Mouseac

Gene expression data from the Mouse Dementia Network, University College London Mouse DemNet UCL

The aim of Mouseac is to provide to the scientific community an easy to use tool to investigate gene expression changes in a number of mouse models of dementia across their lifespan relating to neurodegenerative disorders such as Alzheimer's disease.

Overview

Mouseac is an interface that provides access to the dataset presented in Salih *et al.* (2018) (https://www.biorxiv.org/content/early/2018/10/08/437657) and Matarin *et al.* (2015) (https://www.cell.com/cell-reports/fulltext/S2211-1247(14)01094-8). The aim of Mouseac is to provide a tool with which to explore the gene expression dataset resulting from RNA-seq of the hippocampus, or genome-wide microarrays of 3 brain regions, across 4 ages in 5 transgenic mouse models of dementia and their wild-type counterparts.

Detailed methodology can be found in the main manuscripts:
https://www.biorxiv.org/content/early/2018/10/08/437657
https://www.cell.com/cell-reports/fulltext/S2211-1247(14)01094-8

All procedures were performed in agreement with the UK Animals (Scientific Procedures) Act, 1988, under HO PPL licence 70/7279 with local ethical agreement at UCL and following the GlaxoSmithKline statement on the use of animals.

Mouse models studied

The transgenic mouse models of dementia included in the study were developed by GlaxoSmithKline and incorporate mutant human genes responsible for familial forms of dementia.

TAS10 mice carry a human gene for amyloid precursor protein (*APP*) harbouring the Swedish mutation (K670N/M671L) that causes early-onset familial Alzheimer's disease.

TPM mice carry a human gene for presenilin 1 (*PSEN1*) harbouring the M146V mutation that causes early-onset familial Alzheimer's disease.

Heterozygous (HET) TASTPM mice are transgenic for both genes in the TAS10 and TPM mice.

Homozygous (HO) TASTPM mice carry twice the number of copies of both genes in the HET TASTPM.

TAU mice carry a human microtubule-associated protein tau (*MAPT*) gene harbouring the P301L mutation, which causes Frontotemporal dementia with Parkinsonism linked to chromosome 17.

WILD TYPE mice were C57BL/6 mice, which are the background strain for each of the transgenic mice including WT littermates from the TAS10, TPM and TAU mice.

Ages and brain regions studied

Gene expression has been determined within the hippocampus, cerebral cortex or cerebellum from mice aged 2, 4, 8 and 18 months of age.

Correlation to pathology

The presence of pathology (amyloid plaques for TAS, TPM, HET-TASTPM and HO-TASTPM; presence of neurofibrillary tangles for TAU mice) was assessed using fluorescent immunohistochemistry in brain sections from the contralateral brain hemispheres of the same mice used for RNA-seq or microarrays. The semi-quantitative assessment of pathology within the hippocampus and cortex are presented alongside the RNA-seq or microarray data. No plaques or tangles were identified in the cerebellum of transgenic mice at any age.

Correlations of the pathology to genetic expression data are presented in Matarin *et al.* (2015) https://www.cell.com/cell-reports/fulltext/S2211-1247(14)01094-8

RNA-seq dataset

Total RNA was used from the same mice as described in Matarin *et al.* (2015). RNA-seq library preparation and sequencing was performed by Eurofins Genomics (strand-specific cDNA libraries with polyA selection), by Illumina (HiSeq 2500) sequencing (2x 100 bp paired-end; multiplex 12 samples per lane - 28M reads). Adaptors and low quality base pairs were removed from FASTQ files using Trim Galore (Babraham Bioinformatics). Transcripts were quantified with Salmon, using gene annotation from ENSEMBL GRCm38. Salmon was used because it incorporates GC correction and accounts for fragment positional bias. To get gene level quantification from the transcripts, and correct for average transcript length and library size, expressed as transcripts per million (TPM), the tximport R package was used. TPM values were $\log_2$ transformed, and genes were considered expressed when $\log_2$ TPM values displayed a mean >1·5 for a given gene for at least one group of mice, when gene TPM values were averaged for each genotype at each age (resulting in a total of 18,562 genes expressed). Further details in Salih *et al.* (2018) https://www.biorxiv.org/content/early/2018/10/08/437657 The dataset of gene quantification expressed as TPM is available in Mouseac.

Microarray dataset

Genome-wide microarrays were performed on tissue from each brain region obtained from at least 3 male mice of each genotype at each age point using the MouseRef8 v2 (Illumina) microarray platform. Raw expression data were $\log_2$ transformed and all samples were quantile normalized together. After quality control steps, described in detail in Matarin et al. (2015) https://www.cell.com/cell-reports/fulltext/S2211-1247(14)01094-8 Data were available for at least 3 samples per group, representing 12,588 genes. The normalised dataset is available in Mouseac.

Using the interface

Use of the interface is simple. Type the official mouse gene name (MGI; http://www.informatics.jax.org) into the search box, select which mice you are interested in (by default, all are selected) and press SUBMIT. It may take several seconds for changes to be applied. The resulting plots can be downloaded as a Portable Document Format (*.pdf) file or the raw data from each mouse (including information on brain region, age and mouse model) can be downloaded as a comma delimited (*.csv) file that can be opened in most spreadsheet applications.

Statistics

Statistics have not been included in this online-database. Any statistics carried out from downloaded data should be corrected appropriately for multiple comparisons.