

## **Supplementary Data file titles / legends**

### **Supplementary Data 1. Quality control for RNA-seq libraries**

Sequencing, Alignment and expression count statistics of every sample prepped for RNA-sequencing. Samples that failed quality control or sequencing quality control are indicated. For each library the number of detected genes are presented in the table. A gene is considered 'detected' if at least 1 fragments aligns to it. Genes are included in the differential expression analysis if they have a count  $\geq 5$  in at least 4 samples for HC and NS, and a count  $\geq 5$  in at least 8 samples for FC.

### **Supplementary Data 2. List of genes contributing to sample-sample principal component analysis.**

### **Supplementary Data 3. Differential gene expression analysis**

Differential expression analysis of all genes with an FDR adjusted  $P$ -value $<0.05$  along with their base mean, log<sub>2</sub> fold change, log fold standard error, WALD statistics,  $P$ -value and FDR adjusted  $P$ -value is provided for the home-cage (HC) group in sheet 1, no-shock (NS) group in sheet 2, and fear conditioned (FC) group in sheet 3. The immediate early gene *Arc* has been highlighted in blue for each group.

### **Supplementary Data 4. Comparison to previously published data sets.**

Comparison of HC, NS and FC data sets to previously published transcriptome analyses, based on significantly regulated genes (FDR corrected  $P$ -value $<0.05$  with absolute log<sub>2</sub> fold change  $> 1.0$ ) with corresponding heat maps.

1) Hermey G, Mahlke C, Gutzmann JJ, Schreiber J, Bluthgen N, Kuhl D. Genome-wide profiling of the activity-dependent hippocampal transcriptome. *PLoS One* 8, e76903 (2013): 2 data sets, 24 h and 1 h after seizure induction, whole hippocampus.

- 2) Lacar B, *et al.* Nuclear RNA-seq of single neurons reveals molecular signatures of activation. *Nat Commun* 7, 11022 (2016): 1 data set, 1 h after novelty exposure, Fos+ neurons from the DG
- 3) Cho J, *et al.* Multiple repressive mechanisms in the hippocampus during memory formation. *Science* 350, 82-87 (2015): 4 data sets, 5 min, 10 min, 30 min and 4 h after contextual fear conditioning, whole hippocampus.
- 4) Cho JH, Huang BS, Gray JM. RNA sequencing from neural ensembles activated during fear conditioning in the mouse temporal association cortex. *Sci Rep* 6, 31753 (2016): 1 data set, 6 h after auditory fear conditioning, temporal association cortex (TeA), dVenus+ cells (pooled from FC and shock only control) versus whole TeA.

Every column indicates 1 data set and the log<sub>2</sub> fold change of overlapping genes is listed.

**Supplementary Data 5. List of enriched genes in the pathway analysis described in Fig. 2e and Supplementary Fig. 10.**

**Supplementary Data 6. List of upstream regulators with significant overlap *P* values for the FC data set.**