**Material and Methods**

**RNA sequencing from mice cortex**

Total mRNA from cortex of B6 and 5 transgenic mice strains (Bin1+/-, Clu-/-, Cd2ap+/-, Apoe-/-, Apoehg) were extracted with Qiagen RNeasy Mini Kits (Qiagen, Hilden, Germany) in 6 replicates. Poly-A-enriched mRNA was reverse transcribed and amplified using the Nugen Ovation Kit (NuGEN, San Carlos, CA, USA). Paired-end cDNA was sequenced with an Illumina MiSeq at 106 base pair length (Illumina, San Diego, CA, USA). Reads were checked with FASTX-Toolkit (http://hannonlab.cshl.edu/fastx\_toolkit), trimmed with Trimmomatic (Bolger et al., 2014), and aligned to the GRCm38.73 assembly transcriptome with Bowtie (Langmead et al., 2009). Transcript expression levels were estimated in transcripts per million (TPM) using RSEM (Li and Dewey, 2011).

To identify marker genes for each mouse strain, we model each gene’s expression profile by a group factor using a linear model. The linear model was estimated in Bayesian framework with Stan (http://mc-stan.org/). Marker genes for each strain were defined by the following two criteria: (1) 95% credible interval from Bayesian estimation bigger than 6 for the strain. This is to define reliably transcribed genes. (2) Remove genes that appear to express in 3 or more strains.

**Identify marker genes for 47 cortical cell types**

A total of 47 molecularly distinct cell classes were identified by single cell RNA-sequencing of 3005 cortical cells and BackSPIN clustering (Zeisel et al., 2015). To identify marker genes for each of the 47 cell types, we modeled each gene’s expression profile across the 3005 samples with a generalized linear model, in which gene expression values were modeled with a negative binomial model, and mean of the binomial model was modeled with two predictors: a 47 levels factor describing cell types and a basal variable describing the basal expression levels. Model parameters were estimated with Stan in the Bayesian framework.

* *μ* = *βastrocyte*∗*astrocyte* + *βneuron*∗*neuron* +...+ *βbasal*∗*basal*
* *y* ∼ *NB*(*μ*,*ρ*)

To assign a gene as a marker of a specific cell type, 95% credible interval of the *β* from model estimate needs to be bigger than 3. Removing genes that appear in more than 10 cell types identified cell type-specific genes.