

Supporting Information

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Fig. S1. Every reported strain difference in the drug target panel (49 genes) with a representative comparison in the region of interest. A table of contents summarizes the differences, and each panel caption states the type (density, intensity, or both) and direction of difference. Every difference exhibits a similar pattern across comparable sections within each replicate (included when available). Solid line arrows indicate increased expression; and dashed lines decreased expression relative to C57. Subtle differences may be best appreciated by consulting the original data available at <http://www.brain-map.org>.

[Fig. S1](#)

Fig. S2. Tyrosine hydroxylase (*Th*) in the C57 and PWD strains shows similar expression patterns in the substantia nigra compacta, ventral tegmental area, and olfactory bulb. When compared with the C57 reference strain the PWD strain shows greater density of expression in the medial amygdala, nucleus of the lateral lemniscus, subiculum of the hippocampus, and the reticular nucleus of the thalamus, but lower expression in the Purkinje layer of the cerebellum.

[Fig. S2](#)

Fig. S3. Results from Fig. 1 reorganized by major brain division and then by structure within each division. Relative expression differences were categorized as either decreased (green cells) or increased (red cells), with black cells indicating no difference. Gene categories are listed with the number of different probes run for each category and the number of differences found for each category.

[Fig. S3](#)

Fig. S4. Results from Fig. 1 reorganized by gene category and then by major brain division and then by structure within each division. Relative expression differences were qualitatively binned as either decreased (green cells) or increased (red cells), with black cells indicating no difference. Gene categories are listed with the number of different probes run for each category and the number of differences found for each category.

[Fig. S4](#)

Fig. S5. Exemplar comparison of 5-hydroxytryptamine receptor 2A (*htr2a*) expression elucidates a scored difference in superficial layer 2/3 of motor cortex between CAST and the C57 reference strain. This comparison demonstrates how all differences were assessed in context of surrounding brain regions, noting generally similar expression patterns and cytoarchitectonic composition between strains. (A) Successive sections (lateromedial order) were compared between the strains to confirm putative expression difference in MO layer 2/3 by considering local context of both expressing and nonexpressing regions. The CAST does not exhibit the density of expression in superficial layer 2/3 found in the C57 (red arrows); however similar apparent expression patterns between the strains are noted in layer 5, layer 6b, and CLA (dark blue arrows), whereas layer 6 exhibits similar low or undetectable expression (light blue arrows). Nearest respective Nissl sections are shown in column 4. (B) Representative atlas plates taken from the Allen Mouse Reference Atlas showing where sections were taken. (C) Higher-magnification images (green boxes in B indicate location) reveal a difference in expression in superficial layer 2/3 (higher in C57) in context of similar expression in other layers. An expression intensity mask for each section is also shown to highlight the expression difference in superficial layer 2/3 in context of layers 5 and 6. Respective nearest Nissl sections shown in column 4 indicate similar cytoarchitecture.

[Fig. S5](#)

Fig. S6. Representative images of microdissections in C57 and comparison strain mice for each structure used for rtPCR.

[Fig. S6](#)

Dataset S1. Drug target information

[Dataset S1](#)

List of sample size, gene symbol, gene name, class, category, and probe sequence. Asterisks denote where female C57 mice were used for the replicate experiment for five genes.

Dataset S2. Atlas abbreviations and structure names

[Dataset S2](#)

Table of structures within major brain divisions. Boldface indicates structures that exhibit strain differences.

Dataset S3. rtPCR data and graphs

[Dataset S3](#)

Differences in the average values between C57 ($n = 3$) and comparison strains ($n = 2$) are congruent with reported ISH differences. Values (ΔC_p) for each animal are shown for all structure/gene comparisons (lower values indicate greater relative mRNA content). A 95% confidence interval derived for the mean of the C57 values was exceeded by both respective comparison strain values in all cases. The cycle of threshold values is also listed. Graphs show average values between groups (error bars are SEM taken from all group replicates). A twofold difference in relative content found in all comparisons is indicated by a difference of ~ 1 cycle. Relative difference in superficial MO layer 2 (>1 cycle) is greater than MO layers 5 and 6 (<1 cycle), which were selected as similar between strains based on ISH. (Fig. S5). Black boxes indicate paired structure experiments, derived from the same animals, which were predicted from ISH to vary in the opposite direction.