

Author Supplemental Figure S1: Clustered neuronal (NeuN+) H3K4me3 profiles within a ± 2 kb window around all RefSeq TSSs. (A) infant controls C1-C4, (B) child and adult controls C5-C14, (C) four autism cases A5, A8, A9 and A13 with spreading profiles as described in Results, and (D) other autism cases. See **Figure 2** and main text for further details.

Author Supplemental Figure S2: H3K4me3 ChIP-qPCR on neuronal nuclei. (A) UCSC genome browser tracks illustrate H3K4me3 signal at *AHCYL1* gene on chr1, showing spreading phenotype in PFC neurons of cases A5 and A13 (indicated with blue arrows). Orange tracks correspond to NeuN+ chromatin in autism cases, green tracks correspond to NeuN+ chromatin of controls. (B-E) qPCR data, Y-axis shows relative levels of H3K4me3 (expressed as E^{-ct} , with E = primer amplification efficiency and ct = cycle threshold) for (B) housekeeping gene *B2MTSS* for cases and controls shown in (C), (D). (C) *NR4A1* TSS for A1, A4 and A11 (which showed loss of signal in ChIP-seq; see **Author Supplemental Figure S6**) and controls C10, C11, and C12. (D) *ARC* TSS for autism cases A4, A11, and A16 (affected by loss of signal in ChIP-seq; see **Author Supplemental Figure S6**) and controls C4, C5, C8 and C9. Notice consistent deficit in *NR4A1*- and *ARC*-associated H3K4me3, but not in *B2M*-associated histone methylation in the affected autism cases, in comparison to controls. One outlier sample was excluded in (B), (C). (E) *AHCYL1*-associated spreading peaks (boxed area in (A)) of cases A5 and A13, and for comparison, controls C9, C11 and C12.

Author Supplemental Figure S3: Line graphs (left) represent average H3K4me3 profiles in NeuN- nuclei, in a ± 2 kb window around the TSSs in each cluster, with clusters defined as in **Figure 2A**. Heatmaps (right) depict H3K4me3 profiles in NeuN- nuclei for individual TSSs, each being one row in the graph, clustered as in **Figure 2A**. Six heatmaps are shown, for the four

spreading autism cases A5, A8, A9, and A13 and two controls C15 and C16, as indicated. For further details, see **Figure 2** and main text.

Author Supplemental Figure S4: Bar graphs listing the number of autism-up peaks (as listed in **Table S4**) and autism-down peaks (as listed in **Table S4**) on a case-by-case basis. The criteria for detecting these peaks are as described in main text: >2-fold increase (decrease) compared to each of the ten controls C5-C14. Notice that the majority of peak changes is contributed by the four cases with abnormal 'spreading' of H3K4me3 profiles (A5, A8, A9, and A13).

Author Supplemental Figure S5: Heatmaps showing relative H3K4me3 intensities across the 16 autism samples A1-A16 and control samples C1-C14. The intensities were normalized to the strongest peak. (A) Multiple housekeeping genes, as indicated. (B) Autism-up peaks, as listed in **Table S4**. (C) Autism-down peaks, as listed in **Table S4**.

Author Supplemental Figure S6: Gene-specific H3K4me3 alterations in subsets of autism subjects. UCSC genome browser tracks show H3K4me3 profiles at (A) six genes with decreased H3K4me3 and (B) three genes with increased H3K4me3, in subset of autism cases (orange), compared with non-infant controls (green), as indicated. Affected cases are highlighted by blue arrows. Note correlation between decreased H3K4me3 density with lower levels of corresponding transcript in most cases, as indicated, and increased H3K4me3 and RNA levels for two out of three genes tested. Each transcript is independently normalized to

two different housekeeping genes. Three transcripts are also normalized by geometric mean of six different housekeeping genes as listed in **Table S6**. Scale bar for H3K4me3 tracks for 10 ppm.

Author Supplemental Figure S7: Two autism down peaks affecting A16 overlap with a copy number variation (loss) reported previously.