**Study description:** Mice were bred in the Transgenic Mouse Facility at UCI and maintained in a 12/12-hour light/dark cycle. To minimize gene expression variation between mice, all mice in experimental cohorts were bred in the same mouse room and were aged together (to the extent possible). Littermate mice aged 4 and 12 months old were used in this study; left hemisphere hippocampus from females and males was micro-dissected and assessed.

**Sample processing:** Total RNAs were extracted by using RNeasy Mini Kit (Qiagen) on a QIAcube (Qiagen) liquid handling platform. RNA integrity number (RIN) was measured by Qubit RNA IQ Assay (Invitrogen) and samples with RIN >= 7.0 were kept for cDNA synthesis. cDNA synthesis and amplification were performed followed by Smart-seq2 [1] standard protocol.

**Library preparation:** Libraries were constructed by using DNA Prep Kit (Illumina) on an epMotion 5070 TMX (Eppendorf) automated pipetting system. Libraries were base-pair selected based on Agilent 2100 Bioanalyzer profiles and normalized determined by KAPA Library Quantification Kit (Roche).

**Sequencing:** The libraries were sequenced using paired-end 100bp mode on Illumina NextSeq2000 platform with around 28 million reads per sample.

**Data processing:** Pair-end RNA-seq reads were aligned using STAR v.2.7.3a [2] with parameters ‘outFilterMismatchNmax 10 outFilterMismatchNoverReadLmax 0.07 --outFilterMultimapNmax 10’ to the reference genome GRCm38/mm10. We used STAR to then convert to transcriptome-based mapping with gene annotation Gencode v.M8. Gene expression was measured using RSEM v.1.3.3 [3] with expression values normalized into transcripts per million (TPM).

**References**

Picelli, S., et al. Nature Protocols. 2014. 9(1): p. 171.

Dobin, C.A., et al. Bioinformatics. 2013. 29: p. 15-21.

Li, B., et al. BMC Bioinformatics. 2011. 12: 323.