

## Supplementary Materials for

### Deconvolution of transcriptional networks identifies TCF4 as a master regulator in schizophrenia

Abolfazl Doostparast Torshizi, Chris Armoskus, Hanwen Zhang, Marc P. Forrest, Siwei Zhang, Tade Souaiaia, Oleg V. Evgrafov, James A. Knowles, Jubao Duan\*, Kai Wang\*

\*Corresponding author. Email: [jduan@uchicago.edu](mailto:jduan@uchicago.edu) (J.D.); [wangk@email.chop.edu](mailto:wangk@email.chop.edu) (K.W.)

Published 11 September 2019, *Sci. Adv.* **5**, eaau4139 (2019)  
DOI: 10.1126/sciadv.aau4139

#### The PDF file includes:

- Fig. S1. Representation of the top active MRs identified in the CMC data.
- Fig. S2. GOSlim summary of the up-regulated genes on day 3.
- Fig. S3. GOSlim summary of the down-regulated genes on day 3.
- Fig. S4. GOSlim summary of the up-regulated genes on day 14.
- Fig. S5. GOSlim summary of the down-regulated genes on day 14.
- Fig. S6. Biological pathways altered upon *TCF4* knockdown in hiPSC-derived neuronal cells.
- Fig. S7. MetaCore analysis of top 2000 dysregulated genes upon *TCF4* knockdown in hiPSC-derived neurons.
- Fig. S8. MetaCore analysis of all gene sets dysregulated upon *TCF4* knockdown in hiPSC-derived neurons.
- Fig. S9. The identified *TCF4* interactome and their contributions to expression of *TCF4*.
- Fig. S10. Batch correction of CD07 cell line data.
- Fig. S11. Correlations between the expression profile (summarized as median gene expression of each gene across samples) of the CMC, CNON, and NPC data with the 53 tissues from the GTEx consortium.

#### Other Supplementary Material for this manuscript includes the following:

(available at [advances.sciencemag.org/cgi/content/full/5/9/eaau4139/DC1](https://advances.sciencemag.org/cgi/content/full/5/9/eaau4139/DC1))

- Table S1 (Microsoft Excel format). Targets of the identified hub genes in the CMC network.
- Table S2 (Microsoft Excel format). Network structure created from the CMC data.
- Table S3 (Microsoft Excel format). Network structure created from the CNON data.
- Table S4 (Microsoft Excel format). Targets of the identified hub genes in the CNON network.
- Table S5 (Microsoft Excel format). Targets of five MRs in the CMC and CNON data.
- Table S6 (Microsoft Excel format). List of the altered pathway upon *TCF4* knockdown in NPCs and Glut\_Ns in the SCZ cell line.

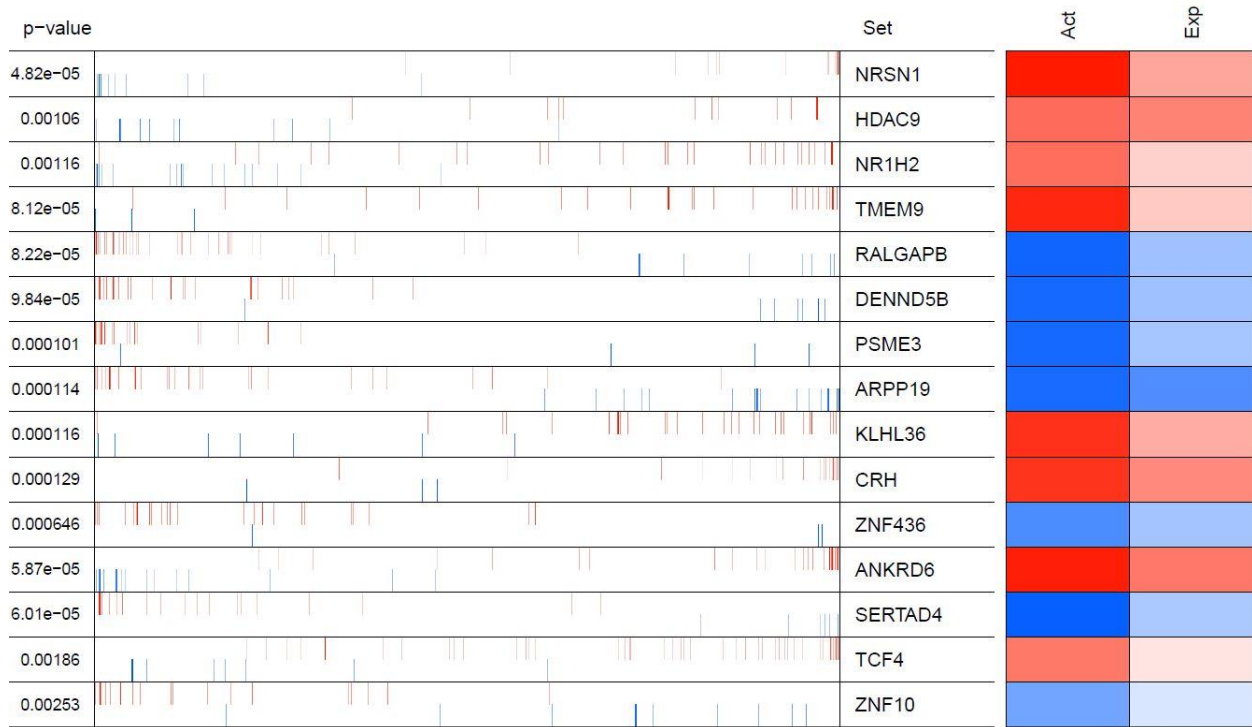
Table S7 (Microsoft Excel format). List of differentially expressed genes in NPCs and Glut\_Ns in the SCZ cell line.

Table S8 (Microsoft Excel format). MetaCore enrichment analysis on NPCs in the SCZ cell line.

Table S9 (Microsoft Excel format). MetaCore enrichment analysis on Glut\_Ns in the SCZ cell line.

Table S10 (Microsoft Excel format). List of TCF4 targets in other studies.

Table S11 (Microsoft Excel format). VIPER enrichment scores of the identified MRs in the CMC and CNON data.



**Fig. S1. Representation of the top active MRs identified in the CMC data.**

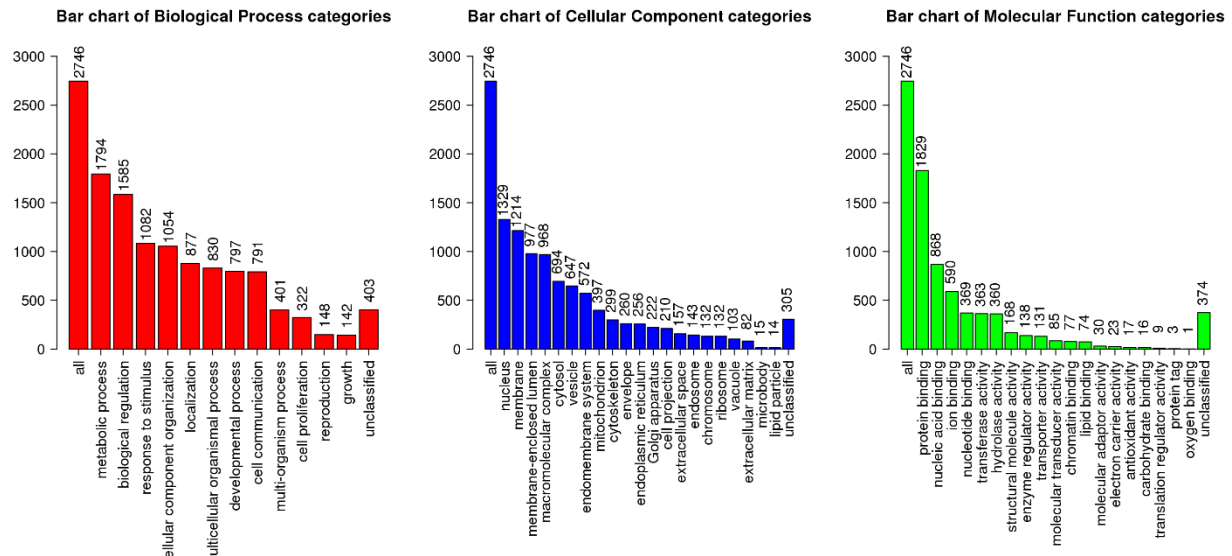


Fig. S2. GOSlim summary of the up-regulated genes on day 3.

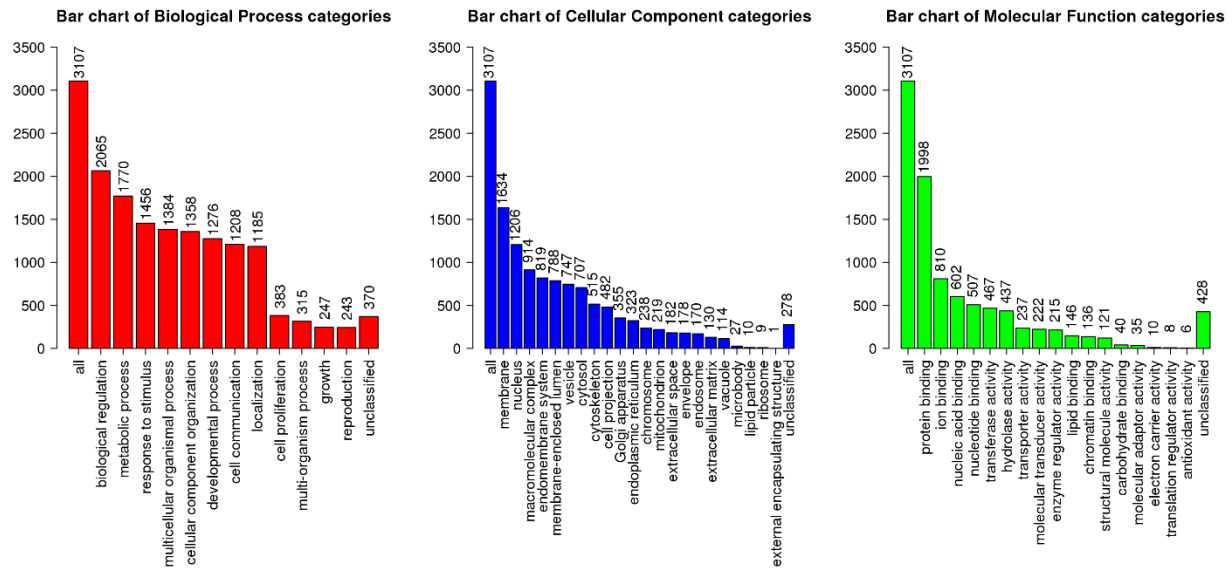


Fig. S3. GOSlim summary of the down-regulated genes on day 3.

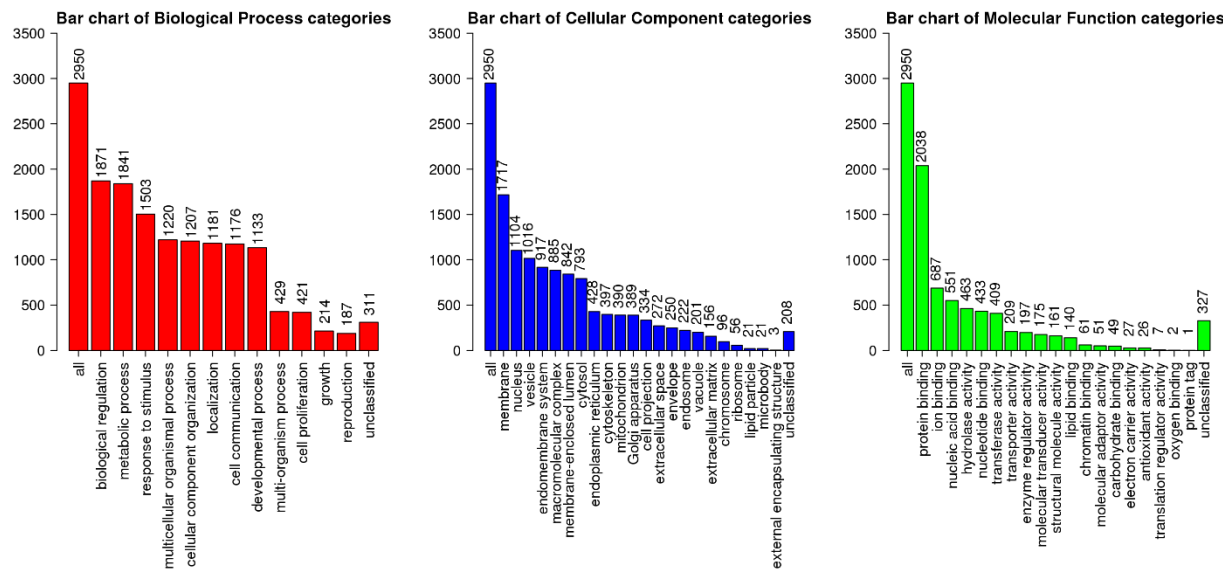


Fig. S4. GOSlim summary of the up-regulated genes on day 14.

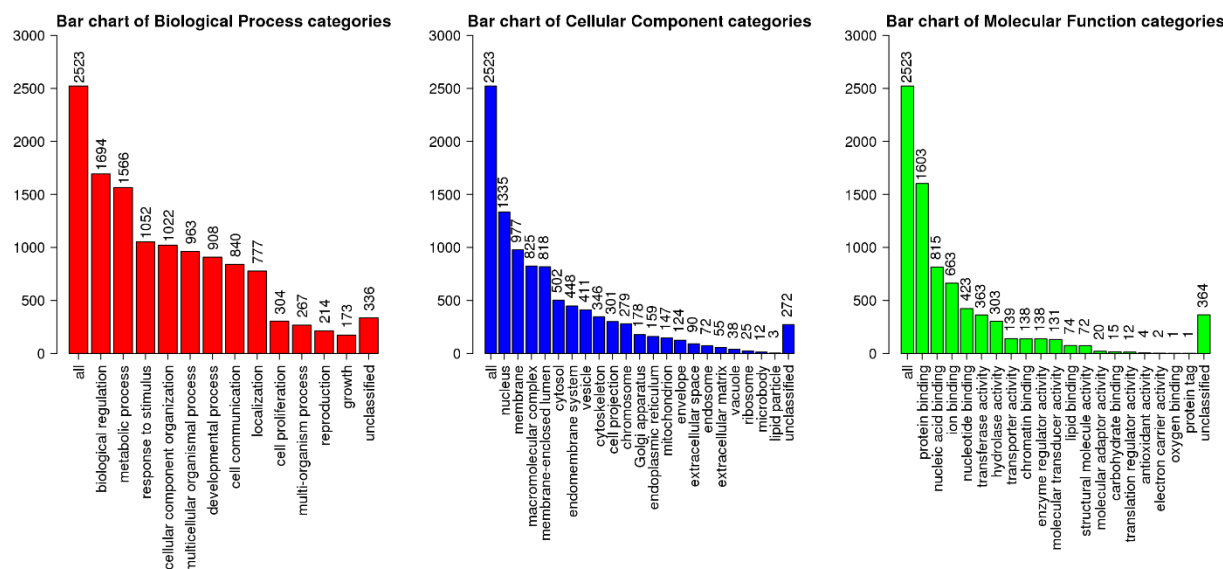
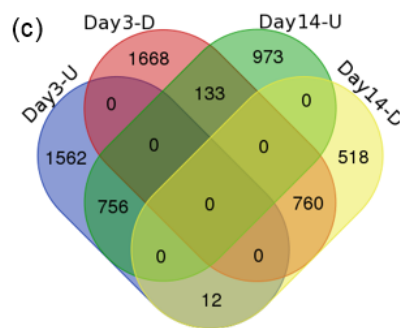
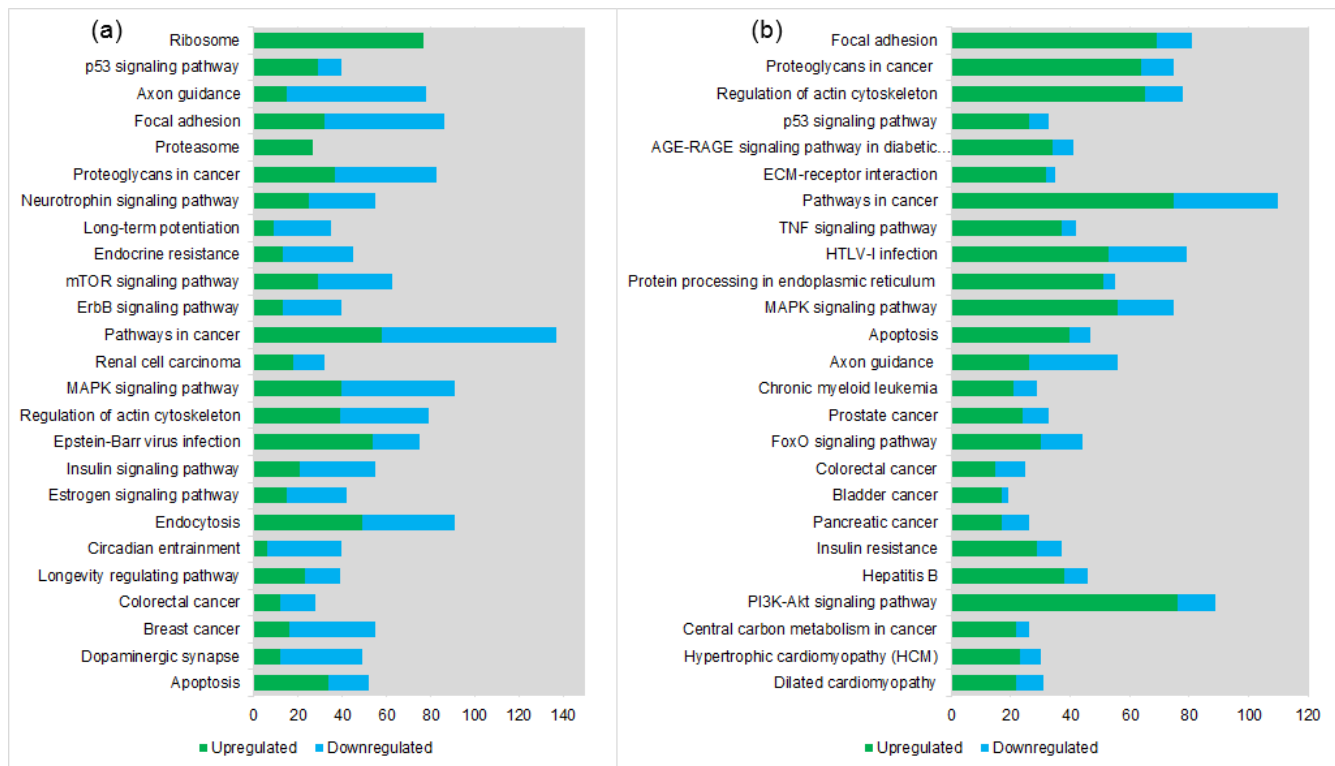
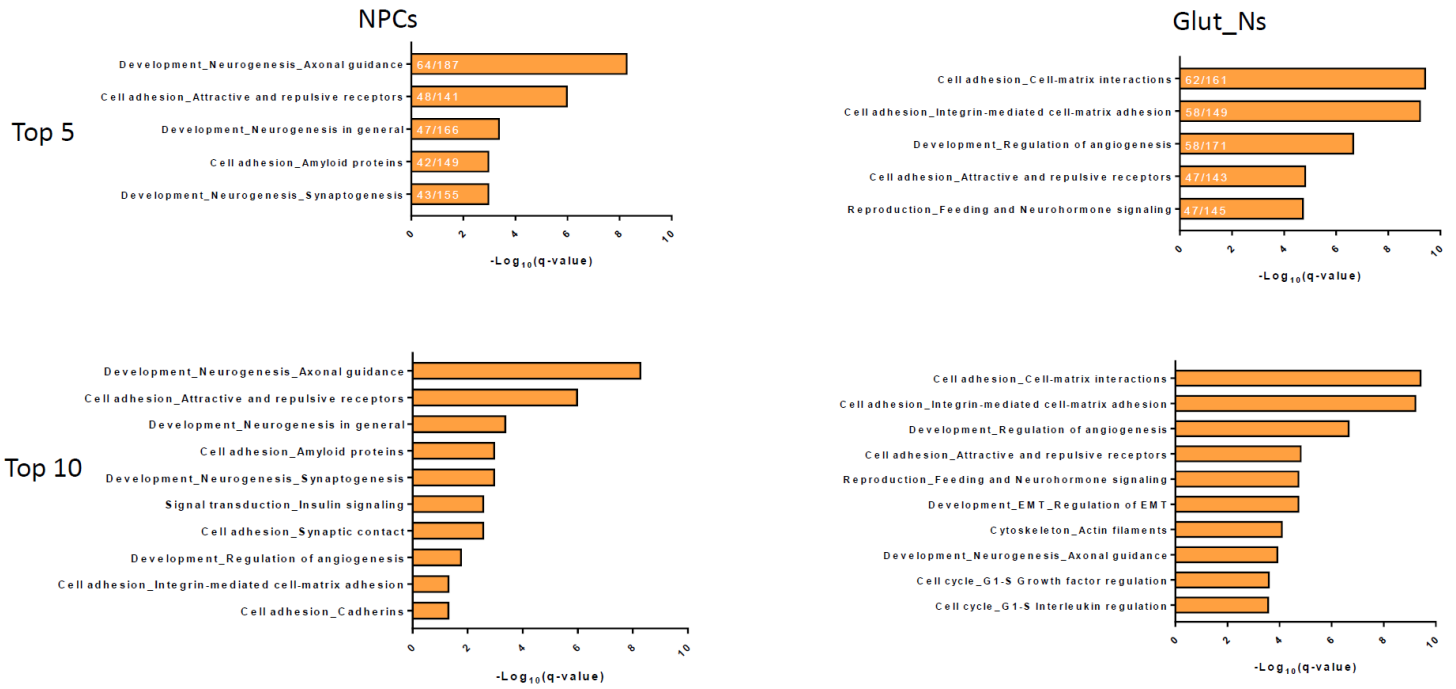


Fig. S5. GOSlim summary of the down-regulated genes on day 14.



**Fig. S6. Biological pathways altered upon *TCF4* knockdown in hiPSC-derived neuronal cells.** The top 25 biological pathways enriched in the DE genes sorted based on Bonferroni-Hochberg FDR-corrected P-values (a) at Day 3; (b) at Day 14; (c) overlap of differentially expressed genes after *TCF4* knockdown at days 3 and 14.



**Fig. S7. MetaCore analysis of top 2000 dysregulated genes upon *TCF4* knockdown in hiPSC-derived neurons.**

Top 2000

upregulated

downregulated

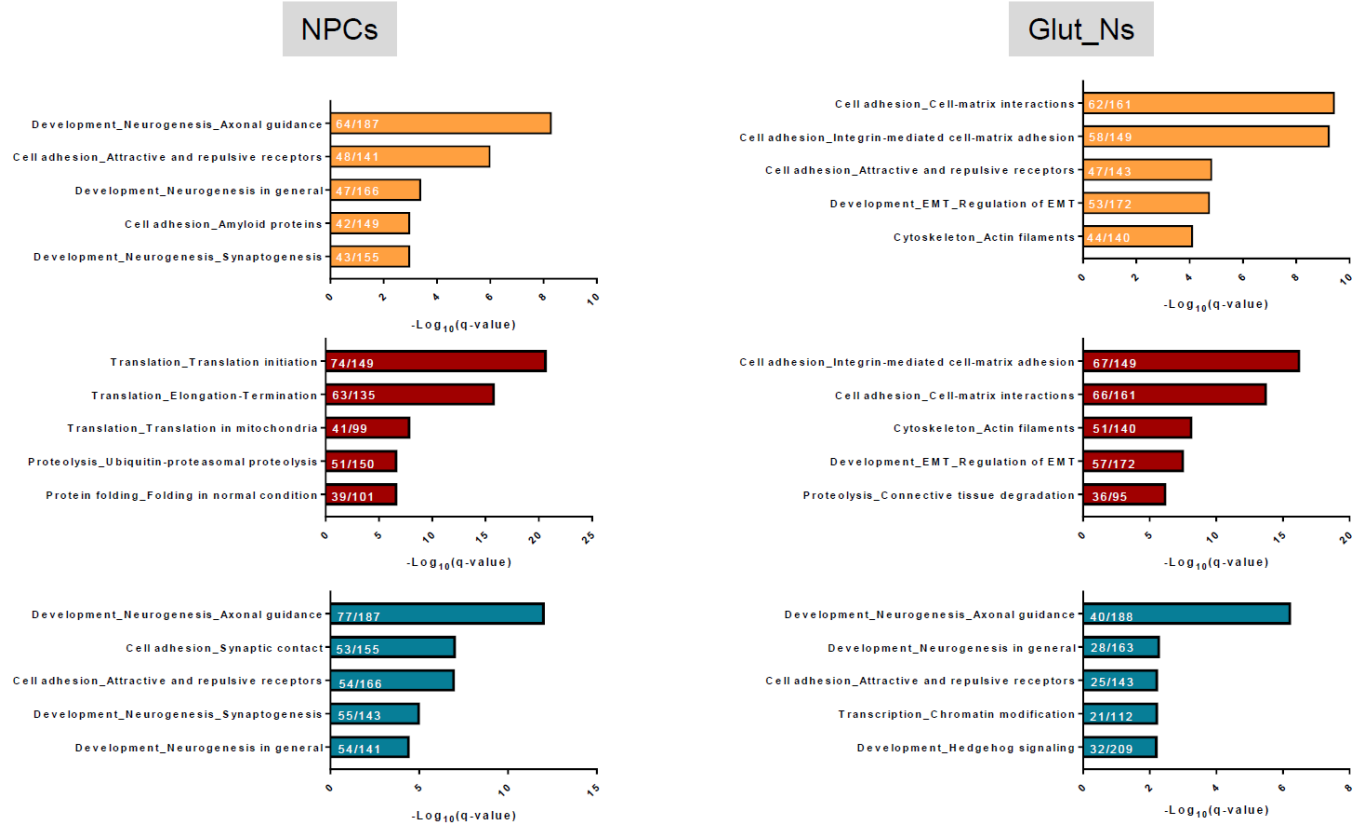
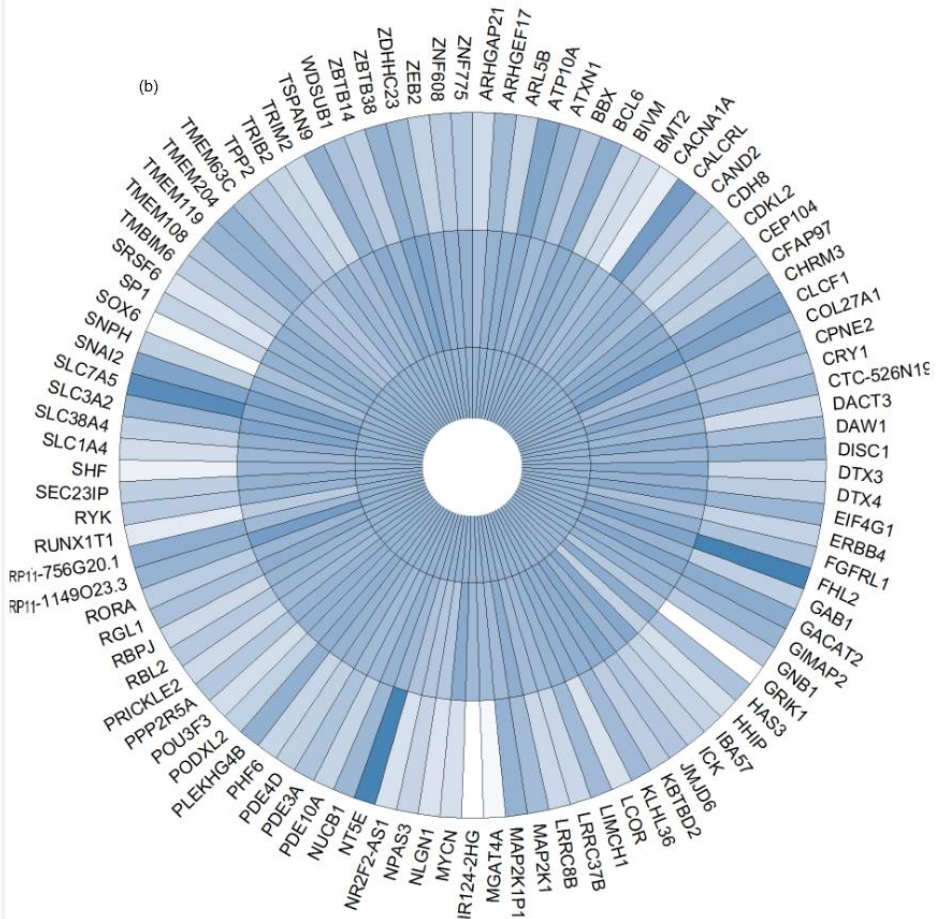
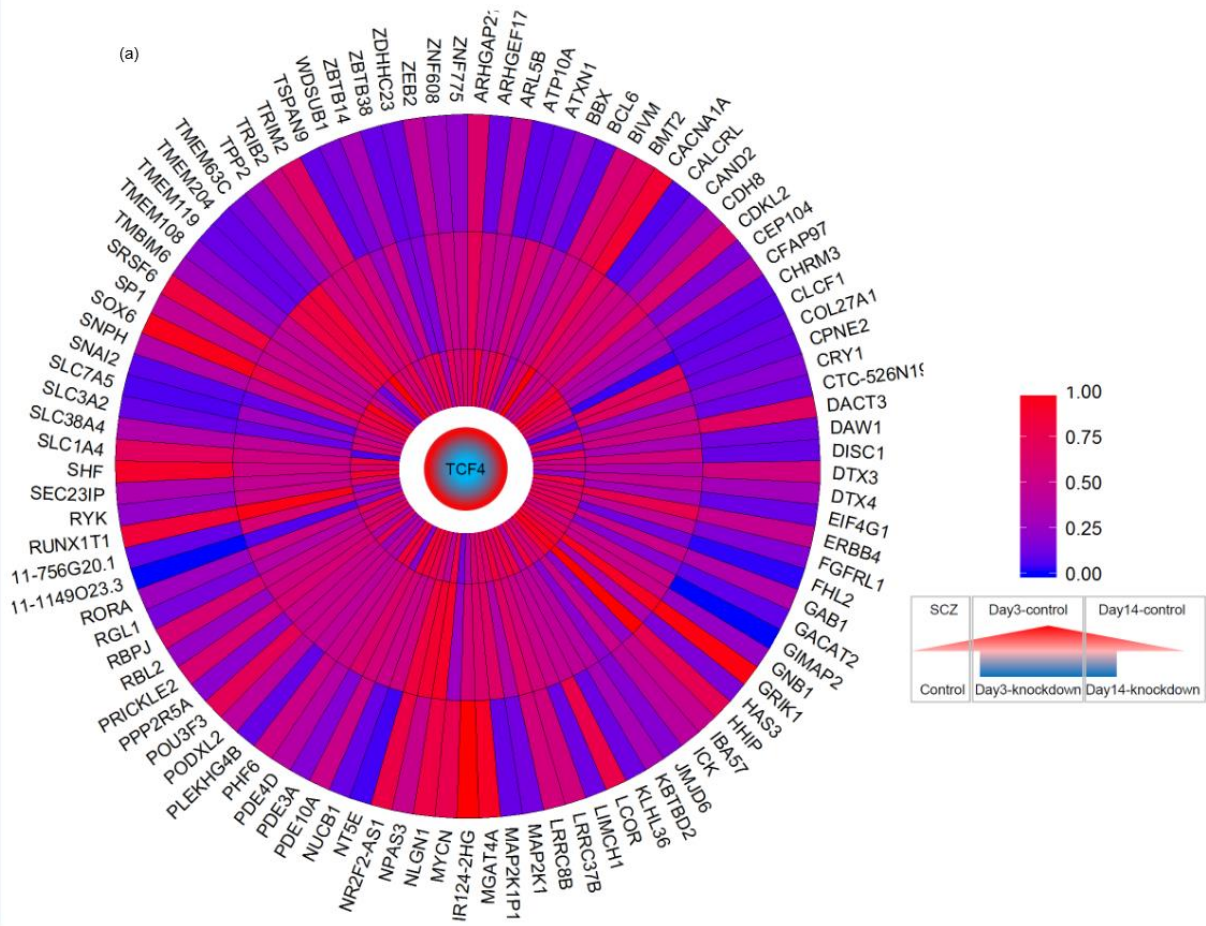
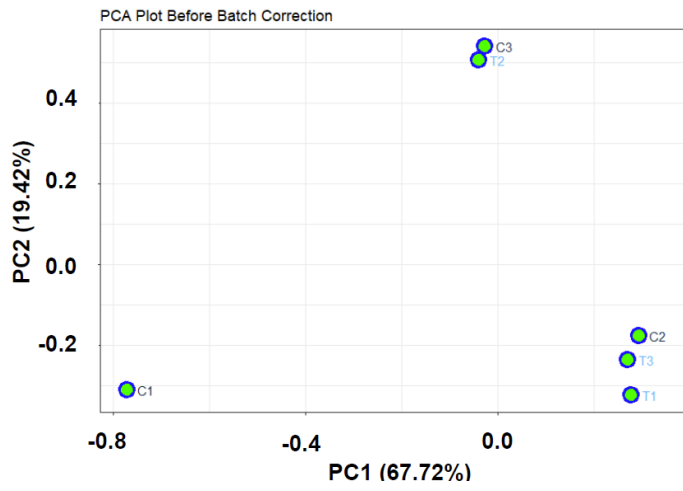


Fig. S8. MetaCore analysis of all gene sets dysregulated upon TCF4 knockdown in hiPSC-derived neurons.

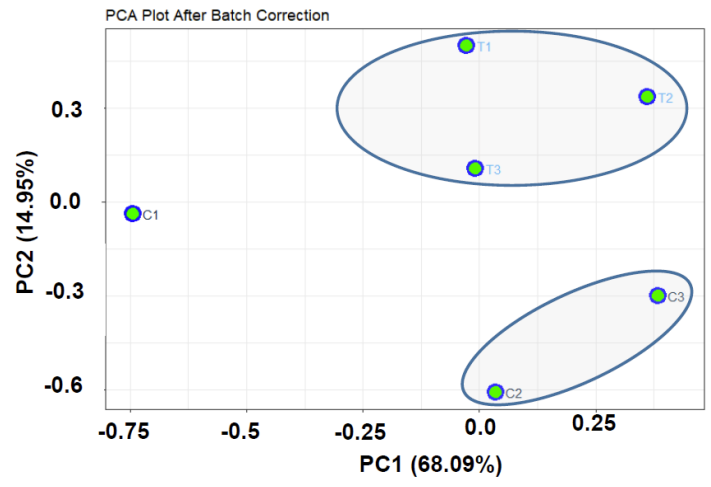




**Fig. S9. The identified TCF4 interactome and their contributions to expression of TCF4.** The inner track represents the expression contribution in CMC and CNON data, the middle track represents the TCF4 knockdown RNA-Seq data at day 3 and the outer track represents the TCF4 knockdown RNA-Seq data at day 14. In both panels, results are based on upregulation of TCF4 as indicated in the inner circle of the upper panel; (a) GSEA enrichment score of the TCF4 regulon in three different states; (b) rank metric score of the regulon representing the contribution of each gene to expression pattern of TCF4.



(a)



(b)

**Fig. S10. Batch correction of CD07 cell line data.** (a) PCA plot of the CD07 samples prior to batch correction, (b) Post-batch correction PCA plot of the CD07 samples

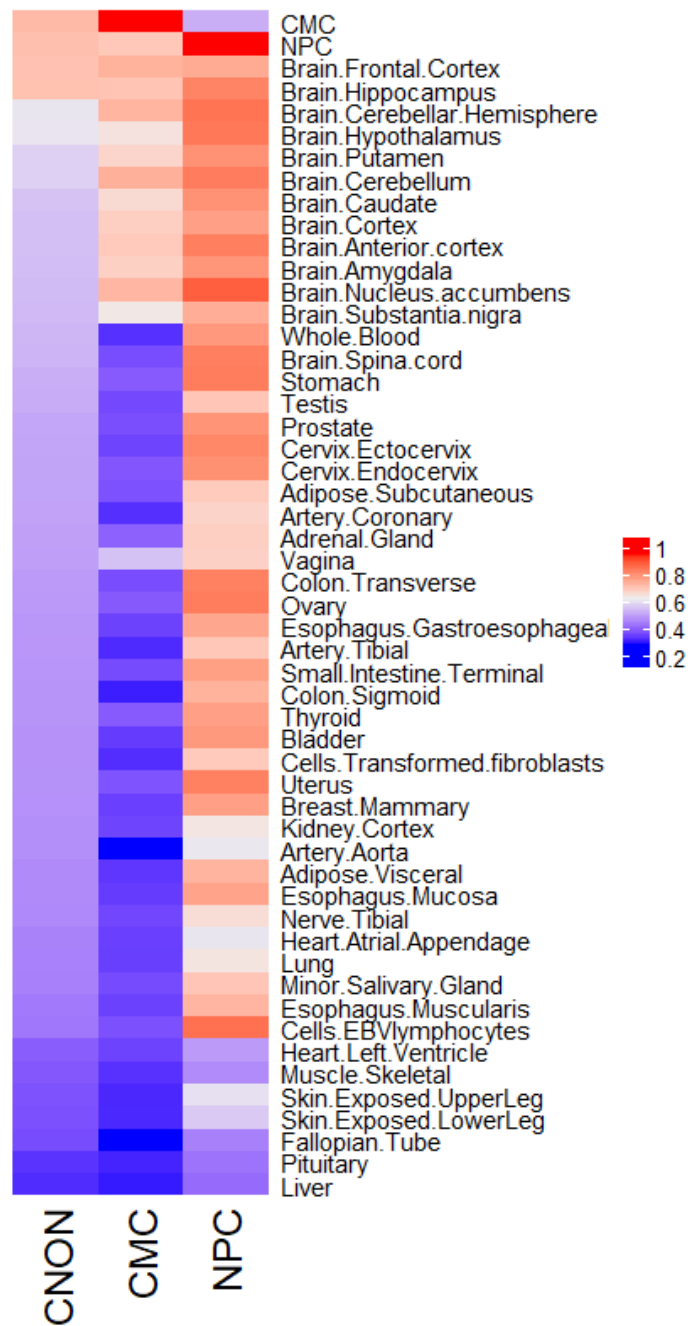


Fig. S11. Correlations between the expression profile (summarized as median gene expression of each gene across samples) of the CMC, CNON, and NPC data with the 53 tissues from the GTEx consortium.