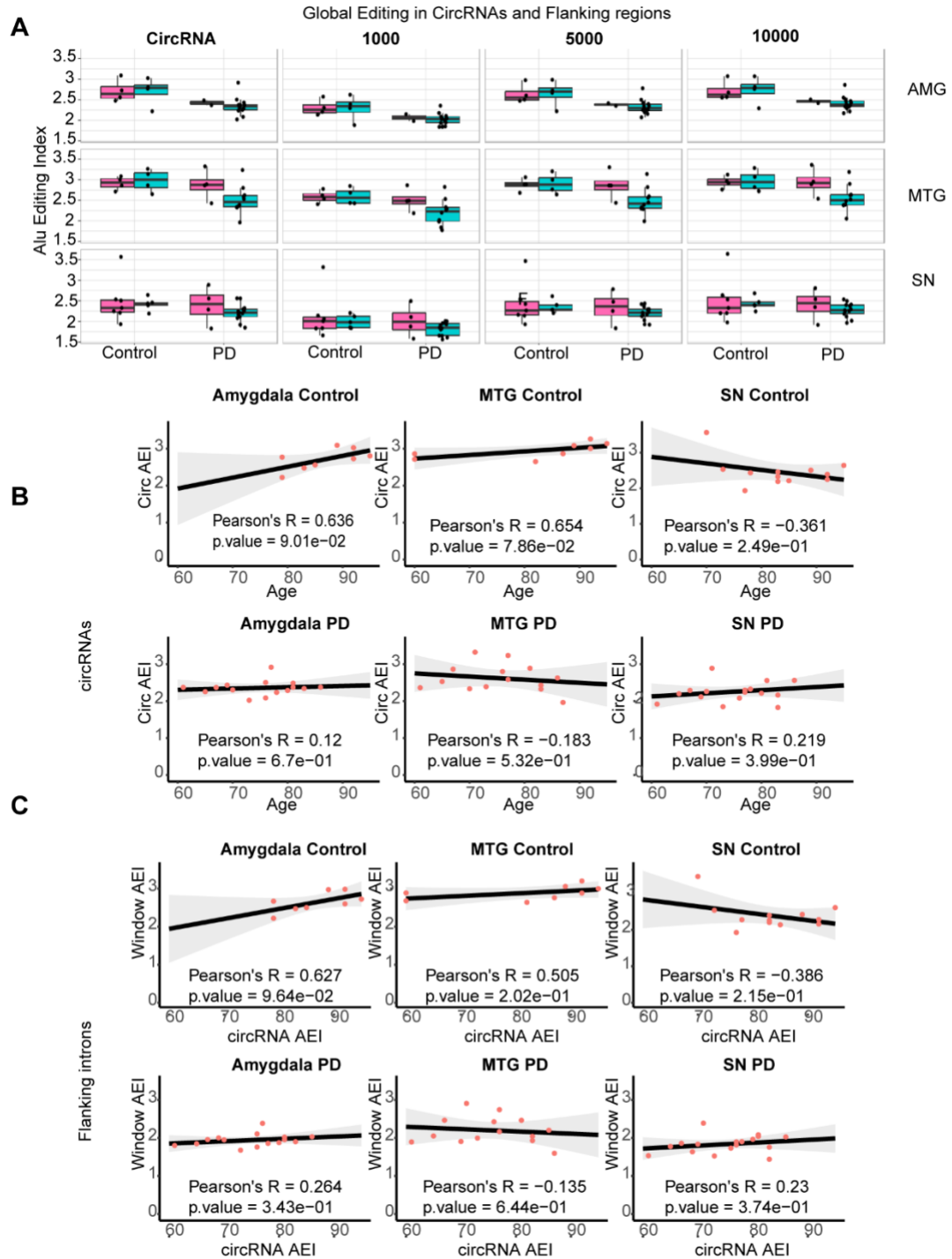


Appendix document

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Appendix figure S1: RNA Editing is not correlated to gender and age:

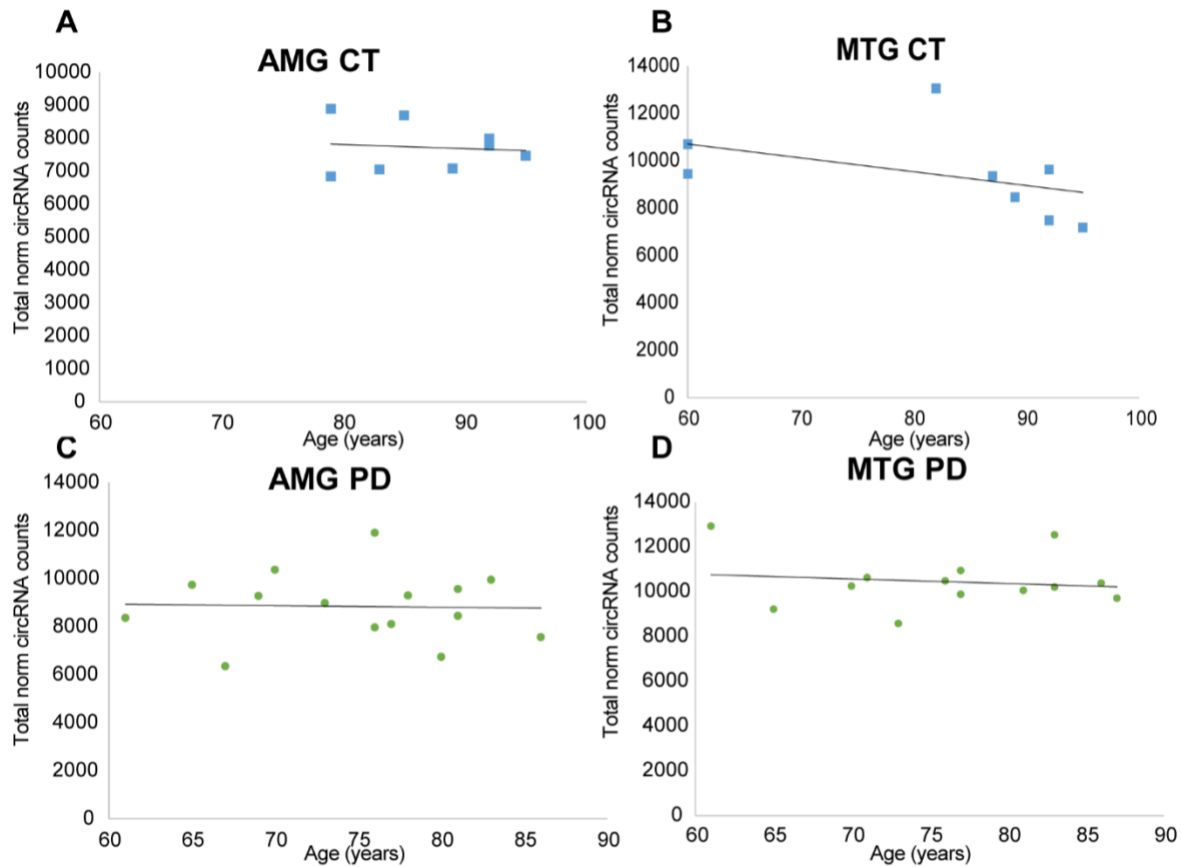


Appendix figure S1: RNA Editing is not correlated to gender and age

(A) RNA editing is not correlated to gender: no statistically significant differences were shown between male & female (T-test $p=0.56$ for control or 0.26 for PD), female marked in pink and males in cyan. $n=8$ for Amygdala control, 15 for Amygdala PD, 8 for MTG control and 13 for MTG PD, 10 for SN control and 15 for SN PD. The box is drawn from Q1 to Q3 with a horizontal line drawn in the middle to denote the median. Whiskers mark minimum or maximum values.

(B-C) RNA editing levels are not correlated to age as measured in circRNAs or in the flanking introns: no statistically significant correlation by Wilcoxon test was found between age and AEI in any of the tested groups.

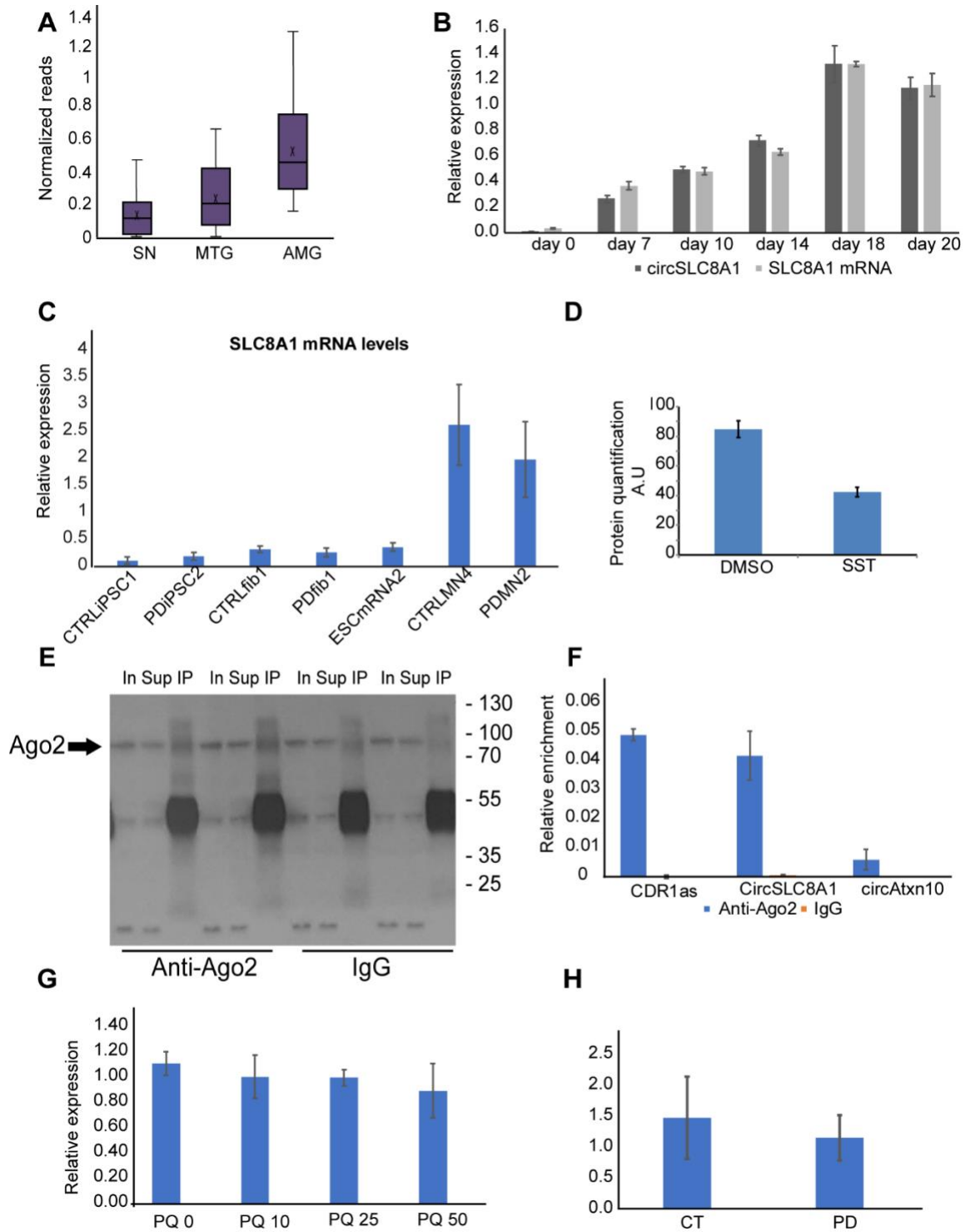
Appendix figure S2: No positive correlation between age and circRNA expression in MTG or Amygdala control and PD samples



Appendix figure S2: No positive correlation between age and circRNA expression in MTG or Amygdala control and PD samples:

(A-D) no correlation in control or PD samples of Amygdala or MTG (Correlation test p value $p=0.81$ and $p=0.91$ for CT and PD AMG and $p=0.27$ and 0.65 for CT and PD in MTG), $n=8$ for AMG CT, 8 for MTG CT, 15 for AMG PD and 13 for MTG PD.

Appendix figure S3: CircSLC8A1 expression in differentiating ES cells, AgoIP validation and miR-128 levels in SN and under oxidation



Appendix figure S3: CircSLC8A1 expression in differentiating ES cells, AgoIP validation and miR-128 levels in SN and under oxidation

(A) circSLC8A1 levels in the three testes brain regions. n=8 for Amygdala control, 15 for Amygdala PD, 8 for MTG control and 13 for MTG PD, 10 for SN control and 15 for SN PD. The box is drawn from Q1 to Q3 with a horizontal line drawn in the middle to denote the median and x marks the average. Whiskers mark minimum or maximum values.

(B) circRNA abundance (left) and SLC8A1 mRNA expression (right) in differentiating human ES cells. n=2 biological replicas for each condition. Data presented as mean \pm SD.

(C) published datasets show upregulated linear SLC8A1 expression in iPSCs differentiation from healthy and PD fibroblasts into neurons, with in no significant difference in SLC8A1 levels between control and PD samples. n=5 for control fibroblasts, 9 for PD fibroblasts, 6 Control iPSC, 7 PD iPSC, 2 ESCs, 5 Control motor neurons and 6 PD motor neurons. p values calculated by T-test. Data presented as mean \pm SD.

(D) quantification of IHC staining using anti-SLC8A1 in SH-SY cells. 10 randomly selected regions of interest (ROIs) from each slide were imaged taking a z-stack of 20um depth to cover the entire area of the cells, 84 cells were analyzed for DMSO and 87 for STT. Data presented as mean \pm SD.

(E) WB of Ago2-Immunoprecipitation or IgG control from SHSY cells: Input (In), Sup and pellet (IP). black arrow marks Ago2 band.

(F) qPCR of Ago2-bound RNA and IgG negative control showing circSLC8A1, circCDR1as as a positive control and circATXN10 as negative control. n=3 biological replicas for each condition, Data presented as mean \pm SD.

(G) miR-128 levels expression in SHSY cells treated with PQ. n=3 biological replicas for each condition. Data presented as mean \pm SD.

(H) miR-128 levels expression in SN of control and PD brains. n=12 for control SN and 17 for PD SN. Data presented as mean \pm SD.