAGGTGCTGAAAGCGAG |
| CTD-neo-Seq-rev | CTGGCGTAATAGCGAAGAGG |

**Supplementary Table 14**. Primers used in BAC recombineering to delete SVA in *CHAF1B* (BAC clone RP11-108J14).

| **Oligo name** | **Oligo Sequence (5' – 3')** |
|---|---|
| *CHAF1B* left arm For | AGACAGTTAGCCAGGATGG |
| *CHAF1B* left arm Rev | TCCCTGTTGAAATGCTTGG |
| Zeocin For construction | TAGCTGGGACTACAGGTGCATCGGATCCACTAGTAACGGC |
| Zeocin Rev construction | TGTAATCCCAGCTACTCGGGCGCCAGTGTGATGGATATCTG |
| *CHAF1B* right arm For | TACAGGCCTGCACCACTATG |
| *CHAF1B* right arm Rev | CAGGCAGAGATTGCAGTGAG |

**Supplementary Table 15**. Primers used to clone zeocin resistance gene.

| **Oligo name** | **Oligo Sequence (5' – 3')** |
|---|---|
| Zeo Res For | TCGGATCCACTAGTAACGGC |
| Zeo Res Rev | CGCCAGTGTGATGGATATCTG |

**Supplementary Table 16**. Table of IDT primers and probes used in gene expression studies.

| **Primer ID** | **Sequence (5'-3')** |
|---|---|
| *AK057321* FWD 1 | GCTACTAGAACCACTGACTTCAT |
| *AK057321* REV 1 | GAGAATCAGGCAGGGATGTT |
| *AK057321* PRB 1 | 5'/56-FAM/AAGATGCAG/ZEN/TCTCCCTCTGA |
| *AK057321* FWD 2 | GCTACTAGAACCACTGACTTCATC |
| *AK057321* REV 2 | AGGCTGAGGCAGGAGAA |
| *AK057321* PRB2 | 5'/56-FAM/ACCATCTCG/ZEN/GCTCACTGCAACATC/3IABkFQ/3' |
| *ZNF91* FWD[1] | CCAGACCTGATTAGTTATCTGG |
| *ZNF91* REV[1] | ACATTTTTCATATTTTCTCAGTAATAC |
| *CDK5RAP2* | Prime Time Std qPCR Assay; Hs.PT.58.28138308 |
| *CDK5RAP2* | Prime Time Std qPCR Assay; Hs.PT.58.22477909 |
| *NIPBL* | Prime Time qPCR Primers; Hs.PT.58.4309431 |
| *SPATA5* | Prime Time qPCR Primers; Hs.PT.58.5 |
| *ATRX* | Prime Time Std qPCR Assay; Hs.PT.58.939584 |
| *WAPL* | Prime Time Std qPCR Assay; Hs.PT.58.27929275 |
| *KDM6A* | Prime Time qPCR Primers; Hs.PT.58.19290698 |
| *ANKDR11* | Prime Time qPCR Primers; Hs.PT.27139934 |
| *CHAF1B* FWD 1 | GGGCACCGTTCTACTTCTTC |
| *CHAF1B* REV 1 | TGACGGTGCCTCTGACT |
| *CHAF1B* PRB1 | 5'/56-FAM/TCCGGGTCC/ZEN/CTCCAGCATTT/3IABkFQ/3' |
| *CHAF1B* FWD 2 | CATCTCCTCCCGSTGCTAAA |
| *CHAF1B* REV 2 | TTTTTCCCCTTCGAGACTCA |

| | |
|---|---|
| *CHAF1B* PRB2 | 5'/56-FAM/TCTTGCTCG/ZEN/TCATACCAAAGCCGT/3IABkFQ/3' |
| *RBL1* | Prime Time qPCR Primers; Hs.PT.58.4123862 |
| *SCN8A* | Prime Time Std qPCR Assay; Hs.PT.58.2478730 |
| *SCN8A* | Prime Time Std qPCR Assay; Hs.PT.58.1641962 |
| *WNK3* | Prime Time Std qPCR Assay; Hs.PT.58.25141664 |
| *KCNJ6* | Prime Time qPCR Primers; Hs.PT.58.1954078 |
| *KCNH1* | Prime Time Std qPCR Assay; Hs.PT.58.27443267 |
| *CASK* | Prime Time Std qPCR Assay; Hs.PT.58.20249400 |
| *MYO5A* | Prime Time Std qPCR Assay; Hs.PT.58.26606668 |
| *NRXN1* | Prime Time Std qPCR Assay; Hs.PT.58.3713581 |
| *NRXN2* | Prime Time Std qPCR Assay; Hs.PT.58.1397376 |
| *GRID1* | Prime Time Std qPCR Assay; Hs.PT.58.19812755 |
| *SHANK2* | Prime Time Std qPCR Assay; Hs.PT.58.2960615 |
| *ABL2* | Prime Time qPCR Primers; Hs.PT.58a.3158121.g |
| *CNTN4* | Prime Time Std qPCR Assay; Hs.PT.58.20752389 |
| *NRCAM* | Prime Time Std qPCR Assay; Hs.PT.58.2794163 |
| *MAPKAP1* | Prime Time qPCR Primers; Hs.PT.58.24858668 |
| *RPTOR* | Prime Time qPCR Primers; Hs.PT.58.26749458 |
| *BRAF1* | Prime Time qPCR Primers; Hs.PT.56a.27823863 |
| *AGPAT3* | Prime Time Std qPCR Assay; Hs.PT.58.28067831 |
| *LETM1* | Prime Time Std qPCR Assay; Hs.PT.58.40993934 |
| *RANBP2* | Prime Time Std qPCR Assay; Hs.PT.58.3984483 |
| *HUNK* FWD | GGTGCCATCAGTTTCCTGCGC |
| *HUNK* REV | TGCCCGTGTAATTCTCATTAA |
| *LSS* FWD | CGCAAGGGTGGCTTCTCCTTCA |
| *LSS* REV | CTCAGCCGTGCAGTCAGAAAC |
| *B2M* | Prime Time Std qPCR Assay; Hs.PT.58v.18759587 |
| *GAPDH* | Prime Time Std qPCR Assay; Hs.PT.39a.22214836 |
| *B2M* | Prime Time qPCR Primers; Hs.PT.58v.18759587 |
| *GAPDH* | Prime Time qPCR Primers; Hs.PT.39a.2214836 |
| *POU5F1* | Prime Time Std qPCR Assay; Hs.PT.58.24436403 |
| *NANOG* | Prime Time Std qPCR Assay; Hs.PT.58.21480849 |
| *SOX2* | Prime Time Std qPCR Assay; Hs.PT.58.237787.g |
| *POFUT2* | Prime Time Std qPCR Assay; Hs.PT.58.24436403 |
| *PCBP3* | Prime Time Std qPCR Assay; Hs.PT.58.25131904 |
| *CDK5RAP2* | Prime Time Std qPCR Assay: Hs.PT.58.28138308 |
| *FOXG1* | Prime Time Std qPCR Assay; Hs.PT.58.26906112.g |
| *RWDD2B* | Prime Time Std qPCR Assay; Hs.PT.58.4429456 |
| *JAM2* | Prime Time Std qPCR Assay; Hs.PT.58.2739820 |
| *Pofut2* | Prime Time Std qPCR Assay; Mm.PT.58.6904698 |
| *Chaf1b* | Prime Time Std qPCR Assay; Mm.PT.58.12985685 |
| *Kcnj6* | Prime Time Std qPCR Assay; Mm.PT.58.13521340 |
| *Agpat3* | Prime Time Std qPCR Assay; Mm.PT.58.5384170 |
| *Pcbp3* | Prime Time Std qPCR Assay; Mm.PT.14265841 |
| *Rwdd2b* | Prime Time Std qPCR Assay; Mm.PT.12650934 |
| *Jam2* | Prime Time Std qPCR Assay; Mm.PT.5384170 |
| *ADARB1* FWD | GCACAGATGTTAAAGATGCCA |

| | |
|---|---|
| *ADARB1* REV | GATCTCCGAGATATTATTTCT |
| *DYRK1A* FWD | AGGTGCGTCAGCAATTTCCTG |
| *DYRK1A* REV | ACCTGTGTAGGAGCTTCAGTG |
| *MRPL39* FWD | ATTTATAGCAACATCGCC |
| *MRPL39* REV | CTTTCTCTTTATTAAAGAGAT |
| *PDXK1* FWD | TGGCCTGTGAGAAGACCGTGT |
| *PDXK1* REV | TGCATGGGGCTGGGCCTCACT |
| *TRAPCC10* FWD | TCGACAACAGTAGCAACTGGG |
| *TRAPCC10* REV | GCAGCTTTTCCCACACACTGCCCA |
| *N6AMT1* FWD | ACTGATATCAACCCTGAGGCA |
| *N6AMT1* REV | ATAACTGGTTGAATGTGAACT |
| *ATP5PF* FWD | TGAAGATCCCAAATTTGAAGT |
| *ATP5PF* REV | GAACACACTCAACATCACCAA |

**Supplementary Table 17**. Table of Eurofin primers used in gene expression studies. Primers that recognize both human and mouse transcripts for data shown in Supplementary Fig. 19 are bolded.

| **Primer Name** | **Oligo Sequence (5'-3')** |
|---|---|
| *RPL13A* For | CGCTGTGAAGGCATCAACATTTC |
| *RPL13A* Rev | GCTGTCACTGCCTGGTACTTC |
| *AK057321* For1 | GGCTCCTTACCAGCTCACCT |
| *AK057321* Rev1 | CTCCTCACATCCCAGACGAT |
| *AK057321* For2 | ATGCAGTCTCCCTCTGATGC |
| *AK057321* Rev2 | CTCCTCACATCCCAGACGAT |
| *HTT* For | ACAAGCAAGAGACCCGAAGA |
| *HTT* Rev | GTCAGGGTTTGCAGAAGCTC |
| *Htt* For | GTCTAGTGCCCTTGCTCCAG |
| *Htt* Rev | ACCAACAGAACCAGGAGTGG |
| ***CHAF1B* For** | GGGGCCACTTAGAAGATGTGTATGA |
| ***CHAF1B* Rev** | ACTTCATGCTGTCGTCGTGAAAC |
| ***IARS* For** | TGGATGCTTCAGGCTGCTTCAC |
| ***IARS* Rev** | GGGGGTGCCCCAGTATCTGTTT |
| ***PI4K2β* For** | TGACCGTGCAAAATCAAGAGGCAAA |
| ***PI4K2β* Rev** | TTGAGGAAGCCAAGCCCAGTGAA |
| ***OSBP* For** | ATCAACCTCGCCACAGCCAAC |
| ***OSBP* Rev** | CTGGGCTAACATGAGGAAATCTCTGC |
| ***FNIP2* For** | ACTGGAAGTAACCTAGCACACAGCA |
| ***FNIP2* Rev** | CCTGTTCATGTGAGATTCAAACAGGGG |
| ***APOD* For** | GAAGATGGTACGAAATTGAGAAGATC |
| ***APOD* Rev** | TCGGTGGCCAGGATCCAGTA |
| ***PSD95* For** | GTGACAACCAAGAAATACCGCTAC |
| ***PSD95* Rev** | CCACCAGGAATGATCTTGGTGAT |
| ***ACTB* For** | ACCCAGATCATGTTTGAGACCTTC |
| ***ACTB* Rev** | CTTGCGCTCAGGAGGAGCAA |
| ***GAPDH* For** | CATCACCATCTTCCAGGAGCG |
| ***GAPDH* Rev** | CCACAGTCTTCTGGGTGGCA |

**Supplementary Table 18.** Primers used for relative quantitative PCR (rqPCR) for *AK057321*

expression analysis in Supplementary Fig. 17.

| **Oligo name** | **Oligo Sequence (5' – 3')** |
|---|---|
| *AK057321* rqFor1 | GGCTCCTTACCAGCTCACCT |
| *AK057321* rqRev1 | CTCCTCACATCCCAGACGAT |
| *AK057321* rqFor2 | ATGCAGTCTCCCTCTGATGC |
| *AK057321* rqRev2 | CTCCTCACATCCCAGACGAT |

**Supplementary Table 19**. Thermocycler conditions for reverse transcriptase and polymerase chain reactions.

| **Figures/Panels** | **Reaction Mix** | **Cycling Conditions** | **Instrument** |
|---|---|---|---|
| **1c**, **1g**, **1i-j**, **2b-c**, **3c-e**, **6a-e**, **7b**, **7i**, Supplementary Figs 2, 3, 13a-c, 15b, 15d, 18, 19b, 21a | M-MuLV Reverse Transcriptase (NEB M0254) with random primer mix (NEB S1330) | mix RNA with random primer mix and incubate at 65 ℃ for 5 minutes and chill on ice. Then add remaining components and incubate: 25℃ 5 minutes, 42℃ 60 minutes, 65℃ 20 minutes; use immediately or store at -20℃ | eppendorf Mastercycler nexus |
| **5b-e**, Supplementary Figs. 17, 19a | M-MLV Reverse Transcriptase (ThermoFisher 28025013) | mix RNA and primers and incubate at 65 ℃ for 5 minutes and chill on ice. Then add remaining components except enzyme and incubate at 37℃ 2 minutes, and then add enzyme and incubate at 25 ℃ for 10 minutes, 37℃ for 50 minutes, 70℃ 15 minutes; use immediately or store at -20℃ | eppendorf Mastercycler nexus |
| **1c**, **1g**, **1i-j**, **2b**, **3c-e**, **6a**, **6e**, **7b-e**, **7i**, Supplementary Figs. 2, 3, 13a-c, 13b, 13d, 21a | Taqman Gene Expression master mix (ThermoFisher; 4369016) | 1. 50℃ for 2 minutes<br>2. 95℃ for 10 minutes<br>3. 95℃ for 15 seconds<br>4. 60℃ for 1 minute<br>5. GoTo 3 for 40 cycles | BioRad CFX384 Touch Real-Time PCR Detection System |
| **1g, 2c**, **5b-e**, **6b-d**, | PowerUp Sybr | 1. 50℃ for 2 minutes | BioRad CFX384 |

| | | | |
|---|---|---|---|
| **7f-g**, Supplementary Figs. 17, 18, 19 | Green Master Mix (ThermoFisher; A25779) | 2. 95°C for 2 minutes<br>3. 95°C for 15 seconds<br>4. 60°C for 1 minute<br>5. GoTo 3 for 40 cycles | Touch Real-Time PCR Detection System |
| **1h**, **3b**, **4a**, Supplementary Figs. 8, 12, 14, 15b, 16, 21b, 22 | Azura 2X Taq Red Mix (Azura; AZ-1322) | 1. 95°C for 1 minute<br>3. 95°C for 15 seconds<br>4. 55°C for 15 seconds<br>5. 72°C for 30 seconds<br>6. GoTo 3 for 35 cycles | eppendorf Mastercycler nexus |
| All cloning reactions excluding SVAs (requires high fidelity) | Phusion High Fidelity DNA Polymerase with HF buffer (NEB; M0530) | 1. 98°C for 30 seconds<br>3. 60°C for 30 seconds<br>4. 72°C for 15 seconds per kb<br>5. GoTo 3 for 35 cycles<br>6. 72°C for 10 minutes | eppendorf Mastercycler nexus |
| SVA cloning reactions (performed on pure BAC clone templates containing each respective SVA; for luciferase assays shown in Supplementary Fig. 20 | Phusion High Fidelity DNA Polymerase with GC buffer and 3% DMSO (NEB; M0530) | 1. 98°C for 30 seconds<br>3. 55°C for 30 seconds<br>4. 72°C for 30 seconds per kb<br>5. GoTo 3 for 35 cycles<br>6. 72°C for 10 minutes | eppendorf Mastercycler nexus |

**Supplementary Table 20**. Genomic IDT primers and probes used in SVA-lncRNA *AK057321* binding studies.

| **Primer Name** | **Oligo Sequence (5'-3')** |
|---|---|
| *CHAF1B* genomic SVA FWD | AAGATCATGCCACTGCACTC |
| *CHAF1B* genomic SVA REV | ACTGCGACCGGTCAGATATAG |
| *CHAF1B* genomic SVA PRB 1 | /56-FAM/AGCTATAGC/ZEN/TAATATAGTGCCAGTGGA/3IABkFQ/ |
| *CDK5RAP2* genomic SVA FWD | GGAGTGTTATTGCCTCTAGGATT |
| *CDK5RAP2* genomic SVA REV | CACACACACACACAGAGAATTG |
| *SCN8A* genomic SVA FWD | GTTGTGTTAAGGGTCAACTGAATAG |
| *SCN8A* genomic SVA REV | AGTTGGTTTCTCTGACAGGATT |