

Supplementary Materials for  
**The Emerging Biology of Autism Spectrum Disorders**

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## Methods

We selected six representative genes reflecting prior discoveries in both idiopathic and syndromic ASD (*NLGN4X*, *NRXN1*, *TSC-1*, *SHANK3*, *FMRI*, and *SHANK2*) and six newly identified ASD risk genes (*CHD8*, *GRIN2B*, *DYRK1A*, *SCN2A*, *POGZ*, and *KATNAL2*) based on a threshold of at least two independent de novo loss-of-function mutations identified in unrelated affected individuals, as described in four recent whole-exome sequencing studies (1–4). To evaluate expression profiles, we used a previously published human brain data set (5) generated by exon arrays. The raw data is available from the Human Brain Transcriptome database (<http://www.humanbraintranscriptome.org>) and the NCBI Gene Expression Omnibus (accession number GSE25219). The entire data includes 1340 samples and covers 16 human brain regions (including 11 neocortical areas), evaluated at 15 developmental periods ranging from embryonic development to late adulthood. The methods for evaluating gene expression in each region and at each period are detailed in Kang *et al.* (5). For panel B of the figure, the expression data for each of the genes noted above was evaluated across the 11 neocortical areas for all developmental periods. We used a loess function in the R software package (<http://www.r-project.org>) (6) to perform a local polynomial regression fitting and then plot the smoothed curves across all developmental periods. In the figure, the different-colored curves represent distinct autism-related genes, as noted at the top of the figure. The *x* axis is labeled with the developmental periods on a logarithmic time scale. The *y* axis is the log<sub>2</sub>-transformed exon array signal intensity.

## References

1. S. J. Sanders *et al.*, *Nature* **485**, 237 (2012).
2. B. M. Neale *et al.*, *Nature* **485**, 242 (2012).
3. B. J. O’Roak *et al.*, *Nature* **485**, 246 (2012).
4. I. Iossifov *et al.*, *Neuron* **74**, 285 (2012)
5. H. J. Kang *et al.*, *Nature* **478**, 483 (2011).
6. R Development Core Team (2008). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. ISBN 3-900051-07-0, URL <http://www.R-project.org>.