Supplementary information

Extension of cortical synaptic development distinguishes humans from chimpanzees and macaques

Supplementary Methods

Sample collection

We used prefrontal cortex (PFC) and cerebellar cortex (CBC) samples from postmortem brains of 33 human (aged 0-98 years), 14 chimpanzee (aged 0-44 years) and 44 rhesus macaque individuals (aged 0-28 years) (Table S1). Human samples were obtained from the NICHD Brain and Tissue Bank for Developmental Disorders at the University of Maryland, USA, the Netherlands Brain Bank, Amsterdam, Netherlands and the Chinese Brain Bank Center, Wuhan, China. Informed consent for use of human tissues for research was obtained in writing from all donors or their next of kin. All subjects were defined as normal by forensic pathologists at the corresponding brain bank. All subjects suffered sudden death with no prolonged agonal state. Chimpanzee samples were obtained from the Yerkes Primate Center, GA, USA, the Anthropological Institute & Museum of the University of Zürich-Irchel, Switzerland and the Biomedical Primate Research Centre, Netherlands (eight Western chimpanzees, one Central/Eastern and five of unknown origin). Rhesus macaque samples were obtained from the Suzhou Experimental Animal Center, China. All non-human primates used in this study suffered sudden deaths for reasons other than their participation in this study and without any relation to the tissue used. CBC dissections were made from the cerebellar cortex. PFC dissections were made from the frontal part of the superior frontal gyrus. All samples contained an approximately 2:1 grey matter to white matter volume ratio.

RNA microarray hybridization

RNA isolation, hybridization to microarrays, and data preprocessing were performed as described previously (Khaitovich et al. 2005). In brief, total RNA was extracted from 100 mg of dissected CBC and PFC samples (humans, n=22/23; chimpanzees, n=12/12;

macaques, n=24/26, respectively; see Table S1) using Trizol reagent (Invitrogen), and purified with the QIAGEN® RNeasy MiniElute kit. RNA quality was assessed with the Agilent® 2100 Bioanalyzer system (Table S1). For each sample, 2 μg of isolated RNA was hybridized to an Affymetrix® Human Gene 1.0 ST array. For human and rhesus macaque samples, the microarray experiments were carried out in two batches, with similar age distributions of subjects across batches (Table S1); in total, the hybridizations were performed in five batches per brain region: human1, chimpanzee, rhesus1, human2, rhesus2. To estimate technical variance, gene expression in two individuals in human PFC and CBC sets, and three individuals in the rhesus PFC set, were measured in technical replicates (Table S1). The 12 macaque prenatal/neonatal PFC samples were measured together following the above mentioned procedure (Table S1).

Microarray data preprocessing

All Affymetrix microarray probes (N= 693,765) were aligned to the reference human, chimpanzee and rhesus genomes (hg18, panTro2, and rheMac2, respectively) downloaded from the UCSC Genome Browser database, using BLAT (Karolchik et al. 2008). Among them, 680,139, 508,073, 241,363 are uniquely and perfectly mapped on human, chimpanzee, and rhesus macaque genome, respectively. 209,310 probes are perfectly and uniquely mapped to all three genomes. These probe annotation is available at http://www.picb.ac.cn/Comparative/data_ms_age_divergence_2010.html.

To check how the location of probes within genes might be affected by the above masking process, we assigned probes into CDS, 5'UTR, 3'UTR categories, by mapping probes to each human transcript (Ensembl, version 54), using Bowtie (Langmead et al. 2009). If a probe was mapped to different categories based on different transcripts of a certain gene, it was preferentially assigned to the CDS, and secondarily to the 5'UTR or 3'UTR categories. Importantly, genes showing human-specific developmental expression had similar probe location distributions across gene regions, such as CDS, 5'UTR and 3'UTR, as other genes expressed in the brain (Figure S3, and Table S6). Specifically, there were no significant differences in probe location among genes in the 5 PFC modules, in the 2 CBC modules, all genes detected in PFC or CBC, or all age-related genes found in PFC or CBC (Wilcoxon test, all $p>0.05$).

Probe intensities were exacted using R package "affy" (Gautier et al. 2004). Probe intensities were then corrected for background, $\log_2$ transformed and quantile normalized. To detect expressed transcripts in each brain region, the following criteria were used (Fu et al. 2009; Somel et al. 2010): (1) for each sample in each species, we only considered probes that perfectly and uniquely mapped to the corresponding genome. If the expression level for a certain probe is higher than the 95% percentile of the control probes with the same GC content, it was considered as detected in this sample. (2) In each sample, a transcript was considered detected if it contained >7 detected probes and more than half of the probes were detected. (3) In each species, a transcript, detected in more than 25% samples, was considered as detected in this species. (4) For each detected transcript, we determined the probes detected in at least one species that uniquely and perfectly mapped to all three species' genes. These probes were used to calculate intensity values as the expression value for this transcript, using median polishing (Gautier et al. 2004) (Hubbard et al. 2007) (http://www.ensembl.org). We then chose one Ensembl gene per transcript; if a gene corresponded to multiple transcripts, we chose the one with highest mean expression level. The PFC dataset of postnatal individuals (n=61) and the PFC prenatal/neonatal macaque dataset (n=12), were preprocessed separately. To combine these two datasets, for each gene measured in both, the expression level in the PFC prenatal/neonatal macaque dataset were normalized by a linear transformation that equated both the mean expression values and standard deviations between the 6 neonatal macaques in this dataset and the 14 neonatal macaques with age < 3 years in the PFC postnatal dataset.

RNA sequencing (RNA-seq)

To generate the first RNA-seq dataset, we prepared three human samples (newborn, young, old), two chimpanzee samples (newborn, young), and 2 rhesus samples (newborn, young) using pooled total RNA from PFC and CBC of five individuals (Table S1). Total RNA was isolated using Trizol® reagent (Invitrogen, Carlsbad, CA). Oligo(dT) selection was performed twice using Oligotex® mRNA Midi Kit (Qiagen). After selection, 100 ng mRNA was first fragmented by addition of 5X fragmentation buffer (200 mM Tris acetate, pH 8.2, 500 mM potassium acetate and 150 mM magnesium acetate) and heating

at 94 °C for 2 min 30 s in a thermocycler, then transferred to ice and run over a Sephadex-G50 column (USA Scientific) to remove the fragmentation ions (Mortazavi et al. 2008). We used random hexamer primers (Invitrogen, Cat. No. 48190-011) for reverse transcription of fragmented mRNA to double-strand cDNA. Sequencing libraries were prepared according to the paired-end sample preparation protocol (http://www.illumina.com). Each sample was sequenced in a separate lane in the Illumina® Genome Analyzer II system, using the 75-bp paired-end sequencing protocol.

For the second RNA-seq dataset, RNA libraries were constructed according to the Illumina strand-specific RNA-seq library preparation procedure for 14 human, and the Illumina non strand-specific RNA-seq library preparation procedure for 14 chimpanzee and 15 macaques (Table S1). Briefly, total RNA was isolated using the Trizol® reagent (Invitrogen, Carlsbad, CA). We then performed two round selection using Sera-Mag® Magnetic oligo(dT) beads (Thermo scientific). 100 ng poly(A)-selected RNA was first fragmented by 5X fragment buffer (Illumina) and then reverse transcribed to cDNA using random primers (Invitrogen, Cat. No. 48190-011). After reverse transcription and 15 cycles of amplification, the cDNA was ligated to 3' and 5' adaptors following the corresponding Illumina library preparation procedure. Libraries were sequenced in a separate lane in the Illumina® Genome Analyzer II system to a length of 100-bp.

We obtained 11-15 million read pairs per sample in the first dataset and 16-39 million reads per sample in the second sample dataset (Table S7). The raw sequence reads were mapped to the reference genomes (hg19, panTro2, and rheMac2), allowing a maximum of four mismatches using the "Tophat" program (http://tophat.cbcb.umd.edu/) (Trapnell et al. 2009) for the first dataset and allowing a maximum of three mismatches using "Bowtie" program (Langmead et al. 2009) for the second dataset. Only uniquely mapped reads were used in downstream analysis. Human gene annotation was downloaded from Ensembl (v56; http://www.ensembl.org). Chimpanzee and rhesus macaque gene annotations were constructed from human gene annotation using the UCSC "Liftover" tool (http://www.genome.ucsc.edu/cgi-bin/hgLiftOver). Gene annotations were filtered to only include transcripts with similar size in all three species (i.e. the difference in transcript length between species is less than the length of the shorter transcript). For the

first dataset, normalized transcript expression levels were calculated using the "Cufflinks" program (http://cufflinks.cbcb.umd.edu/), employing the mapping result from "Tophat" and conserved exon annotation from "Liftover" software (Trapnell et al. 2010). If a gene contained more than one transcript, the expression value of the longest one was chosen as representative. For the second dataset, the read coverage for each conserved exon was calculated based on the mapping result from "Bowtie". Exons with at least one read supported in more than half of the samples for each species were considered as expressed exons. We then divided all exons that could be reciprocally mapped among species into two categories: constitutive exons - exons present in all transcripts of a given gene, based on human Ensembl annotation (v56), and alternative exons - exons absent in some of the gene's transcripts. For brevity, exons partially present in other transcripts were also considered to be present in this transcript. To avoid any influence of alternative splicing or exon usage on our gene expression estimates, we then removed all exons with low or variable inclusion frequency in each of the three species. Specifically, we first calculated the inclusion ratio for each alternative exon as the average nucleotide coverage within an exon, divided by the average nucleotide coverage within the expressed constitutive exons of the corresponding gene:

$$inclusion\ ratio = \frac{\mathrm{cov}(exon)/\mathrm{length}(exon)}{\mathrm{cov}(gene)/\mathrm{length}(gene)}$$

Only the constitutive exons and alternative exons with an inclusion ratio greater than 0.5 in more than 10 individuals within each of the 3 species were then used in gene expression level calculations. Gene expression levels were calculated by normalizing the read coverage by each gene's length, and the total number of reads mapped to genes, per sample.

Identifying response genes upon neuronal activation

The culture of cortical neurons, RNA isolation, hybridization to microarrays, data preprocessing and analysis were performed as described in (Flavell et al. 2008). In brief, cortical neurons isolated from 15-day-old embryo mouse (C57bl/6) were cultured in vitro for 12 days, at which stage they are undergoing extensive synaptic development changes and form mature neuronal network in vitro. To identify genes that are responsive upon

neuronal activation, we exposed neurons to 25uM extracellular bicuculline (Bic), a specific GABAA receptors blocker, or 50mM potassium chloride (KCl) for 6 hours, which all lead to strong neuronal activation and membrane depolarization. Using Agilent whole mouse genome oligo microarray (4x44k), we measured the gene expression profile of cultured neurons under either stimulus or without stimulus (control). Three biological replicates were performed for each group. Arrays were scanned by a DNA microarray scanner (Agilent G2565BA). The Agilent G4462AA Feature Extraction software (v10.5.1.1) was used for image analysis with default settings to get the probe intensities. The probe intensities were further $\log_2$ transformed and quantile normalized.

To identify the probes that show different expression profiles between stimuli and control, probes under $p<0.05$ (t-test) and 2 times fold-change were selected. All probes were mapped to the mouse Ensembl gene ID. The mouse Ensembl gene IDs represented on the array was then transformed to orthologous human gene ID, using the Ensembl human-mouse ortholog annotation (version 56).

Standardization of expression levels across species

In order to compare age-expression profiles across species, without the influence of mean expression level differences (Figure S1A), we standardized expression profiles in each species, taking into account the differences in the sample age distribution among species. Our standardization procedure additionally aimed to exclude possible batch effects (caused by array hybridizations at different times). For the microarray datasets, we used the following procedure: *(i)* We standardized expression levels of each batch in each species to mean = 0 and standard deviation = 1. For the two macaque batches, the normalization was based on individuals with overlapping ages, as the age distribution of the two batches were slightly different. *(ii)* We chose sample subsets consisting of 10 individuals within each species, using both the stage-of-life matched approach and the chronological matched approach (Figure S1C-D). In the stage-of-life matched subsets, a similar age distribution across the lifespan of each species was required, using 40, 60 and 120 years as maximum lifespan for macaques, chimpanzees and humans, respectively (de Magalhães and Costa 2009). In the chronological matched subsets, calendar matched ages were used for each species. *(iii)* We standardized the mean and standard deviation

across the three species based on these subsets: for each gene, for each species, we subtracted the 10 individuals' mean from all individuals' expression levels, and divided the result by the 10 individuals' standard deviation. In cases where gene expression was measured twice in the same individual as technical duplicates, we randomly chose and removed one of the duplicates in the downstream analyses. To include the PFC prenatal/neonatal macaques dataset into standardized PFC postnatal dataset, for each gene measured in both, the expression level in the PFC prenatal/neonatal macaque dataset were normalized by a linear transformation which equated both the mean expression values and standard deviations between the 6 neonatal macaques in prenatal/neonatal macaques dataset and the 14 neonatal macaques with age < 3 years in the standardized PFC postnatal dataset.

Age scale

For all analyses we used a $\log_2$ transformed age scale: *i.e.* $\log_2$(days of age+1), as one chimpanzee was 0 days old. Log-transformation of age is a common procedure to ensure efficient and accurate modeling of developmental changes where the rate of change in the dependent variable, expression level, decreases with increasing age (Clancy et al. 2001; Lu et al. 2001; Shupe et al. 2006). Compared to the use of the linear age scale, this transformation yields a relatively uniform error distribution across samples (Sokal and Rohlf 1995). For calculating developmental timing shifts between species (see below), we used the following gestation time estimates for species: 280 days, 220 days and 165 days for humans, chimpanzees and macaques, respectively (de Magalhães and Costa 2009).

Age-test and differential expression tests

To choose age-related genes, we tested the effect of age on expression levels using polynomial regression models, as described previously(Somel et al. 2009) . Briefly, for each gene, we choose the best polynomial regression with age as predictor and expression level as response, using families of polynomial regression models and the "adjusted r^2" criterion (Faraway 2002). The most complex of these models is defined in the formula:

$$Y_{ij} = \beta_{0i} + \beta_{1i} A_j + \beta_{2i} A_j^2 + \beta_{3i} A_j^3 + \varepsilon_{ij},$$

where Y_{ij} is the expression level for gene i and subject j, A_j is the age of the subject j, and ε_{ij} is the error term. Alternative models are the above models' subsets, including linear and quadratic ones. The significance of the chosen regression model was estimated using the F-test, and the false discovery rate (FDR) was calculated by 1,000 random permutations of age across samples (Table S3). The median of the permutation distribution was used as the null expectation. Each species was tested independently. For both the PFC and CBC datasets, age-related genes were defined as those showing significant age-effect in at least one species. In the analyses using subsets of 10 individuals per species, to make the analysis more conservative, we defined age-related genes as those showing significant age-effect in all three species.

The test for differential expression between a pair of species is based on analysis of covariance, or ANCOVA (Faraway 2002), described in (Somel et al. 2009). Briefly, the test aims to identify whether two species have different curves for expression change with age, or not. First, one of the two species is selected as reference. For each age-related gene, we use the polynomial regression model chosen in the above-described age-test (for the reference species). We then test if such a regression model, but with species-specific parameters, is significantly better than the model with common parameters for both species, given the expression-age distribution of the two species. For example, in a comparison of human and chimpanzee, if the null model for gene *i* was a linear one:

$$Y_{ij} = \beta_{0i} + \beta_{1i}A_j + \varepsilon_{ij},$$

we compare it to the alternative model:

$$Y_{ij} = \beta_{0iC} + \beta_{0iH} + \beta_{1iC}A_{jC} + \beta_{1iH}A_{jH} + \varepsilon_{ij},$$

where Y_{ij} is the expression level of individual *j*, β_{0iC} and β_{1iC} are the chimpanzee-specific intercept and slope, β_{0iH} and β_{1iH} are the human-specific intercept and slope, A_{jC} and A_{jC} are chimpanzee and human ages, respectively. The null model (with no species-specific parameters) and alternative models are compared using the F-test. We test each sub-model of the full alternative model, each containing one or more species-specific parameters. Note that applying the differential expression test using ages normalized for lifespan differences between species, does not alter our results (i.e. the excess of human-specific genes in the PFC compared to CBC; data not shown). The R language code can

for the age- and differential expression tests can be found at http://www.picb.ac.cn/Comparative/data_methods/neoteny/somel_R_functions_1.r.

The permutation is performed by dividing the age-range into 10 sections, and randomly permuting species identifiers among samples within each section, in order to preserve the age-structure in the data. FDR was calculated by 1,000 random permutations of species identifiers (Table S3).

To identify species-specific genes, the differential expression test is performed on each species pair twice, using either species as a reference. For each gene, if either of the two tests was significant at a defined cutoff, we considered this gene as differentially expressed between these two species. If a gene showed no significant differential expression between chimpanzees and macaques, but significant differential expression between humans and the other two primate species, this gene was assigned to the human-specific gene set. Chimpanzee- and macaque-specific genes were defined by the analogous criteria. To avoid any bias due to the unequal sample size and sample age distribution among the three species, we used the subsets of 10 individuals per species (described above; Figure S1C-D). The numbers of overlapping of species-specific genes between this 30-individuals dataset and the full dataset, as well as between PFC and CBC, are shown in Table S4.

Interpolation of expression curves

Here, for each gene, for each species, we interpolated expression values at 15 equally distributed points along the species' age range, from birth until old age: 0-80 years for human; 0-40 years for chimpanzee; 0-28 years for rhesus macaques. These ranges were chosen to cover two thirds of maximum lifespan in each species (based on (de Magalhães and Costa 2009)), given the fact that the oldest macaque individual used in our analyses is 28 years old. We used cubic spline regression for interpolation, restricting the fit to three degrees of freedom, in order to avoid over-fitting.

Human-specific expression modules

For defining modules, we first constructed dendrograms of species-specific genes by hierarchical clustering, using the Pearson correlation coefficient (r) between expression curves of pairs of genes as the distance measure (*i.e.* 1-r). The correlations were

calculated based on expression profiles of all three species. To ensure equal power across species, we used interpolated expression levels for each species (described above). We used the "complete" method for hierarchical clustering and cut the tree at a height determined by manual examination of cluster profiles and by observing cluster functional properties at different levels (h=1.5; Figure S2A-B). Within each group, we only retained genes with median Pearson correlation coefficient >0.5 to the others genes, in all three species. We discarded groups containing <20 genes yielded 5 PFC and 2 CBC modules with strong within-group correlations. Genes assigned to the modules are listed in Table S5.

We note that, in the PFC analysis, dividing the hierarchical clustering tree into two main clusters, or using k-means clustering with two subgroups, yields gene sets where one set has similar profile and functional properties as PFC module 1 (data not shown). This indicates that the exact parameters used for clustering have limited effect on our results for PFC module 1 genes.

Functional enrichment analysis

Kyoto Encylopedia of Genes and Genomes (KEGG) pathway annotation (Kanehisa et al. 2008) and Gene Ontology (GO) annotation (Ashburner et al. 2000) for human were downloaded from KEGG (http://www.genome.jp/kegg/) and Ensembl (v54) databases, respectively. We used the GO "term" and "graph path" tables downloaded from the GO database (http://archive.geneontology.org/latest-termdb/) to associate each GO term with higher terms. To identify overrepresented KEGG pathways or GO terms, we used the hypergeometric test, and adjusted *p*-values for multiple-testing by Bonferroni correction. Only pathways/terms containing ≥5 genes were tested. Enrichment analysis of cell type-specific genes was performed as described previously (Somel et al. 2009). Briefly, we used 1,155 and 578 human Ensembl genes described to be enriched in gray- and white-matter, respectively, in a published experiment from the human frontal cortex (Erraji-Benchekroun et al. 2005). For the cell-type analysis, we used expression levels measured from purified mouse neurons, astrocytes and oligodendrocytes (Cahoy et al. 2008). We defined 1116, 965, and 991 human-mouse one-to-one orthologs (based on Ensembl v54) as neuron-, astrocyte- and oligodendrocyte-specific, using an effect size cutoff equal to 2.

Metabolite analyses

Metabolite data in PFC of 50 humans, 12 chimpanzees and 49 rhesus macaques measured using gas chromatography mass spectrometry (GC-MS) were from (Fu et al. 2011). Samples from almost all individuals were measured in duplicates. As the vast majority of metabolites in macaque show long-term stability (Fu et al. 2011), we included all detected metabolites and all individuals with or without technical replicates in this study. In detail, metabolites with >35% missing values across all individuals were removed. The remaining missing values were predicted using R package "EMV". The dataset was $\log_2$ transformed and quantile normalized. This yielded 151 metabolites with reliable detection levels (excluding spike-in controls and 13C-sorbitol, which was used for standardization). Among the 151 metabolites, 6 are classified as neurotransmitters in the "neuroactive ligand-receptor pathway" in the KEGG database. We standardized the mean and standard deviation based on 10 individuals per species (with similar age distribution across each species' lifespan). We tested all 151 metabolites for human-specific profiles using the ANCOVA test for differential expression, as described above, using the mean per replicate where possible. Seventeen metabolites were identified as human-specific, 3 of which were among the 6 neurotransmitters. For these 3 neurotransmitters, in order to test whether the human points in development are significantly different from the others, we firstly combined individuals with similar ages to four groups (0-1 month; 1 month-1 year; 1-10 years; >10 years) to reduce individual variation. We then used the z-test to estimate difference between human-macaque or human-chimpanzee comparison, by interpolating the chimpanzee/macaque curve and using the human variance across the human spline curve. We found that in the youngest age group (0-1 month) human points were lower than chimpanzee and macaque ($p<0.001$ for glutamate and aspartate; $p<0.1$ for GABA human-macaque comparison).

Estimating time-shift by dynamic time warping

We used a modified dynamic time warping algorithm, DTW-Significance (DTW-S) algorithm, to estimate the time shifts between the time series expression curves of two species (Yuan et al. 2011). The R package "*TimeShift*" for DTW-S is available at http://www.picb.ac.cn/Comparative/data.html. Briefly, the input for the algorithm

consists of two time series expression data with samples of possibly different size and age distribution between the two species. An alignment between the two time series assigns each point in one time series to another point in the other time series with the maintenance of their respective age orders. By searching the space of all such alignments (with a subset size constraint) between the two time series, the method selects the alignment with minimal expression level differences, and reports the corresponding age differences as the estimation of time shifts for each point between the two time series. For implementing this algorithm in this analysis, the gene expression curve alignments were carried out by sampling 20 values among 40 time points interpolated along the fitted spline curve in one species with longer lifespan (with subset size constraint of 20) and calculating the distance to the 20 time points interpolated along the fitted spline curve in the other species with shorter lifespan. For each gene in each pair of species, the alignment with the minimal distance was chosen as output. For this procedure, we interpolated cubic spline curves (degrees of freedom=3) using estimated conception ages and the interpolated curves ranged from rhesus macaque birth age to each species' maximum lifespan. To ensure efficient mapping between expression curves, whenever there was a minimum or maximum predicted point in the expression profiles, we used that point as the first point in the estimation procedure (under the assumption that peak ages correspond to the same biological age among species; see Figure 3A). Otherwise, we used macaque birth age as the first point in the estimation. For each module, we estimated the time shift for each gene separately, calculated the average shift for that module and estimated variance by randomly resampling among module members with replacement 1,000 times. For comparison, we also estimated the shift for each age-related gene in PFC and CBC and randomly sampled gene sets with the same number of genes as the respective module, 1,000 times. For each of the 20 time points, the quantile value of the average shift for a specific module with respect to the distribution of the above 1000 random sampling shifts was recorded. We calculated an estimated *p*-value by (1-the mean value of the 20 quantile values) to assess the statistical significance of the module shift against random background. For Figure 3B, we estimated the shift for human and chimpanzee brain volume growth using the same procedure. Specifically, we used data from (Leigh 2004) and converted these volume measurements into percentages by

dividing them by the adult brain volume. We then applied the dynamic time warping algorithm to these volume percentage estimates.

TF binding site enrichment analysis

The conserved TF binding sites (TFBS) were estimated as follows: Promoter regions (+/- 2,000 bp around the transcription start site) for each gene were extracted based on the gene annotation from Ensembl (v54). Predicted TFBS in each promoter were identified using the Match™ algorithm, employing the TFBS sequences from the TRANSFAC® database (Kel et al. 2003). The average Phastcons scores of each predicted TFBS were calculated using the UCSC Genome Browser 17-way vertebrate Conserved Element Table (Siepel et al. 2005). We defined conserved TFBS as those for which ≥80% of nucleotides had Phastcons scores and the average score was ≥0.6. For each conserved TFBS, we used the hypergeometric test to check whether there was an excess of TFBS in species-specific modules, compared to all age-related genes in that brain region. The enriched TFBS were defined at p-value<0.05. We further estimated the expected-by-chance number of TFBS enriched at this significance cutoff by randomly sampling the same number of age-related genes as within the tested module, and repeating the enrichment test 1,000 times.

The TFs with enriched TFBS were then tested for correlation with their targets in corresponding Module in terms of their expression profiles. The TF-target correlations were compared to correlations between the same TF and its age-related targets outside the Module, using the Wilcoxon test. The test was conducted using all three species' expression profiles, as well as taking each species' expression profile separately.

Evolutionary conservation analysis

For estimating conservation of protein coding sequence, we used human-mouse dN/dS ratios downloaded from the Ensembl database (v55). For estimating promoter conservation, we used the PhastCons 18-way Placental Mammal Conservation Track (a subset of the 28-way Placental Track) from the UCSC Genome Browser (Siepel et al. 2005). For each Ensembl gene, we computed mean PhastCons score per proximal promoter (+/- 2,000 bp around the transcription start site (Xie et al. 2005)). For genes

with multiple transcripts, we chose the one with the highest number of exons. To estimate the basal mutation rate per gene, we used intronic conservation (excluding first introns, excluding 100 bp around each splice site, and considering only 2,500 bp at each end of an intron (Haygood et al. 2007)). When comparing gene sets, for each gene, we used the promoter conservation measure divided by the intron conservation measure. For polymorphism analysis, we used 1,236,401 Perlegen "type A" SNPs, which were discovered by re-sequencing in a panel of African Americans and European Americans (Hinds et al. 2005). The SNP locations were mapped from human genome version hg16 to hg19 locations using the UCSC Genome Browser "Liftover" tool (http://www.genome.ucsc.edu/cgi-bin/hgLiftOver). We compared genes by the number of Perlegen SNPs per proximal promoter defined as defined above. In the results presented in the main text and Figure S6B-D, we compared specific module members with all 8,613 age-related genes using the Wilcoxon test.

Western blot analysis

Western blot were performed as described elsewhere (Glantz et al. 2007). In brief, samples with equal amount of total protein (15 μg for synaptophisin and 20 μg for PSD95) were separated by 10% Mini-PROTEAN TGX gel and transferred onto PVDF membrane (Cat. RPN303F, GE Healthcare). After transfer, wash the membrane with PBS for 5 minutes at room temperature. The membrane was then blocked with blocking buffer (5% BSA mixed in PBS containing 0.1% Tween 20 (PBST)) overnight at 4°C. The membrane was then incubated at room temperature for 2 h in blocking buffer with primary antibodies as follows, mouse anti-SYP (s5768, Sigma, 1:3000), rabbit anti-PSD (#3450, Cell Signaling, 1:800), mouse anti-β-actin (A5441, Sigma, 1:5000) or rabbit anti-β-tubulin III (T2200, Sigma, 1:3000). The actin and tubulin were used as controls for DLG4 and synaptophysin, respectively, to ensure the equal amounts of protein was loaded in each lane. After being washed three times with PBS-T, the membrane was incubated with HRP-conjugated anti-mouse secondary antibody (#7076, Cell Signaling, 1:8000) or HRP-conjugated anti-rabbit antibody (#7074, Cell Signaling, 1:8000) for 45 min at room temperature. Then the membrane was washed three times with PBS-T, and developed with Luminol/enhancer and peroxide buffer solution (Immun-Star HRP

Substrate,170-5041, Bio-Rad) as recommended by the manufacturers. The immunoreactivity was visualized with Fujifilm LAS-4000 system. PSD95 and actin, or synaptophysin and tubulin, from samples in each species in each tissue were processed in the same membrane and visualized in the same condition to minimize experimental variation. The integrated optical density (IOD) of each band was measured by the Gel-Pro Analyzer.

Positive selection analysis

The analysis of positive selection on the human evolutionary lineage after the separation from the Neanderthal linage was carried out following (Green et al. 2010). Specifically, the human SNPs data from 5 modern humans, human reference genome and 6 Neandertal samples were downloaded from UCSC (http://genome.ucsc.edu/Neandertal/). The SNPs were classified as modern human derived, when at least four of the six modern human genomes showed derived allele, while all observed Neanderthal alleles were ancestral, using chimpanzee genome as outgroup. An overrepresentation of such SNPs in a genomic region beyond random expectation would imply that the region had undergone positive selection in the modern human lineage since divergence from Neanderthals (Green et al. 2010). The analysis was done using a sliding window approach with window size of 50 kb moved by 10 kb steps across the human genome.

Supplementary figures

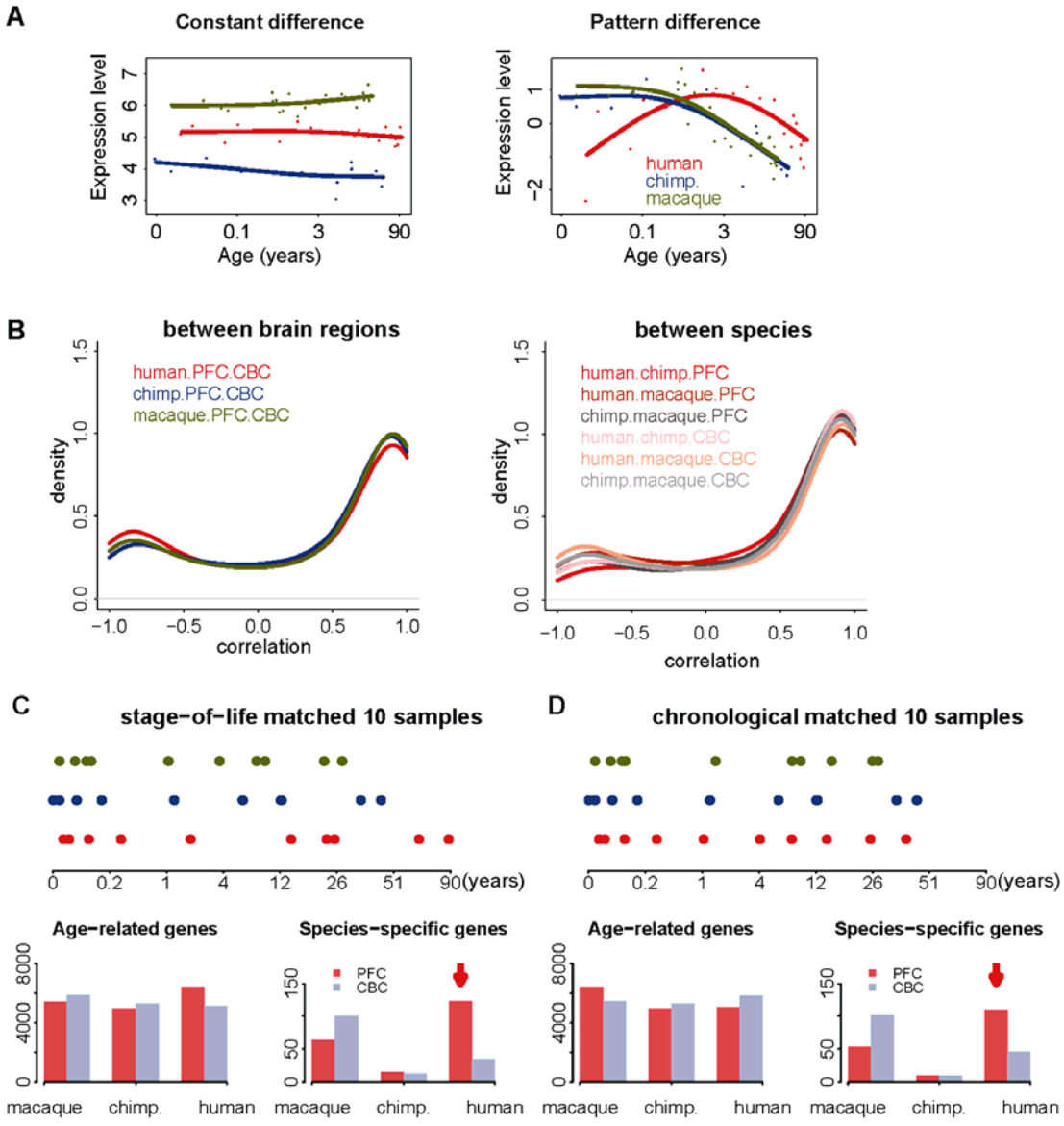

Figure S1. Age-related gene expression change between different brain regions or different species, or using 10 species subsets.

(A) Examples of constant and pattern differential expression. Two examples of differential expression, reflecting expression level differences among species that are constant with age (left panel), and reflecting differences in the timing of expression changes across species (right panel). In the right panel, expression levels are standardized for the mean and variance per species (Supplementary Methods). The genes shown are

C14orf126 and carbonic anhydrase X (*CA10*), respectively. The x-axis represents individuals' ages in $\log_2$ scale.

(B) Correlation of age-related expression change between different brain regions or different species. The Pearson correlation coefficients were calculated using 15 interpolated points across expression-age cubic spline curves per species per brain region (Supplementary Methods). All the correlation coefficients were based on genes identified as age-related in at least one brain region and detected in both regions (N=9,714).

(C-D) Age-related gene expression change in the PFC and CBC using the subset of 10 individuals per species. To avoid any bias due to the unequal sample size and sample age distribution among the three species, subsets of 10 individuals per species based on stage-of-life matching strategy (C) or chronological matching strategy (D) were chosen to redo the analysis (Supplementary Methods). Each point represents an individual. The colors indicate species (red-human, blue-chimpanzee, green-macaque) on the upper panels and brain regions (red-PFC, gray-CBC) on the lower panels. The upper panels' x-axis represents individual age in fourth root ($age^{1/4}$) scale. The lower panels' y-axis shows the numbers of age-related genes and species-specific genes detected in each of the 10 individuals' subsets.

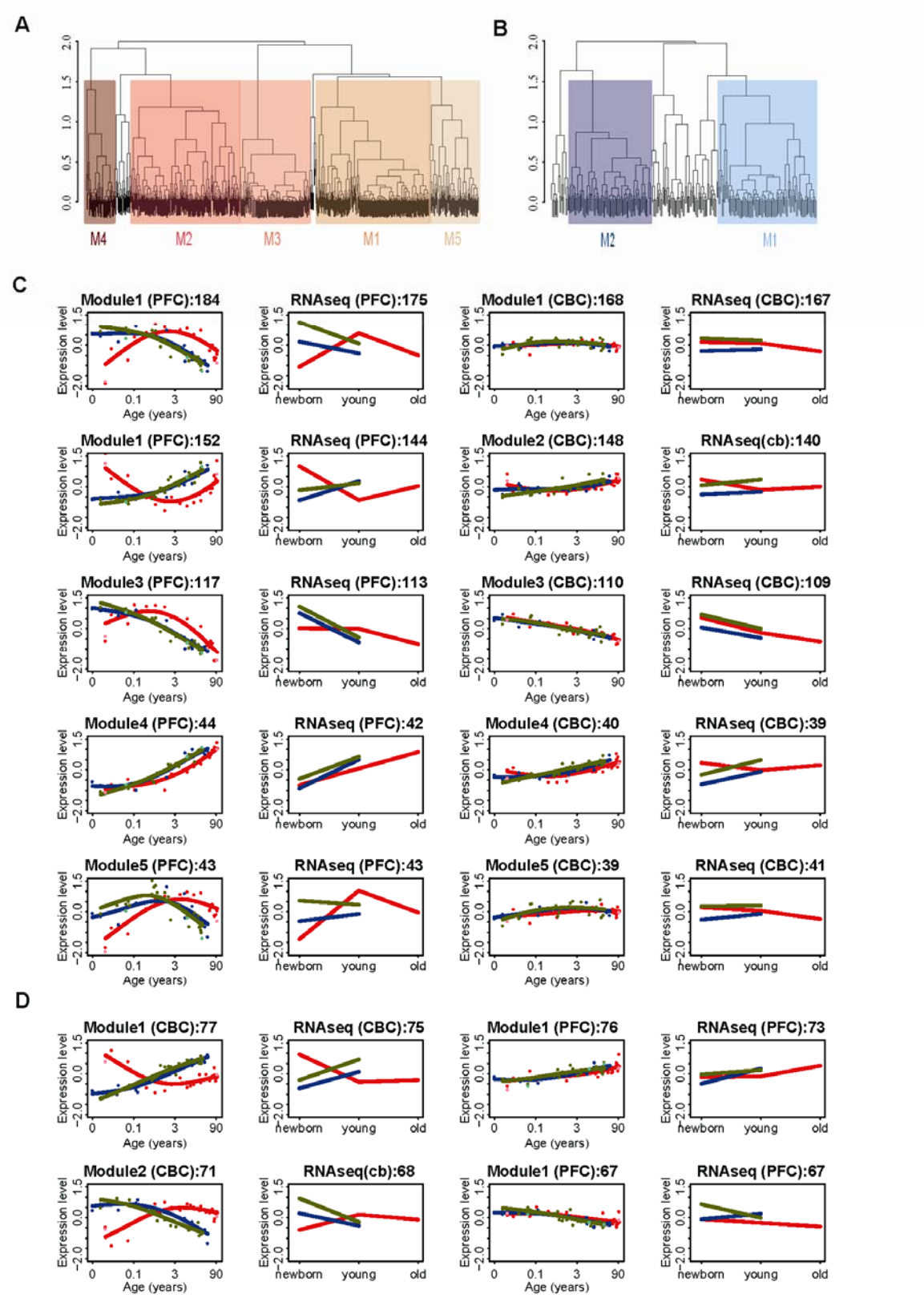
A
M4
M2
M3
M1
M5
B
M2
M1
C
Module1 (PFC):184
RNAseq (PFC):175
Module1 (CBC):168
RNAseq (CBC):167
Module1 (PFC):152
RNAseq (PFC):144
Module2 (CBC):148
RNAseq(cb):140
Module3 (PFC):117
RNAseq (PFC):113
Module3 (CBC):110
RNAseq (CBC):109
Module4 (PFC):44
RNAseq (PFC):42
Module4 (CBC):40
RNAseq (CBC):39
Module5 (PFC):43
RNAseq (PFC):43
Module5 (CBC):39
RNAseq (CBC):41
D
Module1 (CBC):77
RNAseq (CBC):75
Module1 (PFC):76
RNAseq (PFC):73
Module2 (CBC):71
RNAseq(cb):68
Module1 (PFC):67
RNAseq (PFC):67
Expression level
Age (years)
newborn
young
old

Figure S2. Human-specific modules and mean normalized expression profiles of human-specific modules in PFC and CBC.

(A-B) Hierarchical clustering dendrogram of human-specific genes in the PFC (n=702; A) and in the CBC (n=260; B).

The clustering was done using the "complete" method. As distance measure, we used the Person correlation coefficient (specifically, 1 - *r*) between expression-age spline curves of two species (based on 15 points interpolated across lifespan per species; see Supplementary Methods). The colored areas indicate co-expression gene modules, numbered according to their size. Modules with <20 members were not used in the downstream analyses.

(C-D) Mean normalized expression profiles of human-specific modules in the PFC (C) and the CBC (D). Each row represents one module. From the leftmost to rightmost panel: *(i)* the mean expression profile of module genes in the PFC/CBC measured using microarrays and *(ii)* measured using RNA-seq, *(iii)* the mean expression profile of the same genes in the other brain region (in the CBC if the module was defined based on the PFC expression profiles, and vice versa) measured using microarrays and *(iv)* measured using RNA-seq. Each point represents an individual (red-human, blue-chimpanzee, green-macaque, light red-human replicate samples, light green-macaque replicate sample), lines based on microarray measurements show fitted spline curves. The x-axis represents individuals' ages in $\log_2$ scale. Note that the identification and clustering of human-specific genes was done excluding replicates. The numbers above each panel show the number of module member genes expressed in that dataset. Expression levels shown were standardized to mean = 0 and standard deviation = 1 before clustering.

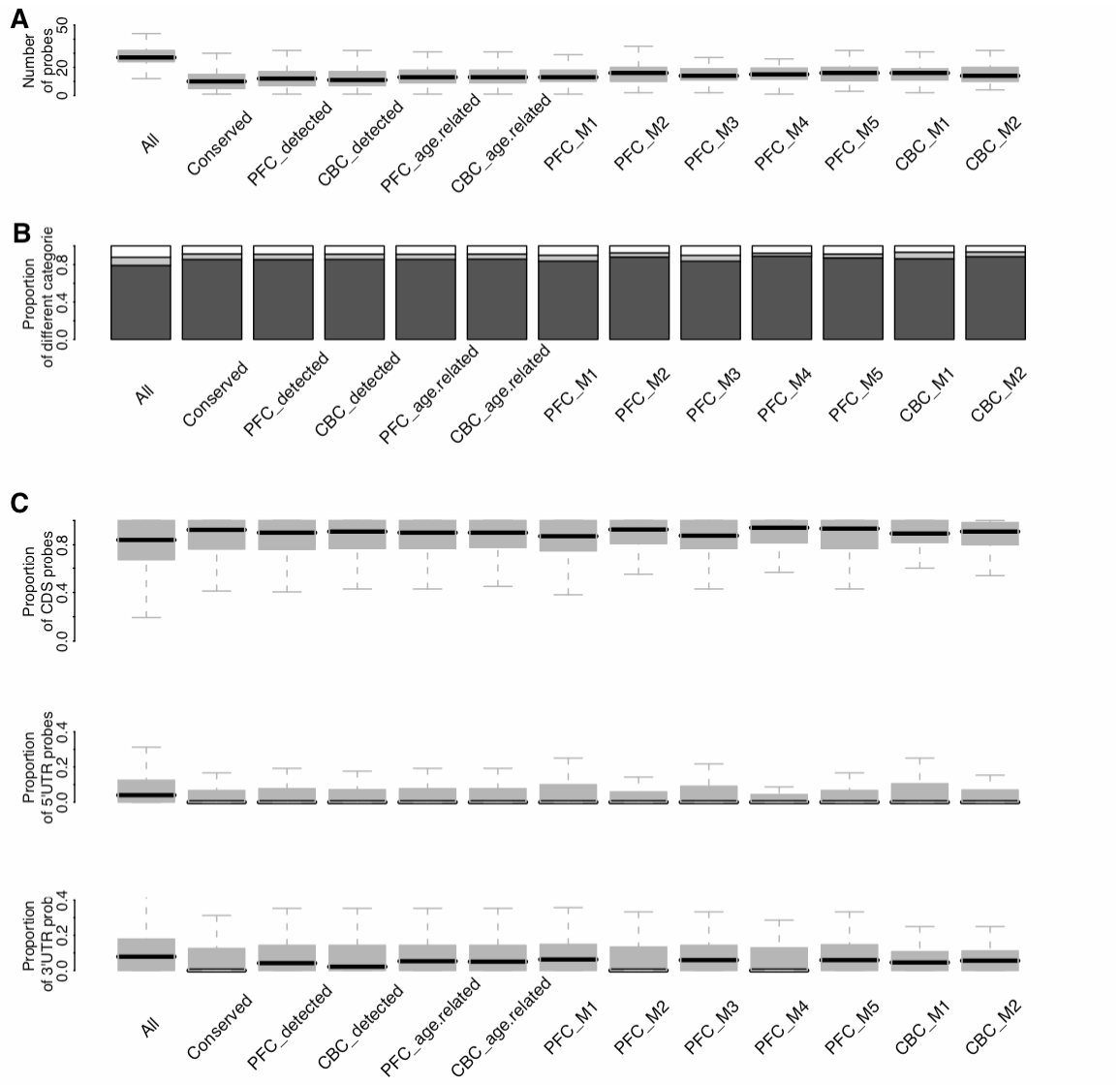

Figure S3. The distribution of numbers of probes per gene and the location of probes within each gene. (A) The distribution of numbers of probes per gene among different gene sets: "All": all genes with all probes; "Conserved": all genes with probes perfectly and uniquely matching to all three genomes; "CBC/PFC_detected": all detected genes with all detected probes in PFC or CBC; "CBC/PFC_age.related": all age-related genes in PFC or CBC; "PFC_M1-5" and "CBC_M1-2": genes in each of the 5 human PFC modules and 2 human CBC modules. Within each gene set, the proportion of probes mapped on CDS (dark gray), 5'UTR (gray), and 3'UTR (white) is shown in (B) and the

distribution of the proportion of probes falling within the three different regions per gene is shown in (C).

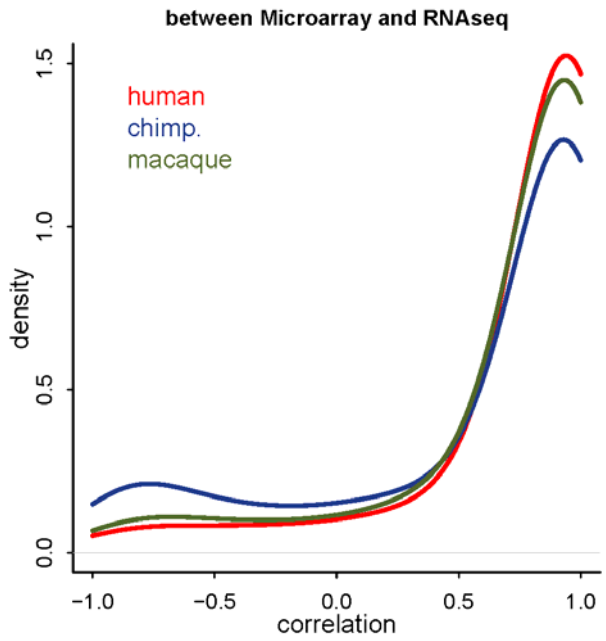

Figure S4. Correlation between age-related expression changes in PFC measured by microarrays and by RNA-seq. Pearson correlation coefficients were calculated using 15 points interpolated across expression-age cubic spline curves fitted for each species based on microarray or RNA-seq (dataset two) expression measurements (Supplementary Methods). All correlation coefficients are based on genes identified as age-related in the PFC based on microarray data and detected in the second RNA-seq dataset (N= 7,697).

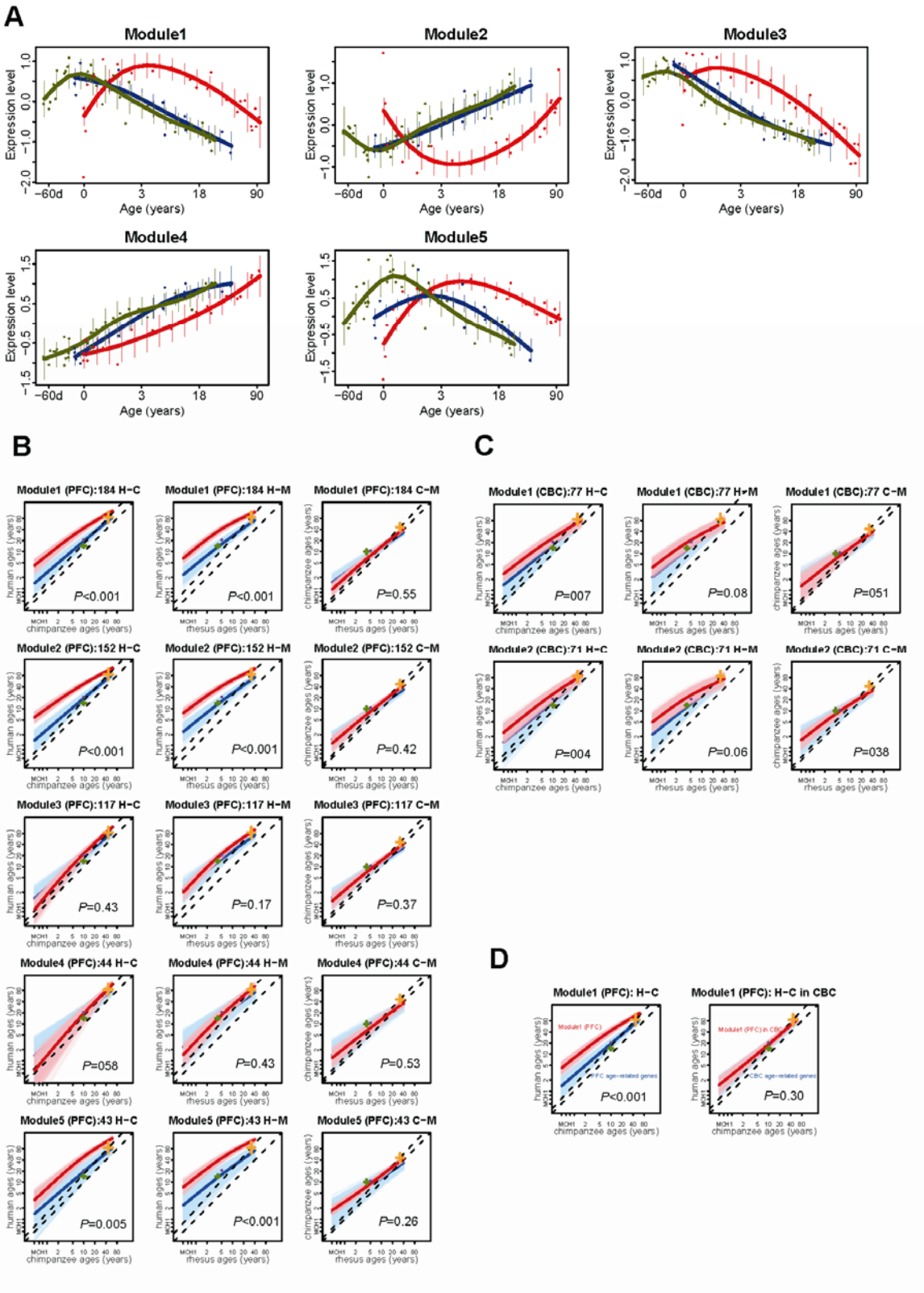
A
Module1
Module2
Module3
Module4
Module5
Expression level
Age (years)
B
C
D
Module1 (PFC):184 H−C
Module1 (PFC):184 H−M
Module1 (PFC):184 C−M
Module2 (PFC):152 H−C
Module2 (PFC):152 H−M
Module2 (PFC):152 C−M
Module3 (PFC):117 H−C
Module3 (PFC):117 H−M
Module3 (PFC):117 C−M
Module4 (PFC):44 H−C
Module4 (PFC):44 H−M
Module4 (PFC):44 C−M
Module5 (PFC):43 H−C
Module5 (PFC):43 H−M
Module5 (PFC):43 C−M
Module1 (CBC):77 H−C
Module1 (CBC):77 H−M
Module1 (CBC):77 C−M
Module2 (CBC):71 H−C
Module2 (CBC):71 H−M
Module2 (CBC):71 C−M
Module1 (PFC): H−C
Module1 (PFC): H−C in CBC
human ages (years)
chimpanzee ages (years)
rhesus ages (years)

Figure S5. Timing differences between human, chimpanzee and rhesus macaque gene expression changes in PFC and CBC.

(A) Expression profiles of human-specific PFC modules including fetal macaque samples. The points represent individuals, (red-human, blue-chimpanzee, green-macaque), The lines represent cubic spline regressions between expression and age for genes within each module. The error bars indicate standard deviation across genes in a module. The x-axis represents individuals' ages on the $\log_2$ scale.

(B-C) Timing differences between human, chimpanzee and rhesus macaque gene expression changes in PFC (B) and CBC (C). The x- and y-axes show ages in years from estimated conception event in a given pair of species (in $\log_2$ scale). The module, brain region and species information are marked above each panel: H-C: human vs. chimpanzee, H-M: human vs. macaque, C-M: chimpanzee vs. macaque. Numbers of genes in each module are shown above each plot. The solid curves show at what age gene expression levels in one species correspond to those in the other species, estimated by aligning the two species' expression profiles using the dynamic time warping algorithm (Supplementary Methods). The red curves show the mean time shift estimates for genes in each human-specific expression module in PFC or CBC. The blue curves show the mean time shift estimates for all age-related genes in the PFC or CBC (transcriptome average). The light red areas show variation in each module's time shift estimate, obtained by bootstrapping the module members 1,000 times. The light blue areas show variation in the transcriptome average's time shift estimate, obtained by sampling the same gene number as the size of the respective module out of all age-related genes (in PFC or CBC), 1,000 times. The other lines and symbols show timing of life-history landmarks: Lower and upper black dashed lines show the diagonal and the line passing through the origin and the maximum lifespan point. The symbols represent the following life-history landmarks: maximum lifespan (orange cross), female sexual maturity (green cross), eruption of last permanent dentition (purple circle) (data from (Smith et al. 1994; de Magalhães and Costa 2009)). "H", "C", "M" axes marks indicate the time of birth for human, chimpanzee and macaque, respectively. The statistical significance of the module shift against random background was show in each panel (Supplementary Methods)

(D) Timing difference between human and chimpanzee expression in the PFC and in the CBC for PFC module 1 genes. The x- and y-axes show human and chimpanzee age in years from estimated conception event (in $\log_2$ scale). The solid curves show at what age human gene expression levels correspond to those of chimpanzee in the PFC (left) and in the CBC (right). The red curves show the mean time shift estimates for PFC module 1 genes. The blue curves show the mean time shift estimates for all age-related genes (transcriptome average). The light red areas show variation in each module's time shift estimate, obtained by bootstrapping the module 1 members 1,000 times. The light blue areas show variation in the transcriptome average's time shift estimate, obtained by sampling the same gene number as the size of the module 1 out of all age-related genes (in PFC or CBC), 1,000 times. The statistical significance of the module shift against random background was show in each panel (Supplementary Methods). The other lines and symbols show timing of life-history landmarks as in (B).

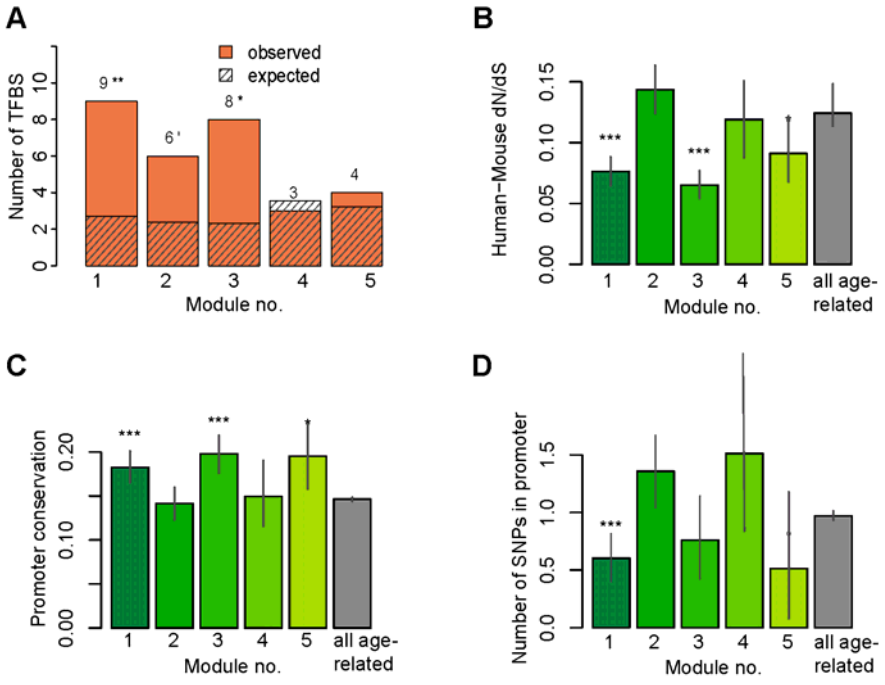

Figure S6. Sequence conservation among genes in human-specific PFC modules compared to sequence conservation among all age-related genes.

(A) Number of enriched transcription factor binding sites (TFBS) in human-specific PFC modules. Shown are the numbers of TFBS enriched among genes within each of the five PFC human-specific expression modules. The streaked bars represent the mean number of TFBS expected by chance, calculated by 1,000 random assignments of the PFC age-related genes to the five modules. The numbers and symbols above each bar show numbers of enriched TFBS among module genes (one-sided hypergeometric test, $p<0.05$), as well as the significance of the number of enriched TFBS based on the 1,000 permutations (**: $p<0.01$; *: $p<0.05$; ': $p<0.1$).

(B) Amino-acid sequence change rates (dN/dS) between mouse and human.

(C) Proximal promoter conservation levels across 18 placental mammals (PhastCons scores; (Siepel et al. 2005)), normalized by intronic mutation rate for each gene.

(D) The number of human SNPs in the proximal promoter (Perlegen "type A" SNPs (Hinds et al. 2005)). Bars indicate mean conservation among genes in a given module

(green bars) or among all 8,613 age-related PFC genes for which the conservation measure can be obtained (gray bars). Error bars indicate 95% confidence intervals estimated by bootstrapping over genes 1,000 times. The asterisks indicate significance levels based on the one-sided Wilcoxon test, comparing each module to all age-related genes (***: $p<0.001$, **: $p<0.01$, *: $p<0.05$, o: $p<0.1$).

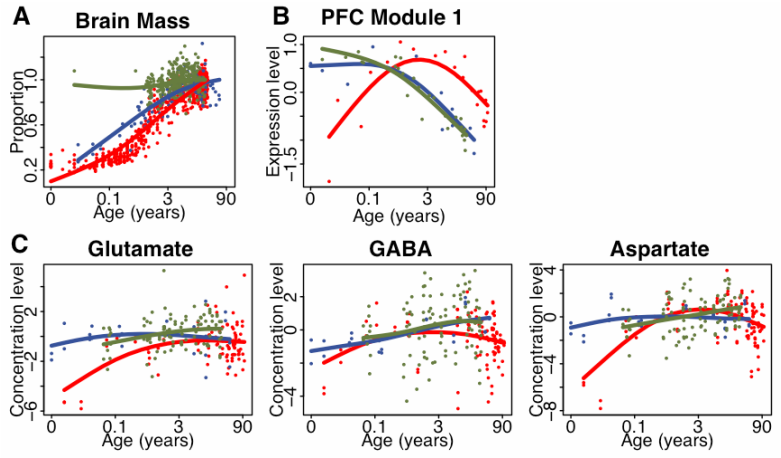

Figure S7. Association of neurotransmitter concentration changes with brain growth curves and PFC Module 1 expression profiles. Each point represents an individual (red-human, blue-chimpanzee, green-macaque). The lines show fitted spline curves. The x-axis represents individuals' ages in $\log_2$ scale. (A) Proportion of the brain mass compared to the maximum value from the fitted spline curve. The brain mass data is taken from (Leigh 2004). (B) Mean expression values of the PFC Module 1 genes. (C) Concentrations of three neurotransmitters, glutamate, GABA and aspartate, in the PFC.

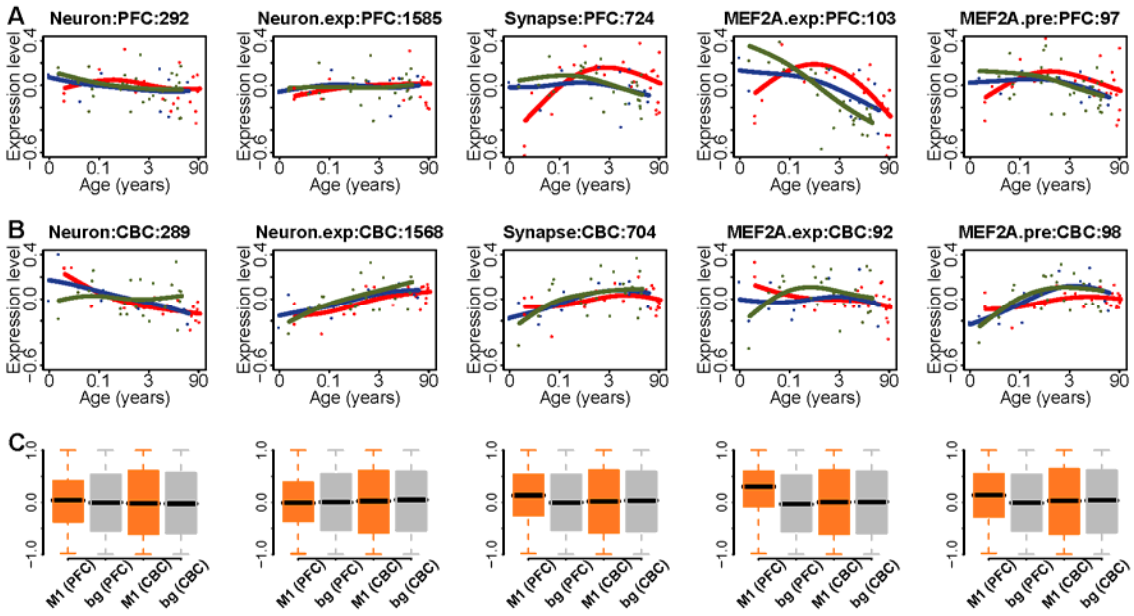

Figure S8. Mean expression profile of neuron, synapse, and MEF2A -related genes. From left to right: (i) neuron-specific ("Neuron") genes were identified by excluding synapse or axon-related genes from neuron-related genes classified according to GO annotation (Ashburner et al. 2000); (ii) genes highly expressed in neurons compared to glia ("Neuron.exp") classified based on (Cahoy et al. 2008); (iii) synapse-related genes ("Synapse") classified according to GO annotation; (iv) activity-dependent targets of MEF2 classified based on (Flavell et al. 2008) ("MEF2A.exp"); (v) predicted MEF2A targets classified based on the TRANSFAC® database ("MEF2A.pre"). (A-B) Each point represents an individual (red-human, blue-chimpanzee, green-macaque), lines based on microarray measurements show fitted spline curves. The x-axis represents individuals' ages on a $\log_2$ scale. The numbers above each panel show the number of each gene set expressed in each brain region. Expression levels were standardized to mean=0 and standard deviation=1 before clustering. (C) Distribution of Pearson correlation coefficients between age-related expression changes of genes in each gene set and each gene in the PFC Module 1 ("M1"). Correlations to all other age-related genes are shown as a background ("bg").

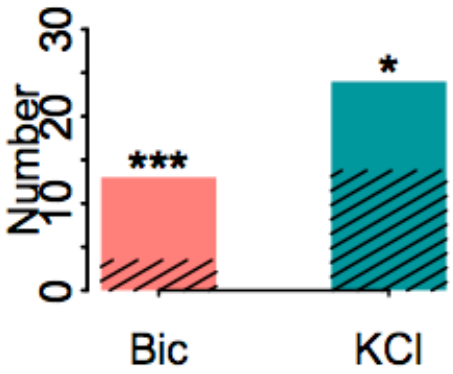

Figure S9. Numbers of PFC Module 1 genes that are up-regulated in neuronal activation.

The streaked bars represent numbers of Module 1 genes expected to be up-regulated by chance. Fisher-exact test was used to calculate the significance of overrepresentation of Module 1 genes among genes up-regulated by Bic or KCl (***: $p<0.001$, *: $p<0.05$).

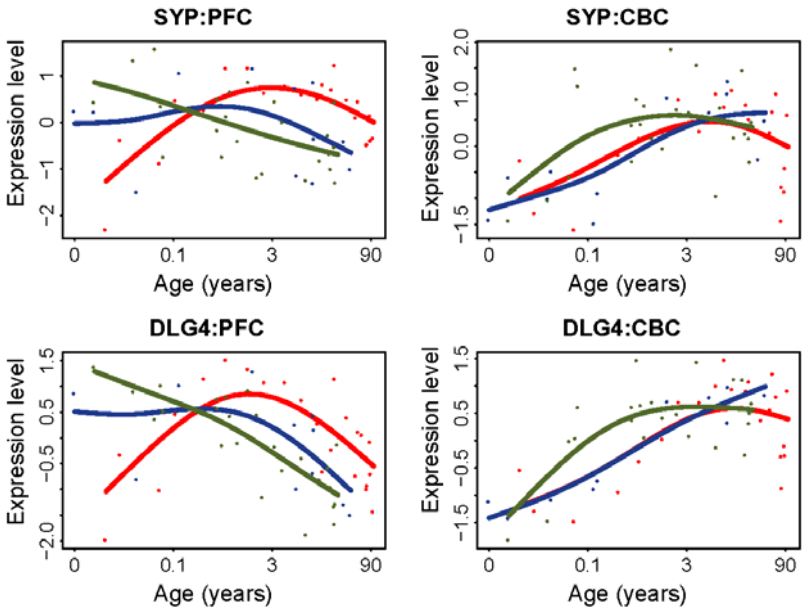

Figure S10. Expression profiles of *SYP* and *DLG4* in PFC and CBC. The points represent individuals, colors represent species: red-humans, blue-chimpanzees, and green-macaques. The lines represent cubic spline regressions between expression and age for each gene. The x-axis represents individuals' ages in $\log_2$ scale.

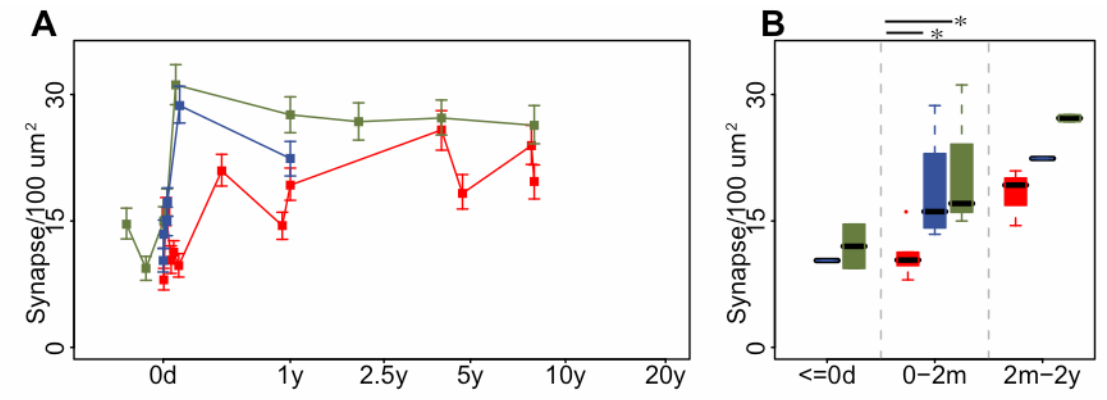

Figure S11. Synaptic density change during human, chimpanzee, and macaque PFC development. The synapses counted by A.O. are shown in this figure and counted by X.J. -- in Figure 7. (A) Mean synaptic density per 100 μm^2 measured in the PFC of humans (red), chimpanzees (blue) and rhesus macaques (green) at different age. The error bars show 95% confidence intervals obtained by bootstrapping synaptic density values within samples 1,000 times. (B) Statistical analysis of synaptic density in three age groups. The distribution of mean synaptic density from samples within each age group is shown in a boxplot. Within the age range of 0-2 months, PFC synaptic density in humans is significantly lower than in both chimpanzees and macaques (one-sided Wilcoxon test, p=0.032 in human-chimpanzee comparison and p=0.036 in human-macaque comparison), while there was no significant synaptic density difference between chimpanzees and macaques (p>0.1). Sample numbers were not sufficient to estimate statistical significance for the other two age intervals.

Supplementary tables

Table S1. Sample information

Species	Experiments	Ages		Sex	PMI	RIN		Batch Information					Cause of death
								Microarray		RNA-seq (dataset1)		RNA-seq (dataset2)	
		Year	Day			PFC	CBC	PFC	CBC	PFC	CBC	PFC	
Homo sapiens	a;b;c;d;f	0	2	m	3	8	7.2	1;2	1;2	newborn	newborn	1	complications of prematurity
Homo sapiens	a;b;c;d;f	0	4	m	5	8.8	7.8	1	1	newborn	newborn	1	congenital heart defect
Homo sapiens	c;d	0	15	f	3	9.1	8.3			newborn	newborn		NA
Homo sapiens	a;b;c;d;f	0	19	f	14	7.1	7.5	2	2	newborn	newborn	1	pneumonia associated with meconium aspiration
Homo sapiens	a;c;d;f	0	34	m	7	7.9	6.9	1		newborn	newborn	1	idiopathic pulmonary hemorrhage
Homo sapiens	a;b;f	0	94	m	12	7.7	7.3	2	2			1	bronchopneumania
Homo sapiens	b	0	196	f	24	7.8	7.9		1				sudden infant death syndrome
Homo sapiens	a;f	0	204	m	6	8.4	7.2	1				1	sudden infant death syndrome
Homo sapiens	a;b;f	1	78	m	19	7.6	7.4	2	2			2	Asthma
Homo sapiens	a;b;f	2	57	f	21	7.5	7.5	2	2			2	acute myocarditis
Homo sapiens	a;b	4	170	f	21	7.7	7.9	2	2				lymphocytic myocarditis
Homo sapiens	a;b	8	2	m	5	8.3	8.1	1	1				cardiac arrhythmia
Homo sapiens	b	10	262	f	22	-	7.6		2				accident, hanging
Homo sapiens	a;b;f	13	360	m	13	8.3	8.1	1	1			2	hanging
Homo sapiens	c;d	16	125	m	16	8.3	8.2			young	young		NA
Homo sapiens	a;c;d	16	271	m	15	9.1	7.6	2		young	young		accident, drowning
Homo sapiens	c;d	18	38	m	6	7.2	6.8			young	young		NA
Homo sapiens	c;d	19	69	f	7	6.5	7			young	young		NA
Homo sapiens	c;d	20	255	m	12	8.7	8.9			young	young		Accident, lightning striking
Homo sapiens	a;b	22	334	m	4	7.3	7.6	2	2				ASCVD
Homo sapiens	a;b;f	25	152	m	19	9.2	8.9	1	1			2	Asthma
Homo sapiens	a;b	39	74	m	12	7.9	7.8	2	2				HASCVD
Homo sapiens	a;b;f	53	112	m	17	8.3	8.5	1	1			2	ASCVD
Homo sapiens	a;b	58	34	m	9	8.4	8.6	2	2				HASCVD
Homo sapiens	a;b;f	66	0	m	10	8.6	8.7	1	1			2	ruptured abdominal aneurysm aorta
Homo sapiens	a;b	78	222	f	3	8	7.8	2	2				natural
Homo sapiens	a;b	80	0	m	7	8.6	8.2	1	1				ventricular fibrillation
Homo sapiens	a;b;c;d;f	88	0	m	7	7.7	7.3	1	1	old	old	2	euthanasia
Homo sapiens	c;d	90	0	f	6	7.8	7.6			old	old		NA
Homo sapiens	a;b	90	0	f	4	7.8	7.9	2	2				natural
Homo sapiens	c;d	96	0	m	6	7.3	7.1			old	old		NA
Homo sapiens	c;d	97	0	f	5	8.4	8			old	old		NA
Homo sapiens	a;b;c;d;f	98	0	m	9	7.3	7.5	1;2	1;2	old	old	2	cardiac tamponade due to bleeding from aorta fissure
Pan troglodytes	a;b;c;d;f	0	0	m	-	7.5	7.4	1	1	newborn	newborn	2	stillbirth
Pan troglodytes	a;b;c;d;f	0	1	f	-	7.2	7.7	1	1	newborn	newborn	2	stillbirth
Pan troglodytes	b;f	0	7	m	-	-	4.2		1			2	NA
Pan troglodytes	a;b;c;d;f	0	8	m	-	7.7	6.4	1	1	newborn	newborn	1	NA
Pan troglodytes	a;b;c;d;f	0	39	m	-	7	6.6	1	1	newborn	newborn	1	NA

Pan troglodytes	b;c;d;f	0	45	f	-	-	5.2		1	newborn	newborn	2	NA
Pan troglodytes	a;b;f	1	160	f	-	7	6.3	1	1			2	NA
Pan troglodytes	a;b;c;d;f	6	123	f	-	6.4	6.1	1	1	young	young	1	NA
Pan troglodytes	a	6	257	f	-	8.6	-	1					NA
Pan troglodytes	f	8	0	f	-	8	-					2	NA
Pan troglodytes	a;b;c;d;f	11	346	m	-	6.5	7.5	1	1	young	young	1	NA
Pan troglodytes	a;b;c;d;f	12	35	m	-	7.5	7.9	1	1	young	young	1	chocked after anestesia
Pan troglodytes	a	12	120	m	-	5.9	-	1					euthanasia
Pan troglodytes	f	27	0	f	-	8.5	-					2	NA
Pan troglodytes	a;b;c;d;f	35	9	m	-	6.3	7.4	1	1	young	young	1	NA
Pan troglodytes	a;b;c;d;f	44	71	f	-	6	7.4	1	1	young	young	1	anemia (clinical)
Macaca mulatta	c;d	0	1	m	0	8.3	6.7			newborn	newborn		-
Macaca mulatta	c;d;f	0	1	m	0	8.6	8.6			newborn	newborn	1	-
Macaca mulatta	a;b;c;d;f	0	1	m	0	8.9	9.1	2	2	newborn	newborn	1	-
Macaca mulatta	c;d	0	2	f	0	8.3	8.5			newborn	newborn		-
Macaca mulatta	a;b;c;d;f	0	7	m	0	8.7	9.9	2	2	newborn	newborn	1	-
Macaca mulatta	a;b;f	0	16	m	0	9.1	9.8	1;2	1			1	-
Macaca mulatta	a;b	0	20	m	0	9.9	9.7	1	1				-
Macaca mulatta	a;b;f	0	22	m	0	9.3	9.5	2	2			1	-
Macaca mulatta	a;b	0	151	m	0	9.1	9	2	2				-
Macaca mulatta	a;b;f	0	153	m	0	9.8	9	1	1			1	-
Macaca mulatta	a;b	0	179	m	0	9.5	8.9	2	2				-
Macaca mulatta	a;b;f	0	207	m	0	9.7	9	1	1			1	-
Macaca mulatta	a;b	0	237	m	0	9	8.9	2	2				-
Macaca mulatta	a;b;f	0	310	m	0	9.5	7.8	1	1			2	-
Macaca mulatta	a;b	1	84	m	0	9.2	8.8	2	2				-
Macaca mulatta	a;b	1	242	m	0	8.6	8.2	2	2				-
Macaca mulatta	a;b;f	2	9	m	0	9	9.8	1	1			2	-
Macaca mulatta	a;b	3	40	m	0	8.7	9.2	2	2				-
Macaca mulatta	a;b;f	4	27	m	0	9	9.7	1	1			2	-
Macaca mulatta	a;b;c;d	8	16	m	0	8.7	9.1	2	2	young	young		-
Macaca mulatta	a;b;c;d;f	9	104	m	0	9	8.2	1	1	young	young	2	-
Macaca mulatta	c;d	10	328	m	0	8.3	9.2			young	young		-
Macaca mulatta	c;d	11	346	m	0	9	8.5			young	young		-
Macaca mulatta	c;d	14	21	m	0	9.5	8.2			young	young		-
Macaca mulatta	a;b;f	15	3	m	0	8.1	8.2	2	2			2	-
Macaca mulatta	a;b	20	91	m	0	9	8.6	1	1				-
Macaca mulatta	a	21	8	m	0	8.7	-	2					-
Macaca mulatta	a;b;f	22	74	m	0	8.5	8.9	1	1			2	-
Macaca mulatta	a	25	0	f	5	8.8	-	2					-
Macaca mulatta	a;b	25	166	f	0	8.2	7.9	2	2				-
Macaca mulatta	a;b;f	26	28	m	0	8.8	9.1	1	1			2	-
Macaca mulatta	a;b;f	28	0	f	0	7.8	9	1;2	1			2	-
Macaca mulatta	e	0	-72	m	0	9	-	-	-	-	-		-
Macaca mulatta	e	0	-57	m	0	9.1	-	-	-	-	-		-
Macaca mulatta	e	0	-53	m	0	9.1	-	-	-	-	-		-
Macaca mulatta	e	0	-42	m	0	8.8	-	-	-	-	-		-
Macaca mulatta	e	0	-35	m	0	8.7	-	-	-	-	-		-
Macaca mulatta	e	0	-30	m	0	8.6	-	-	-	-	-		-

Macaca mulatta	e	0	1	m	0	8.8	-	-	-	-	-	-
Macaca mulatta	e	0	24	m	0	8.1	-	-	-	-	-	-
Macaca mulatta	e	0	182	m	0	8.7	-	-	-	-	-	-
Macaca mulatta	e	0	353	m	0	8.6	-	-	-	-	-	-
Macaca mulatta	e	1	114	m	0	8.2	-	-	-	-	-	-
Macaca mulatta	e	2	101	m	0	8.6	-	-	-	-	-	-

a: RNA microarray for postnatal PFC dataset;

b: RNA microarray for postnatal CBC dataset;

c: RNA-seq for pooled PFC dataset1;

d: RNA-seq for pooled CBC dataset1;

e: RNA microarray for macaque prenatal/neonatal PFC dataset;

f: RNA-seq for PFC dataset2

RIN: RNA integrity values

PMI: Postmortem intervals in hours

ASCVD: arteriosclerotic cardiovascular disease;

HASCVD: hypertensive arteriosclerotic cardiovascular disease.

Table S2. Numbers of detected genes.

Platform	PFC	CBC
RNA Microarray	12,447	12,853
RNAseq Dataset 1	15,183	14,941
RNAseq Dataset 2	14,149	-

Table S3. FDR estimates for the age-test and species difference-test

Dataset	Region	p-value	Age-test						
			Human		Chimpanzee		Macaque		HCM*
			gene no.	FDR	gene no.	FDR	gene no.	FDR	gene no.
Full dataset	PFC	p<0.05	8904	14.4%	5292	24.7%	6878	16.7%	10590
		p<0.01	**7071**	**3.5%**	**3257**	**8.4%**	**4973**	**4.4%**	**8613**
		p<0.001	5022	0.5%	1603	1.6%	3406	0.6%	6234
	CBC	p<0.05	7406	15.1%	5868	21.9%	7038	17.1%	10372
		p<0.01	**5440**	**3.9%**	**3609**	**7.4%**	**5154**	**4.6%**	**7988**
		p<0.001	3609	0.6%	1802	1.6%	3583	0.7%	5526
Stage-of-life matched subset	PFC	**p<0.05**	**6424**	**17.7%**	**4984**	**26.5%**	**5397**	**23.3%**	**2308**
		p<0.01	3925	5.9%	2915	9.6%	3318	8.2%	1091
		p<0.001	1766	1.4%	1275	2.3%	1644	1.9%	400
	CBC	**p<0.05**	**5151**	**24.6%**	**5266**	**24.9%**	**5869**	**22.0%**	**2171**
		p<0.01	2943	9.2%	3031	9.0%	3679	7.6%	1031
		p<0.001	1208	2.5%	1357	2.1%	1782	1.9%	316
Chronological matched subset	PFC	**p<0.05**	**6430**	**19.4%**	**4984**	**25.0%**	**5044**	**25.8%**	**2092**
		p<0.01	3831	6.5%	2915	9.0%	3040	9.4%	945
		p<0.001	1674	1.7%	1275	2.2%	1405	2.1%	321
	CBC	**p<0.05**	**5484**	**23.5%**	**5266**	**26.6%**	**5840**	**21.7%**	**2234**
		p<0.01	3218	8.4%	3031	9.9%	3626	7.8%	1075
		p<0.001	1390	2.1%	1357	2.3%	1799	1.9%	343

Dataset	Region	p-value	Species difference-test						
			Human-Chimp.		Human-Macaque		Chimp.-Macaque		HCM*
			gene no.	FDR	gene no.	FDR	gene no.	FDR	gene no.
Full dataset	PFC	p<0.05	2539	38.4%	4452	18.0%	1199	60.7%	5405
		p<0.01	**1238**	**20.4%**	**2797**	**7.0%**	**486**	**35.0%**	**3407**
		p<0.001	445	6.7%	1508	1.7%	165	11.5%	1788
	CBC	p<0.05	1522	51.4%	3776	23.2%	1839	40.6%	4770
		p<0.01	**637**	**30.1%**	**2221**	**10.9%**	**906**	**20.8%**	**2862**
		p<0.001	225	12.0%	999	3.9%	391	6.9%	1321
Stage-of-life matched subset	PFC	p<0.05	363	59.0%	518	44.0%	210	93.8%	676
		p<0.01	**202**	**25.2%**	**305**	**18.9%**	**109**	**42.2%**	**393**
		p<0.001	61	9.8%	147	5.4%	40	12.5%	184
	CBC	p<0.05	146	110.3%	288	77.8%	217	91.2%	410
		p<0.01	**66**	**59.8%**	**191**	**34.0%**	**136**	**39.0%**	**242**
		p<0.001	22	22.7%	82	8.5%	69	10.1%	116
Chronological matched subset	PFC	p<0.05	337	55.0%	394	57.5%	181	87.8%	545
		p<0.01	**158**	**29.7%**	**248**	**26.4%**	**86**	**46.5%**	**312**
		p<0.001	43	11.6%	119	8.0%	38	13.2%	156
	CBC	p<0.05	128	105.9%	301	74.4%	223	92.8%	405
		p<0.01	**72**	**45.8%**	**196**	**36.2%**	**135**	**41.9%**	**245**
		p<0.001	20	20.0%	106	11.3%	69	11.6%	137

Figures in bold indicate the FDR levels at the cutoffs reported in the main text.
In the Full dataset, genes with p<0.01 for the age-test were considered as age-related genes.
The union of age-related genes among species was then subjected to the differential expression test.
In both 10 samples datasets, genes with p<0.05 for age-test were considered as age-related genes.

The intersection of age related genes among species was then subjected to the differential expression test.

*HCM: For age-test, the number of genes passing the p-value cutoff in at least one species (Full dataset) or in all species (both 10 samples datasets).
For the species difference test, the number of genes passing the p-value cutoff in at least one species.

Table S4. Overlap between identified species-specific gene sets.

1.Among species

Species	Dataset	PFC			CBC		
		Full dataset	Stage-of-life matched subset	Chronological matched subset	Full dataset	Stage-of-life matched subset	Chronological matched subset
Human	Full dataset	702	98 (80%)	91(83%)	260	31 (89%)	41(89%)
	Stage-of-life matched subset	98 (80%)	123	70(64%)	31 (89%)	35	23(66%)
	Chronological matched subset	91(83%)	70(64%)	110	41(89%)	23(66%)	46
Chimpanzee	Full dataset	55	5 (36%)	3(33%)	82	7 (58%)	6(67%)
	Stage-of-life matched subset	5 (36%)	14	6(67%)	7 (58%)	12	4(44%)
	Chronological matched subset	3(33%)	6(67%)	9	6(67%)	4(44%)	9
Macaque	Full dataset	259	38 (60%)	35(66%)	460	80 (80%)	76(75%)
	Stage-of-life matched subset	38 (60%)	64	30(57%)	80 (80%)	100	61(61%)
	Chronological matched subset	35(66%)	30(57%)	53	76(75%)	61(61%)	101

2.Between PFC and CBC

Species	Region	Full dataset		Stage-of-life matched subset		Chronological matched subset	
		PFC	CBC	PFC	CBC	PFC	CBC
Human	PFC	702	32	123	1	110	0
	CBC	32	260	1	35	0	46
Chimpanzee	PFC	55	1	14	0	9	0
	CBC	1	82	0	12	0	9
Macaque	PFC	259	12	64	0	53	0
	CBC	12	460	0	100	0	101

Table S5. Genes with human-specific expression profiles.

Region	Module	Ensemble Gene ID	HGNC ID	Description
PFC	Module1	ENSG00000177181	*RIMKLA*	Ribosomal protein S6 modification-like protein A
PFC	Module1	ENSG00000173126	*PCP4L1*	Purkinje cell protein 4 like 1
PFC	Module1	ENSG00000116584	*ARHGEF2*	Rho guanine nucleotide exchange factor 2
PFC	Module1	ENSG00000185737	*NRG3*	Pro-neuregulin-3, membrane-bound isoform Precursor
PFC	Module1	ENSG00000154478	*GPR26*	Probable G-protein coupled receptor 26
PFC	Module1	ENSG00000107758	*PPP3CB*	Serine/threonine-protein phosphatase 2B catalytic subunit beta isoform
PFC	Module1	ENSG00000169129	*AFAP1L2*	Actin filament-associated protein 1-like 2
PFC	Module1	ENSG00000121653	*MAPK8IP1*	C-jun-amino-terminal kinase-interacting protein 1
PFC	Module1	ENSG00000149177	*PTPRJ*	Receptor-type tyrosine-protein phosphatase eta Precursor
PFC	Module1	ENSG00000152578	*GRIA4*	Glutamate receptor 4 Precursor
PFC	Module1	ENSG00000137486	*ARRB1*	Beta-arrestin-1
PFC	Module1	ENSG00000183715	_	Opioid-binding protein/cell adhesion molecule Precursor
PFC	Module1	ENSG00000139364	*TMEM132B*	Transmembrane protein 132B
PFC	Module1	ENSG00000060140	*STYK1*	Tyrosine-protein kinase STYK1
PFC	Module1	ENSG00000151229	*SLC2A13*	Proton myo-inositol cotransporter
PFC	Module1	ENSG00000135439	*AGAP2*	Arf-GAP, GTPase, ANK repeat and PH domain-containing protein 2
PFC	Module1	ENSG00000197991	*PCDH20*	Protocadherin-20 Precursor
PFC	Module1	ENSG00000100884	*CPNE6*	Copine-6
PFC	Module1	ENSG00000139998	*RAB15*	Ras-related protein Rab-15
PFC	Module1	ENSG00000183092	*BEGAIN*	Brain-enriched guanylate kinase-associated protein
PFC	Module1	ENSG00000186297	*GABRA5*	Gamma-aminobutyric acid receptor subunit alpha-5 Precursor
PFC	Module1	ENSG00000169926	*KLF13*	Krueppel-like factor 13
PFC	Module1	ENSG00000198838	*RYR3*	Ryanodine receptor 3
PFC	Module1	ENSG00000166557	*TMED3*	Transmembrane emp24 domain-containing protein 3 Precursor
PFC	Module1	ENSG00000140538	*NTRK3*	NT-3 growth factor receptor Precursor
PFC	Module1	ENSG00000103528	*SYT17*	Synaptotagmin-17
PFC	Module1	ENSG00000166501	*PRKCB*	Protein kinase C beta type
PFC	Module1	ENSG00000006116	*CACNG3*	Voltage-dependent calcium channel gamma-3 subunit
PFC	Module1	ENSG00000132359	*GARNL4*	Rap1 GTPase-activating protein 2
PFC	Module1	ENSG00000091622	*PITPNM3*	Membrane-associated phosphatidylinositol transfer protein 3
PFC	Module1	ENSG00000154975	*CA10*	Carbonic anhydrase-related protein 10
PFC	Module1	ENSG00000177511	*ST8SIA3*	Sia-alpha-2,3-Gal-beta-1,4-GlcNAc-R:alpha 2,8-sialyltransferase
PFC	Module1	ENSG00000206052	*DOK6*	Docking protein 6
PFC	Module1	ENSG00000136531	*SCN2A*	Sodium channel protein type 2 subunit alpha
PFC	Module1	ENSG00000138028	*CGREF1*	Cell growth regulator with EF hand domain protein 1
PFC	Module1	ENSG00000198369	*SPRED2*	Sprouty-related, EVH1 domain-containing protein 2
PFC	Module1	ENSG00000168702	*LRP1B*	Low-density lipoprotein receptor-related protein 1B Precursor
PFC	Module1	ENSG00000198586	*TLK1*	Serine/threonine-protein kinase tousled-like 1
PFC	Module1	ENSG00000125851	*PCSK2*	Neuroendocrine convertase 2 Precursor
PFC	Module1	ENSG00000166913	*YWHAB*	14-3-3 protein beta/alpha
PFC	Module1	ENSG00000089123	*TASP1*	Threonine aspartase 1
PFC	Module1	ENSG00000157103	*SLC6A1*	Sodium- and chloride-dependent GABA transporter 1

PFC	Module1	ENSG00000170011	*MYRIP*	Rab effector MyRIP
PFC	Module1	ENSG00000175161	*CADM2*	Cell adhesion molecule 2 Precursor
PFC	Module1	ENSG00000184307	*ZDHHC23*	Probable palmitoyltransferase ZDHHC23
PFC	Module1	ENSG00000197584	*KCNMB2*	Calcium-activated potassium channel subunit beta-2
PFC	Module1	ENSG00000175182	*FAM131A*	Protein FAM131A Precursor
PFC	Module1	ENSG00000163491	*NEK10*	Serine/threonine-protein kinase Nek10
PFC	Module1	ENSG00000163288	*GABRB1*	Gamma-aminobutyric acid receptor subunit beta-1 Precursor
PFC	Module1	ENSG00000138759	*FRAS1*	Extracellular matrix protein FRAS1 Precursor
PFC	Module1	ENSG00000109670	*FBXW7*	F-box/WD repeat-containing protein 7
PFC	Module1	ENSG00000169271	*HSPB3*	Heat shock protein beta-3
PFC	Module1	ENSG00000152932	*RAB3C*	Ras-related protein Rab-3C
PFC	Module1	ENSG00000152495	*CAMK4*	Calcium/calmodulin-dependent protein kinase type IV
PFC	Module1	ENSG00000123643	*SLC36A1*	Proton-coupled amino acid transporter 1
PFC	Module1	ENSG00000154162	*CDH12*	Cadherin-12 Precursor
PFC	Module1	ENSG00000171617	*ENC1*	Ectoderm-neural cortex protein 1
PFC	Module1	ENSG00000129625	*REEP5*	Receptor expression-enhancing protein 5
PFC	Module1	ENSG00000135298	*BAI3*	Brain-specific angiogenesis inhibitor 3 Precursor
PFC	Module1	ENSG00000112379	*KIAA1244*	Brefeldin A-inhibited guanine nucleotide-exchange protein 3
PFC	Module1	ENSG00000175048	*ZDHHC14*	Probable palmitoyltransferase ZDHHC14
PFC	Module1	ENSG00000132434	*LANCL2*	LanC-like protein 2
PFC	Module1	ENSG00000006128	*TAC1*	Protachykinin-1 Precursor
PFC	Module1	ENSG00000136297	*MMD2*	Monocyte to macrophage differentiation factor 2
PFC	Module1	ENSG00000186472	*PCLO*	piccolo isoform 1
PFC	Module1	ENSG00000155093	*PTPRN2*	Receptor-type tyrosine-protein phosphatase N2 Precursor
PFC	Module1	ENSG00000185053	*SGCZ*	Zeta-sarcoglycan
PFC	Module1	ENSG00000164794	*KCNV1*	Potassium voltage-gated channel subfamily V member 1
PFC	Module1	ENSG00000119125	*GDA*	Guanine deaminase
PFC	Module1	ENSG00000164946	*FREM1*	FRAS1-related extracellular matrix protein 1 Precursor
PFC	Module1	ENSG00000136928	*GABBR2*	Gamma-aminobutyric acid type B receptor subunit 2 Precursor
PFC	Module1	ENSG00000078725	*DBC1*	Deleted in bladder cancer protein 1 Precursor
PFC	Module1	ENSG00000008086	*CDKL5*	Cyclin-dependent kinase-like 5
PFC	Module1	ENSG00000200473		5S ribosomal RNA
PFC	Module1	ENSG00000162551	*ALPL*	Alkaline phosphatase, tissue-nonspecific isozyme Precursor
PFC	Module1	ENSG00000121905	*HPCA*	Neuron-specific calcium-binding protein hippocalcin
PFC	Module1	ENSG00000117410	*ATP6V0B*	V-type proton ATPase 21 kDa proteolipid subunit
PFC	Module1	ENSG00000162409	*PRKAA2*	5'-AMP-activated protein kinase catalytic subunit alpha-2
PFC	Module1	ENSG00000162631	*NTNG1*	Netrin-G1 Precursor
PFC	Module1	ENSG00000162736	*NCSTN*	Nicastrin Precursor
PFC	Module1	ENSG00000198797	*FAM5B*	Protein FAM5B Precursor
PFC	Module1	ENSG00000133019	*CHRM3*	Muscarinic acetylcholine receptor M3
PFC	Module1	ENSG00000171603	*CLSTN1*	Calsyntenin-1 Precursor
PFC	Module1	ENSG00000121753	*BAI2*	Brain-specific angiogenesis inhibitor 2 Precursor
PFC	Module1	ENSG00000186094	*AGBL4*	Cytosolic carboxypeptidase 6
PFC	Module1	ENSG00000154511	*FAM69A*	Protein FAM69A
PFC	Module1	ENSG00000116991	*SIPA1L2*	Signal-induced proliferation-associated 1-like protein 2

PFC	Module1	ENSG00000189181	*OR14I1*	Olfactory receptor 14I1
PFC	Module1	ENSG00000107862	*GBF1*	Golgi-specific brefeldin A-resistance guanine nucleotide exchange factor 1
PFC	Module1	ENSG00000065621	*GSTO2*	Glutathione S-transferase omega-2
PFC	Module1	ENSG00000156395	*SORCS3*	VPS10 domain-containing receptor SorCS3 Precursor
PFC	Module1	ENSG00000151023	*ENKUR*	Enkurin
PFC	Module1	ENSG00000198915	*RASGEF1A*	Ras-GEF domain-containing family member 1A
PFC	Module1	ENSG00000176769	*TCERG1L*	Transcription elongation regulator 1-like protein
PFC	Module1	ENSG00000110514	*MADD*	MAP kinase-activating death domain protein
PFC	Module1	ENSG00000072518	*MARK2*	Serine/threonine-protein kinase MARK2
PFC	Module1	ENSG00000149577	*SIDT2*	SID1 transmembrane family member 2 Precursor
PFC	Module1	ENSG00000176697	*BDNF*	Brain-derived neurotrophic factor Precursor
PFC	Module1	ENSG00000168539	*CHRM1*	Muscarinic acetylcholine receptor M1
PFC	Module1	ENSG00000172531	*PPP1CA*	Serine/threonine-protein phosphatase PP1-alpha catalytic subunit
PFC	Module1	ENSG00000186642	*PDE2A*	cGMP-dependent 3',5'-cyclic phosphodiesterase
PFC	Module1	ENSG00000135519	*KCNH3*	Potassium voltage-gated channel subfamily H member 3
PFC	Module1	ENSG00000174437	*ATP2A2*	Sarcoplasmic/endoplasmic reticulum calcium ATPase 2
PFC	Module1	ENSG00000151176	*PLBD2*	Putative phospholipase B-like 2 Precursor
PFC	Module1	ENSG00000139645	*ANKRD52*	Serine/threonine-protein phosphatase 6 regulatory ankyrin repeat subunit C
PFC	Module1	ENSG00000153233	*PTPRR*	Receptor-type tyrosine-protein phosphatase R Precursor
PFC	Module1	ENSG00000139318	*DUSP6*	Dual specificity protein phosphatase 6
PFC	Module1	ENSG00000111344	*RASAL1*	RasGAP-activating-like protein 1
PFC	Module1	ENSG00000179841	*AKAP5*	A-kinase anchor protein 5
PFC	Module1	ENSG00000021645	*NRXN3*	Neurexin-3-beta Precursor
PFC	Module1	ENSG00000100505	*TRIM9*	Tripartite motif-containing protein 9
PFC	Module1	ENSG00000166068	*SPRED1*	Sprouty-related, EVH1 domain-containing protein 1
PFC	Module1	ENSG00000137766	*UNC13C*	Protein unc-13 homolog C
PFC	Module1	ENSG00000068305	*MEF2A*	Myocyte-specific enhancer factor 2A
PFC	Module1	ENSG00000058335	*RASGRF1*	Ras-specific guanine nucleotide-releasing factor 1
PFC	Module1	ENSG00000102879	*CORO1A*	Coronin-1A
PFC	Module1	ENSG00000157368	*IL34*	Interleukin-34 Precursor
PFC	Module1	ENSG00000169181	*GSG1L*	Germ cell-specific gene 1-like protein
PFC	Module1	ENSG00000006740	_	Rho GTPase-activating protein RICH2
PFC	Module1	ENSG00000131242	*RAB11FIP4*	Rab11 family-interacting protein 4
PFC	Module1	ENSG00000108352	*RAPGEFL1*	Rap guanine nucleotide exchange factor-like 1
PFC	Module1	ENSG00000120088	*CRHR1*	Corticotropin-releasing factor receptor 1 Precursor
PFC	Module1	ENSG00000132535	*DLG4*	Disks large homolog 4
PFC	Module1	ENSG00000179036	_	_
PFC	Module1	ENSG00000108262	*GIT1*	ARF GTPase-activating protein GIT1
PFC	Module1	ENSG00000161714	*PLCD3*	1-phosphatidylinositol-4,5-bisphosphate phosphodiesterase delta-3
PFC	Module1	ENSG00000041353	*RAB27B*	Ras-related protein Rab-27B
PFC	Module1	ENSG00000128626	*MRPS12*	28S ribosomal protein S12, mitochondrial Precursor
PFC	Module1	ENSG00000160014	*CALM3*	Calmodulin
PFC	Module1	ENSG00000065000	*AP3D1*	AP-3 complex subunit delta-1
PFC	Module1	ENSG00000186111	*PIP5K1C*	Phosphatidylinositol-4-phosphate 5-kinase type-1 gamma

PFC	Module1	ENSG00000118160	*SLC8A2*	Sodium/calcium exchanger 2 Precursor
PFC	Module1	ENSG00000105053	*VRK3*	Serine/threonine-protein kinase VRK3
PFC	Module1	ENSG00000115738	*ID2*	DNA-binding protein inhibitor ID-2
PFC	Module1	ENSG00000162975	*KCNF1*	Potassium voltage-gated channel subfamily F member 1
PFC	Module1	ENSG00000057935	*MTA3*	Metastasis-associated protein MTA3
PFC	Module1	ENSG00000055813	*CCDC85A*	Coiled-coil domain-containing protein 85A
PFC	Module1	ENSG00000170485	*NPAS2*	Neuronal PAS domain-containing protein 2
PFC	Module1	ENSG00000155052	*CNTNAP5*	Contactin-associated protein-like 5 Precursor
PFC	Module1	ENSG00000115896	*PLCL1*	Inactive phospholipase C-like protein 1
PFC	Module1	ENSG00000115194	*SLC30A3*	Zinc transporter 3
PFC	Module1	ENSG00000184261	*KCNK12*	Potassium channel subfamily K member 12
PFC	Module1	ENSG00000138411	*HECW2*	E3 ubiquitin-protein ligase HECW2
PFC	Module1	ENSG00000188674	*C2orf80*	Uncharacterized protein C2orf80
PFC	Module1	ENSG00000101337	*TM9SF4*	Transmembrane 9 superfamily member 4 Precursor
PFC	Module1	ENSG00000101079	*NDRG3*	Protein NDRG3
PFC	Module1	ENSG00000154654	*NCAM2*	Neural cell adhesion molecule 2 Precursor
PFC	Module1	ENSG00000133424	*LARGE*	Glycosyltransferase-like protein LARGE1
PFC	Module1	ENSG00000166862	*CACNG2*	Voltage-dependent calcium channel gamma-2 subunit
PFC	Module1	ENSG00000088538	*DOCK3*	Dedicator of cytokinesis protein 3
PFC	Module1	ENSG00000113966	*ARL6*	ADP-ribosylation factor-like protein 6
PFC	Module1	ENSG00000198919	*DZIP3*	E3 ubiquitin-protein ligase DZIP3
PFC	Module1	ENSG00000031081	_	Cdc42 GTPase-activating protein
PFC	Module1	ENSG00000151789	*ZNF385D*	Zinc finger protein 385D
PFC	Module1	ENSG00000163947	*ARHGEF3*	Rho guanine nucleotide exchange factor 3
PFC	Module1	ENSG00000151276	*MAGI1*	Membrane-associated guanylate kinase, WW and PDZ domain-containing protein 1
PFC	Module1	ENSG00000074416	*MGLL*	Monoglyceride lipase
PFC	Module1	ENSG00000068885	*IFT80*	Intraflagellar transport protein 80 homolog
PFC	Module1	ENSG00000163285	*GABRG1*	Gamma-aminobutyric acid receptor subunit gamma-1 Precursor
PFC	Module1	ENSG00000151834	*GABRA2*	Gamma-aminobutyric acid receptor subunit alpha-2 Precursor
PFC	Module1	ENSG00000178382	_	_
PFC	Module1	ENSG00000158985	*CDC42SE2*	CDC42 small effector protein 2
PFC	Module1	ENSG00000183775	*KCTD16*	BTB/POZ domain-containing protein KCTD16
PFC	Module1	ENSG00000170624	*SGCD*	Delta-sarcoglycan
PFC	Module1	ENSG00000145824	*CXCL14*	C-X-C motif chemokine 14 Precursor
PFC	Module1	ENSG00000184347	*SLIT3*	Slit homolog 3 protein Precursor
PFC	Module1	ENSG00000069122	*GPR116*	Probable G-protein coupled receptor 116 Precursor
PFC	Module1	ENSG00000152034	*MCHR2*	Melanin-concentrating hormone receptor 2
PFC	Module1	ENSG00000185345	*PARK2*	E3 ubiquitin-protein ligase parkin
PFC	Module1	ENSG00000160963	*EMID2*	Collagen alpha-1
PFC	Module1	ENSG00000130226	*DPP6*	Dipeptidyl aminopeptidase-like protein 6
PFC	Module1	ENSG00000058404	*CAMK2B*	Calcium/calmodulin-dependent protein kinase type II beta chain
PFC	Module1	ENSG00000106089	*STX1A*	Syntaxin-1A
PFC	Module1	ENSG00000179603	*GRM8*	Metabotropic glutamate receptor 8 Precursor
PFC	Module1	ENSG00000008853	*RHOBTB2*	Rho-related BTB domain-containing protein 2

PFC	Module1	ENSG00000153317	*ASAP1*	Arf-GAP with SH3 domain, ANK repeat and PH domain-containing protein 1
PFC	Module1	ENSG00000147724	*FAM135B*	Protein FAM135B
PFC	Module1	ENSG00000122733	*KIAA1045*	Protein KIAA1045
PFC	Module1	ENSG00000156017	*C9orf41*	UPF0586 protein C9orf41
PFC	Module1	ENSG00000123091	*RNF11*	RING finger protein 11
PFC	Module1	ENSG00000140104	*C14orf79*	Uncharacterized protein C14orf79
PFC	Module1	ENSG00000140545	*MFGE8*	Lactadherin Precursor
PFC	Module1	ENSG00000144712	*CAND2*	Cullin-associated NEDD8-dissociated protein 2
PFC	Module1	ENSG00000017483	*SLC38A5*	Sodium-coupled neutral amino acid transporter 5
PFC	Module2	ENSG00000169504	*CLIC4*	Chloride intracellular channel protein 4
PFC	Module2	ENSG00000159023	*EPB41*	Protein 4.1
PFC	Module2	ENSG00000077585	*GPR137B*	Integral membrane protein GPR137B
PFC	Module2	ENSG00000036549	*ZZZ3*	ZZ-type zinc finger-containing protein 3
PFC	Module2	ENSG00000170242	*USP47*	Ubiquitin carboxyl-terminal hydrolase 47
PFC	Module2	ENSG00000086848	*FDXACB1*	Ferredoxin-fold anticodon-binding domain-containing protein 1
PFC	Module2	ENSG00000185591	*SP1*	Transcription factor Sp1
PFC	Module2	ENSG00000120802	*TMPO*	Lamina-associated polypeptide 2, isoforms beta/gamma
PFC	Module2	ENSG00000076513	*ANKRD13A*	Ankyrin repeat domain-containing protein 13A
PFC	Module2	ENSG00000111642	*CHD4*	Chromodomain-helicase-DNA-binding protein 4
PFC	Module2	ENSG00000111266	*DUSP16*	Dual specificity protein phosphatase 16
PFC	Module2	ENSG00000134294	*SLC38A2*	Sodium-coupled neutral amino acid transporter 2
PFC	Module2	ENSG00000135108	*FBXO21*	F-box only protein 21
PFC	Module2	ENSG00000100578	*KIAA0586*	Uncharacterized protein KIAA0586
PFC	Module2	ENSG00000140043	*PTGR2*	Prostaglandin reductase 2
PFC	Module2	ENSG00000092201	*SUPT16HP*	FACT complex subunit SPT16
PFC	Module2	ENSG00000184935	_	_
PFC	Module2	ENSG00000166917	_	_
PFC	Module2	ENSG00000144036	*EXOC6B*	Exocyst complex component 6B
PFC	Module2	ENSG00000124226	*RNF114*	RING finger protein 114
PFC	Module2	ENSG00000101384	*JAG1*	Protein jagged-1 Precursor
PFC	Module2	ENSG00000131375	*CAPN7*	Calpain-7
PFC	Module2	ENSG00000169379	*ARL13B*	ADP-ribosylation factor-like protein 13B
PFC	Module2	ENSG00000173889	*PHC3*	Polyhomeotic-like protein 3
PFC	Module2	ENSG00000163961	*RNF168*	E3 ubiquitin-protein ligase RNF168
PFC	Module2	ENSG00000118785	*SPP1*	Osteopontin Precursor
PFC	Module2	ENSG00000109606	*DHX15*	Putative pre-mRNA-splicing factor ATP-dependent RNA helicase DHX15
PFC	Module2	ENSG00000109323	*MANBA*	Beta-mannosidase Precursor
PFC	Module2	ENSG00000109381	*ELF2*	ETS-related transcription factor Elf-2
PFC	Module2	ENSG00000170088	*TMEM192*	Transmembrane protein 192
PFC	Module2	ENSG00000164292	*RHOBTB3*	Rho-related BTB domain-containing protein 3
PFC	Module2	ENSG00000070193	*FGF10*	Fibroblast growth factor 10 Precursor
PFC	Module2	ENSG00000158987	*RAPGEF6*	Rap guanine nucleotide exchange factor 6
PFC	Module2	ENSG00000065615	*CYB5R4*	Cytochrome b5 reductase 4
PFC	Module2	ENSG00000105856	*HBP1*	HMG box-containing protein 1

PFC	Module2	ENSG00000013374	*NUB1*	NEDD8 ultimate buster 1
PFC	Module2	ENSG00000157191	*NECAP2*	Adaptin ear-binding coat-associated protein 2
PFC	Module2	ENSG00000162607	*USP1*	Ubiquitin carboxyl-terminal hydrolase 1
PFC	Module2	ENSG00000189195	*BTBD8*	BTB/POZ domain-containing protein 8
PFC	Module2	ENSG00000143469	*SYT14*	Synaptotagmin-14
PFC	Module2	ENSG00000117525	*F3*	Tissue factor Precursor
PFC	Module2	ENSG00000085465	*OVGP1*	Oviduct-specific glycoprotein Precursor
PFC	Module2	ENSG00000081019	*RSBN1*	Round spermatid basic protein 1
PFC	Module2	ENSG00000143498	*TAF1A*	TATA box-binding protein-associated factor RNA polymerase I subunit A
PFC	Module2	ENSG00000138293	*NCOA4*	Nuclear receptor coactivator 4
PFC	Module2	ENSG00000096717	*SIRT1*	NAD-dependent deacetylase sirtuin-1
PFC	Module2	ENSG00000060339	*CCAR1*	Cell division cycle and apoptosis regulator protein 1
PFC	Module2	ENSG00000214435	*AS3MT*	Arsenite methyltransferase
PFC	Module2	ENSG00000108055	*SMC3*	Structural maintenance of chromosomes protein 3
PFC	Module2	ENSG00000152487	_	_
PFC	Module2	ENSG00000150093	*ITGB1*	Integrin beta-1 Precursor
PFC	Module2	ENSG00000132274	*TRIM22*	Tripartite motif-containing protein 22
PFC	Module2	ENSG00000149054	*ZNF215*	Zinc finger protein 215
PFC	Module2	ENSG00000187079	*TEAD1*	Transcriptional enhancer factor TEF-1
PFC	Module2	ENSG00000042429	*MED17*	Mediator of RNA polymerase II transcription subunit 17
PFC	Module2	ENSG00000110756	*HPS5*	Hermansky-Pudlak syndrome 5 protein
PFC	Module2	ENSG00000137513	*NARS2*	Probable asparaginyl-tRNA synthetase, mitochondrial Precursor
PFC	Module2	ENSG00000149308	*NPAT*	Protein NPAT
PFC	Module2	ENSG00000137656	*BUD13*	BUD13 homolog
PFC	Module2	ENSG00000127311	*HELB*	DNA helicase B
PFC	Module2	ENSG00000135093	*USP30*	Ubiquitin carboxyl-terminal hydrolase 30
PFC	Module2	ENSG00000161800	*RACGAP1P*	Rac GTPase-activating protein 1
PFC	Module2	ENSG00000133858	*ZFC3H1*	Zinc finger C3H1 domain-containing protein
PFC	Module2	ENSG00000139357	*SLC5A8*	Sodium-coupled monocarboxylate transporter 1
PFC	Module2	ENSG00000202335	_	Small nucleolar RNA SNORD50
PFC	Module2	ENSG00000134899	*ERCC5*	DNA repair protein complementing XP-G cells
PFC	Module2	ENSG00000152193	*RNF219*	RING finger protein 219
PFC	Module2	ENSG00000088448	*ANKRD10*	Ankyrin repeat domain-containing protein 10
PFC	Module2	ENSG00000185246	*PRPF39*	Pre-mRNA-processing factor 39
PFC	Module2	ENSG00000165934	*CPSF2*	Cleavage and polyadenylation specificity factor subunit 2
PFC	Module2	ENSG00000213741	*RPS29P9*	40S ribosomal protein S29
PFC	Module2	ENSG00000100522	*GNPNAT1*	Glucosamine 6-phosphate N-acetyltransferase
PFC	Module2	ENSG00000185650	*ZFP36L1*	Butyrate response factor 1
PFC	Module2	ENSG00000119688	*ABCD4*	ATP-binding cassette sub-family D member 4
PFC	Module2	ENSG00000119720	*C14orf102*	UPF0614 protein C14orf102
PFC	Module2	ENSG00000128923	*FAM63B*	Protein FAM63B
PFC	Module2	ENSG00000103671	*TRIP4*	Activating signal cointegrator 1
PFC	Module2	ENSG00000167202	*TBC1D2B*	TBC1 domain family member 2B
PFC	Module2	ENSG00000103187	*COTL1*	Coactosin-like protein

PFC	Module2	ENSG00000070366	*SMG6*	Telomerase-binding protein EST1A
PFC	Module2	ENSG00000074356	*C17orf85*	Uncharacterized protein C17orf85
PFC	Module2	ENSG00000108592	*FTSJ3*	Putative rRNA methyltransferase 3
PFC	Module2	ENSG00000067900	*ROCK1*	Rho-associated protein kinase 1
PFC	Module2	ENSG00000105185	*PDCD5*	Programmed cell death protein 5
PFC	Module2	ENSG00000196357	*ZNF565*	Zinc finger protein 565
PFC	Module2	ENSG00000173960	*UBXN2A*	UBX domain-containing protein 2A
PFC	Module2	ENSG00000080345	*RIF1*	Telomere-associated protein RIF1
PFC	Module2	ENSG00000136535	*TBR1*	T-box brain protein 1
PFC	Module2	ENSG00000163516	*ANKZF1*	Ankyrin repeat and zinc finger domain-containing protein 1
PFC	Module2	ENSG00000068697	*LAPTM4A*	Lysosomal-associated transmembrane protein 4A
PFC	Module2	ENSG00000200003	_	U6 spliceosomal RNA
PFC	Module2	ENSG00000136709	*WDR33*	WD repeat-containing protein 33
PFC	Module2	ENSG00000013441	*CLK1*	Dual specificity protein kinase CLK1
PFC	Module2	ENSG00000144445	*C2orf67*	Uncharacterized protein C2orf67
PFC	Module2	ENSG00000125970	*RALY*	RNA-binding protein Raly
PFC	Module2	ENSG00000101442	*ACTR5*	Actin-related protein 5
PFC	Module2	ENSG00000101109	*STK4*	Serine/threonine-protein kinase 4
PFC	Module2	ENSG00000124171	*PARD6B*	Partitioning defective 6 homolog beta
PFC	Module2	ENSG00000149634	*C20orf165*	Uncharacterized protein C20orf165
PFC	Module2	ENSG00000182541	*LIMK2*	LIM domain kinase 2
PFC	Module2	ENSG00000173200	*PARP15*	Poly polymerase 15
PFC	Module2	ENSG00000155893	*ACPL2*	Acid phosphatase-like protein 2 Precursor
PFC	Module2	ENSG00000176142	*TMEM39A*	Transmembrane protein 39A
PFC	Module2	ENSG00000138231	*DBR1*	Lariat debranching enzyme
PFC	Module2	ENSG00000114127	*XRN1*	5'-3' exoribonuclease 1
PFC	Module2	ENSG00000157796	*WDR19*	WD repeat-containing protein 19
PFC	Module2	ENSG00000118762	*PKD2*	Polycystin-2
PFC	Module2	ENSG00000077684	*PHF17*	Protein Jade-1
PFC	Module2	ENSG00000083896	*YTHDC1*	YTH domain-containing protein 1
PFC	Module2	ENSG00000163297	*ANTXR2*	Anthrax toxin receptor 2 Precursor
PFC	Module2	ENSG00000169836	*TACR3*	Neuromedin-K receptor
PFC	Module2	ENSG00000109771	*LRP2BP*	LRP2-binding protein
PFC	Module2	ENSG00000122008	*POLK*	DNA polymerase kappa
PFC	Module2	ENSG00000133302	*ANKRD32*	Ankyrin repeat domain-containing protein 32
PFC	Module2	ENSG00000112855	*HARS2*	Probable histidyl-tRNA synthetase, mitochondrial Precursor
PFC	Module2	ENSG00000113272	*THG1L*	Probable tRNA
PFC	Module2	ENSG00000113328	*CCNG1*	Cyclin-G1
PFC	Module2	ENSG00000145780	*FEM1C*	Protein fem-1 homolog C
PFC	Module2	ENSG00000168944	*CEP120*	Centrosomal protein of 120 kDa
PFC	Module2	ENSG00000131504	*DIAPH1*	Protein diaphanous homolog 1
PFC	Module2	ENSG00000155868	*MED7*	Mediator of RNA polymerase II transcription subunit 7
PFC	Module2	ENSG00000026950	*BTN3A1*	Butyrophilin subfamily 3 member A1 Precursor
PFC	Module2	ENSG00000118518	*RNF146*	RING finger protein 146
PFC	Module2	ENSG00000213066	*FGFR1OP*	FGFR1 oncogene partner

PFC	Module2	ENSG00000158691	*ZSCAN12*	Zinc finger and SCAN domain-containing protein 12
PFC	Module2	ENSG00000096060	*FKBP5*	FK506-binding protein 5
PFC	Module2	ENSG00000146247	*PHIP*	PH-interacting protein
PFC	Module2	ENSG00000135338	*LCA5*	Lebercilin
PFC	Module2	ENSG00000013375	*PGM3*	Phosphoacetylglucosamine mutase
PFC	Module2	ENSG00000074935	*TUBE1*	Tubulin epsilon chain
PFC	Module2	ENSG00000135597	*REPS1*	RalBP1-associated Eps domain-containing protein 1
PFC	Module2	ENSG00000186625	*KATNA1*	Katanin p60 ATPase-containing subunit A1
PFC	Module2	ENSG00000159840	*ZYX*	Zyxin
PFC	Module2	ENSG00000034677	*RNF19A*	E3 ubiquitin-protein ligase RNF19A
PFC	Module2	ENSG00000122729	*ACO1*	Cytoplasmic aconitate hydratase
PFC	Module2	ENSG00000178966	*RMI1*	RecQ-mediated genome instability protein 1
PFC	Module2	ENSG00000119397	*CEP110*	Centriolin
PFC	Module2	ENSG00000083223	*ZCCHC6*	Zinc finger CCHC domain-containing protein 6
PFC	Module2	ENSG00000046651	*OFD1*	Oral-facial-digital syndrome 1 protein
PFC	Module2	ENSG00000102007	*PLP2*	Proteolipid protein 2
PFC	Module2	ENSG00000184634	*MED12*	Mediator of RNA polymerase II transcription subunit 12
PFC	Module2	ENSG00000196440	*CXorf35*	_
PFC	Module2	ENSG00000208964	_	_
PFC	Module2	ENSG00000125676	*THOC2*	THO complex subunit 2
PFC	Module2	ENSG00000117360	*PRPF3*	U4/U6 small nuclear ribonucleoprotein Prp3
PFC	Module2	ENSG00000187049	*TMEM216*	Transmembrane protein 216
PFC	Module2	ENSG00000120832	*MTERFD3*	mTERF domain-containing protein 3, mitochondrial Precursor
PFC	Module2	ENSG00000136104	*RNASEH2B*	Ribonuclease H2 subunit B
PFC	Module2	ENSG00000102699	*PARP4*	Poly polymerase 4
PFC	Module2	ENSG00000173575	*CHD2*	Chromodomain-helicase-DNA-binding protein 2
PFC	Module2	ENSG00000140199	*SLC12A6*	Solute carrier family 12 member 6
PFC	Module2	ENSG00000120318	*ARAP3*	Arf-GAP, Rho-GAP domain, ANK repeat and PH domain-containing protein 3
PFC	Module3	ENSG00000117154	*IGSF21*	Immunoglobulin superfamily member 21 Precursor
PFC	Module3	ENSG00000117411	*B4GALT2*	Beta-1,4-galactosyltransferase 2
PFC	Module3	ENSG00000117114	*LPHN2*	Latrophilin-2 Precursor
PFC	Module3	ENSG00000117600	_	Lipid phosphate phosphatase-related protein type 4
PFC	Module3	ENSG00000162636	*FAM102B*	Protein FAM102B
PFC	Module3	ENSG00000174151	*CYB561D1*	Cytochrome b561 domain-containing protein 1
PFC	Module3	ENSG00000203685	*C1orf95*	Uncharacterized membrane protein C1orf95
PFC	Module3	ENSG00000143195	*ILDR2*	Immunoglobulin-like domain-containing receptor 2
PFC	Module3	ENSG00000168243	*GNG4*	Guanine nucleotide-binding protein G
PFC	Module3	ENSG00000198879	*SFMBT2*	Scm-like with four MBT domains protein 2
PFC	Module3	ENSG00000150275	*PCDH15*	Protocadherin-15 Precursor
PFC	Module3	ENSG00000182667	*OPCML*	Neurotrimin Precursor
PFC	Module3	ENSG00000051009	*FAM160A2*	UPF0518 protein FAM160A2
PFC	Module3	ENSG00000110400	*PVRL1*	Poliovirus receptor-related protein 1 Precursor
PFC	Module3	ENSG00000166257	*SCN3B*	Sodium channel subunit beta-3 Precursor
PFC	Module3	ENSG00000123352	*SPATS2*	Spermatogenesis-associated serine-rich protein 2

PFC	Module3	ENSG00000176871	*WSB2*	WD repeat and SOCS box-containing protein 2
PFC	Module3	ENSG00000041515	*MYO16*	Myosin-XVI
PFC	Module3	ENSG00000133083	*DCLK1*	Serine/threonine-protein kinase DCLK1
PFC	Module3	ENSG00000089723	*OTUB2*	Ubiquitin thioesterase OTUB2
PFC	Module3	ENSG00000100678	*SLC8A3*	Sodium/calcium exchanger 3 Precursor
PFC	Module3	ENSG00000119682	*KIAA0317*	Protein KIAA0317
PFC	Module3	ENSG00000198752	_	Serine/threonine-protein kinase MRCK beta
PFC	Module3	ENSG00000187446	_	Calcium-binding protein p22
PFC	Module3	ENSG00000140557	*ST8SIA2*	Alpha-2,8-sialyltransferase 8B
PFC	Module3	ENSG00000166206	*GABRB3*	Gamma-aminobutyric acid receptor subunit beta-3 Precursor
PFC	Module3	ENSG00000137817	*PARP6*	Poly polymerase 6
PFC	Module3	ENSG00000169783	*LINGO1*	Leucine-rich repeat and immunoglobulin-like domain-containing nogo receptor-interacting protein 1 Precursor
PFC	Module3	ENSG00000103942	*HOMER2*	Homer protein homolog 2
PFC	Module3	ENSG00000140945	*CDH13*	Cadherin-13 Precursor
PFC	Module3	ENSG00000150394	*CDH8*	Cadherin-8 Precursor
PFC	Module3	ENSG00000140937	*CDH11*	Cadherin-11 Precursor
PFC	Module3	ENSG00000161958	*FGF11*	Fibroblast growth factor 11
PFC	Module3	ENSG00000168256	*NKIRAS2*	NF-kappa-B inhibitor-interacting Ras-like protein 2
PFC	Module3	ENSG00000141485	*SLC13A5*	Solute carrier family 13 member 5
PFC	Module3	ENSG00000063015	*SEZ6*	Seizure protein 6 homolog Precursor
PFC	Module3	ENSG00000108960	*MMD*	Monocyte to macrophage differentiation protein
PFC	Module3	ENSG00000168675	*C18orf1*	Uncharacterized protein C18orf1
PFC	Module3	ENSG00000141431	*ASXL3*	Putative Polycomb group protein ASXL3
PFC	Module3	ENSG00000166974	*MAPRE2*	Microtubule-associated protein RP/EB family member 2
PFC	Module3	ENSG00000105270	*CLIP3*	CAP-Gly domain-containing linker protein 3
PFC	Module3	ENSG00000129990	*SYT5*	Synaptotagmin-5
PFC	Module3	ENSG00000133265	*HSPBP1*	Hsp70-binding protein 1
PFC	Module3	ENSG00000151693	*ASAP2*	Arf-GAP with SH3 domain, ANK repeat and PH domain-containing protein 2
PFC	Module3	ENSG00000157851	*DPYSL5*	Dihydropyrimidinase-related protein 5
PFC	Module3	ENSG00000170340	*B3GNT2*	UDP-GlcNAc:betaGal beta-1,3-N-acetylglucosaminyltransferase 2
PFC	Module3	ENSG00000114999	*TTL*	Tubulin--tyrosine ligase
PFC	Module3	ENSG00000144230	*GPR17*	Uracil nucleotide/cysteinyl leukotriene receptor
PFC	Module3	ENSG00000187123	*LYPD6*	Ly6/PLAUR domain-containing protein 6 Precursor
PFC	Module3	ENSG00000163249	*CCNYL1*	Cyclin-Y-like protein 1
PFC	Module3	ENSG00000114923	*SLC4A3*	Anion exchange protein 3
PFC	Module3	ENSG00000152128	*TMEM163*	Transmembrane protein 163
PFC	Module3	ENSG00000177519	*RPRM*	Protein reprimo
PFC	Module3	ENSG00000118263	*KLF7*	Krueppel-like factor 7
PFC	Module3	ENSG00000171951	*SCG2*	Secretogranin-2 Precursor
PFC	Module3	ENSG00000187957	*DNER*	Delta and Notch-like epidermal growth factor-related receptor Precursor
PFC	Module3	ENSG00000101349	*PAK7*	Serine/threonine-protein kinase PAK 7
PFC	Module3	ENSG00000026559	*KCNG1*	Potassium voltage-gated channel subfamily G member 1
PFC	Module3	ENSG00000154639	*CXADRP2*	Coxsackievirus and adenovirus receptor Precursor
PFC	Module3	ENSG00000100095	*SEZ6L*	Seizure 6-like protein Precursor

PFC	Module3	ENSG00000128203	*ASPHD2*	Aspartate beta-hydroxylase domain-containing protein 2
PFC	Module3	ENSG00000011198	*ABHD5*	1-acylglycerol-3-phosphate O-acyltransferase ABHD5
PFC	Module3	ENSG00000144724	*PTPRG*	Receptor-type tyrosine-protein phosphatase gamma Precursor
PFC	Module3	ENSG00000183662	*FAM19A1*	Protein FAM19A1 Precursor
PFC	Module3	ENSG00000134072	*CAMK1*	Calcium/calmodulin-dependent protein kinase type 1
PFC	Module3	ENSG00000163637	*PRICKLE2*	Prickle-like protein 2
PFC	Module3	ENSG00000004399	*PLXND1*	Plexin-D1 Precursor
PFC	Module3	ENSG00000157005	*SST*	Somatostatin Precursor
PFC	Module3	ENSG00000145147	*SLIT2*	Slit homolog 2 protein Precursor
PFC	Module3	ENSG00000174145	*KIAA1239*	Leucine-rich repeat and WD repeat-containing protein KIAA1239
PFC	Module3	ENSG00000134853	*PDGFRA*	Alpha-type platelet-derived growth factor receptor Precursor
PFC	Module3	ENSG00000174473	*GALNTL6*	Polypeptide N-acetylgalactosaminyltransferase-like 6
PFC	Module3	ENSG00000218336	*ODZ3*	Teneurin-3
PFC	Module3	ENSG00000071127	*WDR1*	WD repeat-containing protein 1
PFC	Module3	ENSG00000113389	*NPR3*	Atrial natriuretic peptide clearance receptor Precursor
PFC	Module3	ENSG00000134982	*APC*	Adenomatous polyposis coli protein
PFC	Module3	ENSG00000112902	*SEMA5A*	Semaphorin-5A Precursor
PFC	Module3	ENSG00000040731	*CDH10*	Cadherin-10 Precursor
PFC	Module3	ENSG00000145632	*PLK2*	Serine/threonine-protein kinase PLK2
PFC	Module3	ENSG00000145681	*HAPLN1*	Hyaluronan and proteoglycan link protein 1 Precursor
PFC	Module3	ENSG00000197283	*SYNGAP1*	Ras GTPase-activating protein SynGAP
PFC	Module3	ENSG00000133627	*ACTR3B*	Actin-related protein 3B
PFC	Module3	ENSG00000153814	*JAZF1*	Juxtaposed with another zinc finger protein 1
PFC	Module3	ENSG00000153956	*CACNA2D1*	Voltage-dependent calcium channel subunit alpha-2/delta-1 Precursor
PFC	Module3	ENSG00000105887	*LUZP6*	Myotrophin
PFC	Module3	ENSG00000157168	*NRG1*	Pro-neuregulin-1, membrane-bound isoform Precursor
PFC	Module3	ENSG00000165084	*C8orf34*	Uncharacterized protein C8orf34
PFC	Module3	ENSG00000104435	*STMN2*	Stathmin-2
PFC	Module3	ENSG00000184156	*KCNQ3*	Potassium voltage-gated channel subfamily KQT member 3
PFC	Module3	ENSG00000147852	*VLDLR*	Very low-density lipoprotein receptor Precursor
PFC	Module3	ENSG00000137094	*DNAJB5*	DnaJ homolog subfamily B member 5
PFC	Module3	ENSG00000107282	*APBA1*	Amyloid beta A4 precursor protein-binding family A member 1
PFC	Module3	ENSG00000198785	*GRIN3A*	Glutamate receptor subunit 3A Precursor
PFC	Module3	ENSG00000165802	*NELF*	Nasal embryonic luteinizing hormone-releasing hormone factor
PFC	Module3	ENSG00000101911	*PRPS2*	Ribose-phosphate pyrophosphokinase 2
PFC	Module3	ENSG00000077264	*PAK3*	Serine/threonine-protein kinase PAK 3
PFC	Module3	ENSG00000185985	*SLITRK2*	SLIT and NTRK-like protein 2 Precursor
PFC	Module3	ENSG00000147044	*CASK*	Peripheral plasma membrane protein CASK
PFC	Module3	ENSG00000171357	*C1orf190*	Uncharacterized protein C1orf190
PFC	Module3	ENSG00000132692	*BCAN*	Brevican core protein Precursor
PFC	Module3	ENSG00000132334	*PTPRE*	Receptor-type tyrosine-protein phosphatase epsilon Precursor
PFC	Module3	ENSG00000111145	*ELK3*	ETS domain-containing protein Elk-3
PFC	Module3	ENSG00000064726	*BTBD1*	BTB/POZ domain-containing protein 1
PFC	Module3	ENSG00000090674	*MCOLN1*	Mucolipin-1
PFC	Module3	ENSG00000105568	*PPP2R1A*	Serine/threonine-protein phosphatase 2A 65 kDa regulatory subunit A

				alpha isoform
PFC	Module3	ENSG00000089057	*SLC23A2*	Solute carrier family 23 member 2
PFC	Module3	ENSG00000156299	*TIAM1*	T-lymphoma invasion and metastasis-inducing protein 1
PFC	Module3	ENSG00000214021	*TTLL3*	Tubulin--tyrosine ligase-like protein 3
PFC	Module3	ENSG00000114853	*ZBTB47*	Zinc finger and BTB domain-containing protein 47
PFC	Module3	ENSG00000114867	*EIF4G1*	Eukaryotic translation initiation factor 4 gamma 1
PFC	Module3	ENSG00000164086	*DUSP7*	Dual specificity protein phosphatase 7
PFC	Module3	ENSG00000114686	*MRPL3*	39S ribosomal protein L3, mitochondrial
PFC	Module3	ENSG00000145708	*CRHBP*	Corticotropin-releasing factor-binding protein Precursor
PFC	Module3	ENSG00000164466	*SFXN1*	Sideroflexin-1
PFC	Module3	ENSG00000198729	*PPP1R14C*	Protein phosphatase 1 regulatory subunit 14C
PFC	Module3	ENSG00000196358	*NTNG2*	Netrin-G2 Precursor
PFC	Module3	ENSG00000152382	*TADA1L*	Transcriptional adapter 1-like protein
PFC	Module4	ENSG00000168710	*AHCYL1*	Putative adenosylhomocysteinase 2
PFC	Module4	ENSG00000148482	*SLC39A12*	Zinc transporter ZIP12
PFC	Module4	ENSG00000148700	*ADD3*	Gamma-adducin
PFC	Module4	ENSG00000133789	*SWAP70*	Switch-associated protein 70
PFC	Module4	ENSG00000148935	*GAS2*	Growth arrest-specific protein 2
PFC	Module4	ENSG00000166535	*A2ML1*	Alpha-2-macroglobulin-like protein 1 Precursor
PFC	Module4	ENSG00000167779	*IGFBP6*	Insulin-like growth factor-binding protein 6 Precursor
PFC	Module4	ENSG00000139190	*VAMP1*	Vesicle-associated membrane protein 1
PFC	Module4	ENSG00000186031	*FMN1*	Formin-1
PFC	Module4	ENSG00000171766	*GATM*	Glycine amidinotransferase, mitochondrial Precursor
PFC	Module4	ENSG00000166848	*TERF2IP*	Telomeric repeat-binding factor 2-interacting protein 1
PFC	Module4	ENSG00000141314	*RHBDL3*	Rhomboid-related protein 3
PFC	Module4	ENSG00000131095	*GFAP*	Glial fibrillary acidic protein
PFC	Module4	ENSG00000105711	*SCN1B*	Sodium channel subunit beta-1 Precursor
PFC	Module4	ENSG00000134324	*LPIN1*	Lipin-1
PFC	Module4	ENSG00000138448	*ITGAV*	Integrin alpha-V Precursor
PFC	Module4	ENSG00000138378	*STAT4*	Signal transducer and activator of transcription 4
PFC	Module4	ENSG00000100307	*CBX7*	Chromobox protein homolog 7
PFC	Module4	ENSG00000114166	*KAT2B*	Histone acetyltransferase PCAF
PFC	Module4	ENSG00000213672	*NCKIPSD*	NCK-interacting protein with SH3 domain
PFC	Module4	ENSG00000114126	*TFDP2*	Transcription factor Dp-2
PFC	Module4	ENSG00000013293	*SLC7A14*	Probable cationic amino acid transporter
PFC	Module4	ENSG00000138639	*ARHGAP24*	Rho GTPase-activating protein 24
PFC	Module4	ENSG00000145390	*USP53*	Inactive ubiquitin carboxyl-terminal hydrolase 53
PFC	Module4	ENSG00000171476	*HOPX*	Homeodomain-only protein
PFC	Module4	ENSG00000151623	*NR3C2*	Mineralocorticoid receptor
PFC	Module4	ENSG00000145715	*RASA1*	Ras GTPase-activating protein 1
PFC	Module4	ENSG00000043143	*PHF15*	Protein Jade-2
PFC	Module4	ENSG00000113327	*GABRG2*	Gamma-aminobutyric acid receptor subunit gamma-2 Precursor
PFC	Module4	ENSG00000153291	*SLC25A27*	Mitochondrial uncoupling protein 4
PFC	Module4	ENSG00000024862	*CCDC28A*	Coiled-coil domain-containing protein 28A
PFC	Module4	ENSG00000078269	*SYNJ2*	Synaptojanin-2

PFC	Module4	ENSG00000132429	*POPDC3*	Popeye domain-containing protein 3
PFC	Module4	ENSG00000001631	*KRIT1*	Krev interaction trapped protein 1
PFC	Module4	ENSG00000104728	*ARHGEF10*	Rho guanine nucleotide exchange factor 10
PFC	Module4	ENSG00000169499	*PLEKHA2*	Pleckstrin homology domain-containing family A member 2
PFC	Module4	ENSG00000123119	*NECAB1*	N-terminal EF-hand calcium-binding protein 1
PFC	Module4	ENSG00000107317	*PTGDS*	Prostaglandin-H2 D-isomerase Precursor
PFC	Module4	ENSG00000175556	*LONRF3*	LON peptidase N-terminal domain and RING finger protein 3
PFC	Module4	ENSG00000135744	*AGT*	Angiotensinogen Precursor
PFC	Module4	ENSG00000119638	*NEK9*	Serine/threonine-protein kinase Nek9
PFC	Module4	ENSG00000138738	*PRDM5*	PR domain zinc finger protein 5
PFC	Module4	ENSG00000152931	_	Prostate-specific and androgen-regulated protein 1
PFC	Module4	ENSG00000164199	*GPR98*	G-protein coupled receptor 98 Precursor
PFC	Module5	ENSG00000081760	*AACS*	Acetoacetyl-CoA synthetase
PFC	Module5	ENSG00000108861	*DUSP3*	Dual specificity protein phosphatase 3
PFC	Module5	ENSG00000116016	*EPAS1*	Endothelial PAS domain-containing protein 1
PFC	Module5	ENSG00000184160	*ADRA2C*	Alpha-2C adrenergic receptor
PFC	Module5	ENSG00000150627	*WDR17*	WD repeat-containing protein 17
PFC	Module5	ENSG00000186479	*RGS7BP*	Regulator of G-protein signaling 7-binding protein
PFC	Module5	ENSG00000112335	*SNX3*	Sorting nexin-3
PFC	Module5	ENSG00000158008	*EXTL1*	Exostosin-like 1
PFC	Module5	ENSG00000143126	*CELSR2*	Cadherin EGF LAG seven-pass G-type receptor 2 Precursor
PFC	Module5	ENSG00000165757	*KIAA1462*	Uncharacterized protein KIAA1462
PFC	Module5	ENSG00000134343	*ANO3*	Anoctamin-3
PFC	Module5	ENSG00000149091	*DGKZ*	Diacylglycerol kinase zeta
PFC	Module5	ENSG00000179292	*TMEM151A*	Transmembrane protein 151A
PFC	Module5	ENSG00000154146	*NRGN*	Neurogranin
PFC	Module5	ENSG00000135119	*RNFT2*	Ring finger and transmembrane domain-containing protein 2
PFC	Module5	ENSG00000181418	*DDN*	Dendrin
PFC	Module5	ENSG00000110931	*CAMKK2*	Calcium/calmodulin-dependent protein kinase kinase 2
PFC	Module5	ENSG00000036530	*CYP46A1*	Cholesterol 24-hydroxylase
PFC	Module5	ENSG00000100711	*ZFYVE21*	Zinc finger FYVE domain-containing protein 21
PFC	Module5	ENSG00000092445	*TYRO3*	Tyrosine-protein kinase receptor TYRO3 Precursor
PFC	Module5	ENSG00000171914	*TLN2*	Talin-2
PFC	Module5	ENSG00000166949	*SMAD3*	Mothers against decapentaplegic homolog 3
PFC	Module5	ENSG00000172575	*RASGRP1*	RAS guanyl-releasing protein 1
PFC	Module5	ENSG00000156642	*NPTN*	Neuroplastin Precursor
PFC	Module5	ENSG00000090581	*GNPTG*	N-acetylglucosamine-1-phosphotransferase subunit gamma Precursor
PFC	Module5	ENSG00000073670	*ADAM11*	Disintegrin and metalloproteinase domain-containing protein 11 Precursor
PFC	Module5	ENSG00000133026	*MYH10*	Myosin-10
PFC	Module5	ENSG00000144357	*UBR3*	E3 ubiquitin-protein ligase UBR3
PFC	Module5	ENSG00000204262	*COL5A2*	Collagen alpha-2
PFC	Module5	ENSG00000135919	*SERPINE2*	Glia-derived nexin Precursor
PFC	Module5	ENSG00000198792	*TMEM184B*	Transmembrane protein 184B
PFC	Module5	ENSG00000138944	*KIAA1644*	Uncharacterized protein KIAA1644 Precursor

PFC	Module5	ENSG00000182247	*UBE2E2*	Ubiquitin-conjugating enzyme E2 E2
PFC	Module5	ENSG00000164061	*BSN*	Protein bassoon
PFC	Module5	ENSG00000163704	*PRRT3*	Proline-rich transmembrane protein 3 Precursor
PFC	Module5	ENSG00000145451	*GLRA3*	Glycine receptor subunit alpha-3 Precursor
PFC	Module5	ENSG00000065833	*ME1*	NADP-dependent malic enzyme
PFC	Module5	ENSG00000071189	*SNX13*	Sorting nexin-13
PFC	Module5	ENSG00000169085	*C8orf46*	Uncharacterized protein C8orf46
PFC	Module5	ENSG00000169933	*FRMPD4*	FERM and PDZ domain-containing protein 4
PFC	Module5	ENSG00000102385	*DRP2*	Dystrophin-related protein 2
PFC	Module5	ENSG00000102003	*SYP*	Synaptophysin
PFC	Module5	ENSG00000124313	*IQSEC2*	IQ motif and SEC7 domain-containing protein 2
CBC	Module1	ENSG00000162889	*MAPKAPK2*	MAP kinase-activated protein kinase 2
CBC	Module1	ENSG00000066027	*PPP2R5A*	Serine/threonine-protein phosphatase 2A 56 kDa regulatory subunit alpha isoform
CBC	Module1	ENSG00000162511	*LAPTM5*	Lysosomal-associated transmembrane protein 5
CBC	Module1	ENSG00000126067	*PSMB2*	Proteasome subunit beta type-2
CBC	Module1	ENSG00000116791	*CRYZ*	Quinone oxidoreductase
CBC	Module1	ENSG00000117500	*TMED5*	Transmembrane emp24 domain-containing protein 5 Precursor
CBC	Module1	ENSG00000143502	*SUSD4*	Sushi domain-containing protein 4 Precursor
CBC	Module1	ENSG00000165443	*PHYHIPL*	Phytanoyl-CoA hydroxylase-interacting protein-like
CBC	Module1	ENSG00000166348	*USP54*	Inactive ubiquitin carboxyl-terminal hydrolase 54
CBC	Module1	ENSG00000107554	*DNMBP*	Dynamin-binding protein
CBC	Module1	ENSG00000133789	*SWAP70*	Switch-associated protein 70
CBC	Module1	ENSG00000187240	*DYNC2H1*	Cytoplasmic dynein 2 heavy chain 1
CBC	Module1	ENSG00000188906	*LRRK2*	Leucine-rich repeat serine/threonine-protein kinase 2
CBC	Module1	ENSG00000119242	*CCDC92*	Coiled-coil domain-containing protein 92
CBC	Module1	ENSG00000088387	*DOCK9*	Dedicator of cytokinesis protein 9
CBC	Module1	ENSG00000139973	*SYT16*	Synaptotagmin-16
CBC	Module1	ENSG00000165533	*TTC8*	Tetratricopeptide repeat protein 8
CBC	Module1	ENSG00000072110	*ACTN1*	Alpha-actinin-1
CBC	Module1	ENSG00000165929	*TC2N*	Tandem C2 domains nuclear protein
CBC	Module1	ENSG00000187446	_	Calcium-binding protein p22
CBC	Module1	ENSG00000087253	*LPCAT2*	Lysophosphatidylcholine acyltransferase 2
CBC	Module1	ENSG00000140950	*KIAA1609*	TLD domain-containing protein KIAA1609
CBC	Module1	ENSG00000167654	*ATCAY*	Caytaxin
CBC	Module1	ENSG00000083844	*ZNF264*	Zinc finger protein 264
CBC	Module1	ENSG00000152527	*PLEKHH2*	Pleckstrin homology domain-containing family H member 2
CBC	Module1	ENSG00000135968	*GCC2*	GRIP and coiled-coil domain-containing protein 2
CBC	Module1	ENSG00000157557	*ETS2*	Protein C-ets-2
CBC	Module1	ENSG00000178075	*GRAMD1C*	GRAM domain-containing protein 1C
CBC	Module1	ENSG00000145012	*LPP*	Lipoma-preferred partner
CBC	Module1	ENSG00000172667	*ZMAT3*	Zinc finger matrin-type protein 3
CBC	Module1	ENSG00000118785	*SPP1*	Osteopontin Precursor
CBC	Module1	ENSG00000164116	*GUCY1A3*	Guanylate cyclase soluble subunit alpha-3
CBC	Module1	ENSG00000163285	*GABRG1*	Gamma-aminobutyric acid receptor subunit gamma-1 Precursor

CBC	Module1	ENSG00000145675	*PIK3R1*	Phosphatidylinositol 3-kinase regulatory subunit alpha
CBC	Module1	ENSG00000145794	*MEGF10*	Multiple epidermal growth factor-like domains 10 Precursor
CBC	Module1	ENSG00000164616	*FBXL21*	F-box and leucine-rich repeat protein 21
CBC	Module1	ENSG00000129625	*REEP5*	Receptor expression-enhancing protein 5
CBC	Module1	ENSG00000043462	*LCP2*	Lymphocyte cytosolic protein 2
CBC	Module1	ENSG00000137393	*RNF144B*	E3 ubiquitin-protein ligase RNF144B
CBC	Module1	ENSG00000198721	*PECI*	Peroxisomal 3,2-trans-enoyl-CoA isomerase
CBC	Module1	ENSG00000135338	*LCA5*	Lebercilin
CBC	Module1	ENSG00000136250	*AOAH*	Acyloxyacyl hydrolase Precursor
CBC	Module1	ENSG00000147454	*SLC25A37*	Mitoferrin-1
CBC	Module1	ENSG00000104725	*NEFL*	Neurofilament light polypeptide
CBC	Module1	ENSG00000104368	*PLAT*	Tissue-type plasminogen activator Precursor
CBC	Module1	ENSG00000198467	*TPM2*	Tropomyosin beta chain
CBC	Module1	ENSG00000188647	*PTAR1*	Protein prenyltransferase alpha subunit repeat-containing protein 1
CBC	Module1	ENSG00000211044	_	_
CBC	Module1	ENSG00000117525	*F3*	Tissue factor Precursor
CBC	Module1	ENSG00000122862	*SRGN*	Serglycin Precursor
CBC	Module1	ENSG00000165322	*ARHGAP12*	Rho GTPase-activating protein 12
CBC	Module1	ENSG00000171714	*ANO5*	Anoctamin-5
CBC	Module1	ENSG00000149084	*HSD17B12*	Estradiol 17-beta-dehydrogenase 12
CBC	Module1	ENSG00000134574	*DDB2*	DNA damage-binding protein 2
CBC	Module1	ENSG00000139278	*GLIPR1*	Glioma pathogenesis-related protein 1 Precursor
CBC	Module1	ENSG00000110880	*CORO1C*	Coronin-1C
CBC	Module1	ENSG00000141404	*GNAL*	Guanine nucleotide-binding protein G
CBC	Module1	ENSG00000141449	*KIAA1772*	GREB1-like protein
CBC	Module1	ENSG00000154040	*CABYR*	Calcium-binding tyrosine phosphorylation-regulated protein
CBC	Module1	ENSG00000178662	*CSRNP3*	Cysteine/serine-rich nuclear protein 3
CBC	Module1	ENSG00000144285	*SCN1A*	Sodium channel protein type 1 subunit alpha
CBC	Module1	ENSG00000124151	*NCOA3*	Nuclear receptor coactivator 3
CBC	Module1	ENSG00000025772	*TOMM34*	Mitochondrial import receptor subunit TOM34
CBC	Module1	ENSG00000159128	*IFNGR2*	Interferon-gamma receptor beta chain Precursor
CBC	Module1	ENSG00000114439	*BBX*	HMG box transcription factor BBX
CBC	Module1	ENSG00000163840	*DTX3L*	Protein deltex-3-like
CBC	Module1	ENSG00000085276	*MECOM*	Ecotropic virus integration site 1 protein homolog
CBC	Module1	ENSG00000164039	*BDH2*	3-hydroxybutyrate dehydrogenase type 2
CBC	Module1	ENSG00000138735	*PDE5A*	cGMP-specific 3',5'-cyclic phosphodiesterase
CBC	Module1	ENSG00000197062	*ZNF187*	Zinc finger protein 187
CBC	Module1	ENSG00000112511	_	PHD finger protein 1
CBC	Module1	ENSG00000112214	*FHL5*	Four and a half LIM domains protein 5
CBC	Module1	ENSG00000146373	*RNF217*	Probable E3 ubiquitin-protein ligase RNF217
CBC	Module1	ENSG00000077063	*CTTNBP2*	Cortactin-binding protein 2
CBC	Module1	ENSG00000186591	*UBE2H*	Ubiquitin-conjugating enzyme E2 H
CBC	Module1	ENSG00000105855	*ITGB8*	Integrin beta-8 Precursor
CBC	Module1	ENSG00000094841	*UPRT*	Uracil phosphoribosyltransferase
CBC	Module2	ENSG00000171729	*TMEM51*	Transmembrane protein 51

CBC	Module2	ENSG00000117154	*IGSF21*	Immunoglobulin superfamily member 21 Precursor
CBC	Module2	ENSG00000117676	*RPS6KA1*	Ribosomal protein S6 kinase alpha-1
CBC	Module2	ENSG00000171385	*KCND3*	Potassium voltage-gated channel subfamily D member 3
CBC	Module2	ENSG00000175470	*PPP2R2D*	Serine/threonine-protein phosphatase 2A 55 kDa regulatory subunit B delta isoform
CBC	Module2	ENSG00000168496	*FEN1*	Flap endonuclease 1
CBC	Module2	ENSG00000066084	*DIP2B*	Disco-interacting protein 2 homolog B
CBC	Module2	ENSG00000135414	*GDF11*	Growth/differentiation factor 11 Precursor
CBC	Module2	ENSG00000072657	*TRHDE*	Thyrotropin-releasing hormone-degrading ectoenzyme
CBC	Module2	ENSG00000111684	_	Lysophospholipid acyltransferase 5
CBC	Module2	ENSG00000177084	*POLE*	DNA polymerase epsilon catalytic subunit A
CBC	Module2	ENSG00000171723	*GPHN*	Gephyrin
CBC	Module2	ENSG00000140455	*USP3*	Ubiquitin carboxyl-terminal hydrolase 3
CBC	Module2	ENSG00000138604	*GLCE*	D-glucuronyl C5-epimerase
CBC	Module2	ENSG00000169330	*KIAA1024*	UPF0258 protein KIAA1024
CBC	Module2	ENSG00000080644	*CHRNA3*	Neuronal acetylcholine receptor subunit alpha-3 Precursor
CBC	Module2	ENSG00000140873	*ADAMTS18*	A disintegrin and metalloproteinase with thrombospondin motifs 18 Precursor
CBC	Module2	ENSG00000108375	*RNF43*	RING finger protein 43 Precursor
CBC	Module2	ENSG00000132646	*PCNA*	Proliferating cell nuclear antigen
CBC	Module2	ENSG00000149639	*C20orf117*	Uncharacterized protein C20orf117
CBC	Module2	ENSG00000011198	*ABHD5*	1-acylglycerol-3-phosphate O-acyltransferase ABHD5
CBC	Module2	ENSG00000152977	*ZIC1*	Zinc finger protein ZIC 1
CBC	Module2	ENSG00000114767	*RRP9*	U3 small nucleolar RNA-interacting protein 2
CBC	Module2	ENSG00000152208	*GRID2*	Glutamate receptor delta-2 subunit Precursor
CBC	Module2	ENSG00000164100	*NDST3*	Bifunctional heparan sulfate N-deacetylase/N-sulfotransferase 3
CBC	Module2	ENSG00000183783	*KCTD8*	BTB/POZ domain-containing protein KCTD8
CBC	Module2	ENSG00000145335	*SNCA*	Alpha-synuclein
CBC	Module2	ENSG00000196782	*MAML3*	Mastermind-like protein 3
CBC	Module2	ENSG00000164418	*GRIK2*	Glutamate receptor, ionotropic kainate 2 Precursor
CBC	Module2	ENSG00000160967	*CUX1*	Protein CASP
CBC	Module2	ENSG00000185900	_	Protein kinase-like protein SgK196
CBC	Module2	ENSG00000196739	*COL27A1*	Collagen alpha-1
CBC	Module2	ENSG00000130713	*EXOSC2*	Exosome complex exonuclease RRP4
CBC	Module2	ENSG00000136805	*C9orf4*	Uncharacterized protein C9orf4
CBC	Module2	ENSG00000165359	*DDX26B*	Protein DDX26B
CBC	Module2	ENSG00000159023	*EPB41*	Protein 4.1
CBC	Module2	ENSG00000163462	*TRIM46*	Tripartite motif-containing protein 46
CBC	Module2	ENSG00000213341	*CHUK*	Inhibitor of nuclear factor kappa-B kinase subunit alpha
CBC	Module2	ENSG00000070961	*ATP2B1*	Plasma membrane calcium-transporting ATPase 1
CBC	Module2	ENSG00000136112	_	_
CBC	Module2	ENSG00000011638	*TMEM159*	Promethin
CBC	Module2	ENSG00000176476	*CCDC101*	SAGA-associated factor 29 homolog
CBC	Module2	ENSG00000089280	*FUS*	RNA-binding protein FUS
CBC	Module2	ENSG00000141098	*GFOD2*	Glucose-fructose oxidoreductase domain-containing protein 2 Precursor
CBC	Module2	ENSG00000161647	*MPP3*	MAGUK p55 subfamily member 3

CBC	Module2	ENSG00000105698	*USF2*	Upstream stimulatory factor 2
CBC	Module2	ENSG00000198633	*ZNF534*	zinc finger protein 534 isoform 2
CBC	Module2	ENSG00000178171	*FAM123C*	Protein FAM123C
CBC	Module2	ENSG00000048991	*R3HDM1*	R3H domain-containing protein 1
CBC	Module2	ENSG00000135951	*TSGA10*	Testis-specific gene 10 protein
CBC	Module2	ENSG00000153234	*NR4A2*	Nuclear receptor subfamily 4 group A member 2
CBC	Module2	ENSG00000130684	*ZNF337*	Zinc finger protein 337
CBC	Module2	ENSG00000130584	*ZBTB46*	Zinc finger and BTB domain-containing protein 46
CBC	Module2	ENSG00000156983	*BRPF1*	Peregrin
CBC	Module2	ENSG00000154928	*EPHB1*	Ephrin type-B receptor 1 Precursor
CBC	Module2	ENSG00000206562	*METTL6*	Methyltransferase-like protein 6
CBC	Module2	ENSG00000173011	_	Transcriptional adapter 2-beta
CBC	Module2	ENSG00000145536	*ADAMTS16*	A disintegrin and metalloproteinase with thrombospondin motifs 16 Precursor
CBC	Module2	ENSG00000040731	*CDH10*	Cadherin-10 Precursor
CBC	Module2	ENSG00000152822	*GRM1*	Metabotropic glutamate receptor 1 Precursor
CBC	Module2	ENSG00000170260	*ZNF212*	Zinc finger protein 212
CBC	Module2	ENSG00000164778	*EN2*	Homeobox protein engrailed-2
CBC	Module2	ENSG00000106603	*C7orf44*	Uncharacterized protein C7orf44
CBC	Module2	ENSG00000147724	*FAM135B*	Protein FAM135B
CBC	Module2	ENSG00000135643	*KCNMB4*	Calcium-activated potassium channel subunit beta-4
CBC	Module2	ENSG00000175198	*PCCA*	Propionyl-CoA carboxylase alpha chain, mitochondrial Precursor
CBC	Module2	ENSG00000171241	*SHCBP1*	SHC SH2 domain-binding protein 1
CBC	Module2	ENSG00000101773	*RBBP8*	Retinoblastoma-binding protein 8
CBC	Module2	ENSG00000151693	*ASAP2*	Arf-GAP with SH3 domain, ANK repeat and PH domain-containing protein 2
CBC	Module2	ENSG00000135074	*ADAM19*	Disintegrin and metalloproteinase domain-containing protein 19 Precursor
CBC	Module2	ENSG00000013392	*RWDD2A*	RWD domain-containing protein 2A

Table S6. Numbers of probes used in gene expression measurements

Category	Probes	CDS probes*	5'UTR probes	3'UTR probes	Genes
All probes	693765	-	-	-	-
Probes mapped to human genome	680139	504332	55497	77242	24427
Probes mapped to chimpanzee genome	508073	-	-	-	-
Probes mapped to macaque genome	241363	-	-	-	-
Probes mapped to three genomes	209310	172072	11950	17189	19222
Detected in PFC	157072	129821	8683	13529	12447
Detected in CBC	159029	131454	8648	13487	12853
Age-related genes in PFC	119403	99223	6338	10371	8613
Age-related genes in CBC	111052	92408	5831	9382	7988
M1 in PFC	2728	2205	164	264	184
M2 in PFC	2454	2070	106	174	152
M3 in PFC	1783	1436	107	174	117
M4 in PFC	686	594	21	52	44
M5 in PFC	694	600	28	60	43
M1 in CBC	1232	1034	83	81	77
M2 in CBC	1080	919	52	67	71

* The probes mapped to each gene's CDS, 5'UTR, or 3'UTR region are defined based on human Ensembl annotation (version 54).

Table S7 Numbers of sequence reads

Dataset	Brain Region	Species	Age	Total read pairs /reads*	Mapped read pairs /reads**
1	PFC	human	newborn	12986849	11201196
1	PFC	human	young	10867452	9701436
1	PFC	human	old	14164681	11924785
1	PFC	chimpanzee	newborn	14769618	12078817
1	PFC	chimpanzee	young	13339060	11168502
1	PFC	macaque	newborn	12154304	10462467
1	PFC	macaque	young	13886464	11564237
1	CBC	human	newborn	14401087	12005990
1	CBC	human	young	11454526	9916738
1	CBC	human	old	12673390	10272699
1	CBC	chimpanzee	newborn	13241671	10362841
1	CBC	chimpanzee	young	13613681	11439778
1	CBC	macaque	newborn	12902755	10218202
1	CBC	macaque	young	12894566	10829456
2	PFC	human	2	21277649	6091528
2	PFC	human	4	21284713	12168005
2	PFC	human	19	20754409	10852823
2	PFC	human	34	23722421	13465717
2	PFC	human	94	23416250	13482878
2	PFC	human	204	22698303	12883134
2	PFC	human	443	23934412	13388858
2	PFC	human	787	17759057	9763113
2	PFC	human	5105	19901399	10530823
2	PFC	human	9277	23201284	12425625
2	PFC	human	19457	16019209	8908398
2	PFC	human	24090	20948595	11819920
2	PFC	human	32120	21032459	12126368
2	PFC	human	35770	20255260	11991680
2	PFC	chimpanzee	12784	35416060	24424709
2	PFC	chimpanzee	2313	39710284	25801319
2	PFC	chimpanzee	4380	38093774	25712276
2	PFC	chimpanzee	4415	38557113	26315737
2	PFC	chimpanzee	16131	37653869	24892859
2	PFC	chimpanzee	39	38457051	24966833
2	PFC	chimpanzee	8	36272005	25443043
2	PFC	chimpanzee	2920	35829591	24025090
2	PFC	chimpanzee	9855	34651138	22818348
2	PFC	chimpanzee	525	33650766	23380267
2	PFC	chimpanzee	7	36037186	24773786
2	PFC	chimpanzee	1	34551179	23319711

2	PFC	chimpanzee	45	34495444	23955705
2	PFC	chimpanzee	0	33730466	22252447
2	PFC	macaque	1	35647306	22680112
2	PFC	macaque	1	36207576	20633109
2	PFC	macaque	7	35368530	20571126
2	PFC	macaque	16	33944540	19868284
2	PFC	macaque	22	35150179	20191511
2	PFC	macaque	153	36074539	21055294
2	PFC	macaque	207	34525819	19902951
2	PFC	macaque	310	31005239	17038410
2	PFC	macaque	739	32143377	16755158
2	PFC	macaque	1487	30998685	16250594
2	PFC	macaque	3389	32106698	16927367
2	PFC	macaque	5478	31450483	17026329
2	PFC	macaque	8104	28942443	15187912
2	PFC	macaque	9518	29315091	15315768
2	PFC	macaque	10220	29042277	14643836

* Total mapped read pairs were counted for Dataset1 and reads were counted for Dataset2.
** For Dataset1, we require at least one read from a pair of reads to be mapped to the genome.

Table S8. Functional characteristics of genes with human-specific expression

Region	Module		Function annotation	Observed	All	p-value
PFC	**M1**	KEGG	Calcium signaling pathway	10	96	8.00E-03
			Neuroactive ligand-receptor interaction	12	112	1.80E-04
			Long-term potentiation	6	46	3.50E-02
		GO	Signal transduction	74	1805	4.50E-05
			Small gtpase mediated signal transduction	20	311	1.48E-02
			G-protein coupled receptor protein signaling pathway	24	418	1.53E-02
			Calcium ion transport	12	107	3.48E-03
			Gamma-aminobutyric acid signaling pathway	5	17	2.21E-02
			Synaptic transmission	20	231	2.44E-04
			Transport	63	1635	5.48E-03
			Cell-cell signaling	23	345	2.40E-03
			Cell communication	85	2040	8.05E-07
			Ion transport	26	480	1.89E-02
			Cation transport	21	366	4.44E-02
			Regulation of synaptic transmission	10	78	6.22E-03
			Transmission of nerve impulse	22	268	1.60E-04
			Neuropeptide signaling pathway	7	34	6.86E-03
			Neurological system process	26	436	4.03E-03
			Regulation of cell communication	29	536	7.25E-03
			Establishment of localization	63	1646	6.77E-03
			Di-, tri-valent inorganic cation transport	12	120	9.84E-03
		Cell type	Neurons	48	793	2.47E-08
		Structure	Grey-matter	71	794	9.31E-12
PFC	**M2**	GO	Nucleobase, nucleoside, nucleotide and nucleic acid metabolic process	59	1990	1.11E-03
			RNA metabolic process	41	1239	5.95E-03
			Nitrogen compound metabolic process	61	2191	5.44E-03
		Structure	White-matter	6	406	1.63E-02
PFC	**M3**	KEGG	Regulation of actin cytoskeleton	7	107	2.07E-03
			Axon guidance	6	87	4.09E-03
		GO	Cell differentiation	28	793	1.54E-03
			Multicellular organismal development	39	1399	4.17E-03
			Neuron projection development	15	190	3.26E-05
			Cell motion	15	319	1.28E-02
			Cell morphogenesis	18	269	1.88E-05
			Anatomical structure morphogenesis	24	618	1.71E-03
			Nervous system development	29	616	2.84E-06
			Axonogenesis	13	141	4.32E-05
			Neuron development	17	198	1.45E-06
			Neurogenesis	22	316	2.95E-07
			Generation of neurons	21	287	3.17E-07
			Neuron projection morphogenesis	13	162	1.88E-04
			Neuron differentiation	20	256	2.82E-07
			Cell development	23	458	4.01E-05

			Cell morphogenesis involved in neuron differentiation	13	152	9.61E-05
			Cell projection organization	18	263	1.37E-05
			Cell morphogenesis involved in differentiation	13	177	4.75E-04
			Anatomical structure development	41	1274	5.37E-05
			Developmental process	44	1557	5.87E-04
		Cell type	Neurons	24	817	2.36E-03
		Structure	Grey-matter	25	840	7.79E-03
PFC	**M5**	GO	Cell communication	21	2104	3.07E-03
			Regulation of cell	9	556	4.29E-02
		Structure	Grey-matter	17	848	1.26E-03
CBC	**M2**	GO	Regulation of synaptic transmission	5	71	6.03E-02
			Regulation of membrane potential	5	74	7.20E-02

Observed: number of genes that overlap between specific gene set and module
All: number of genes that overlap between specific gene set and all age-related genes
p-value: hypergeometric test p-value after Bonferroni correction for multiple testing.

Table S9. Correlation between neurotransmitter profiles and PFC Module 1 profiles or brain mass changes with age.

		Neurotransmitters		
		Glutamate	GABA	Aspartate
Brain Mass*	Whole lifespan	-0.17	-0.06	0.17
	Development***	-0.16	0.03	0.23
PFC M1*	Whole lifespan	0.18	**-0.30**	**0.30**
	Development	**0.47**	0.05	**0.60**
PFC M1**	Whole lifespan	0.23	-0.29	0.27
(Remove the effect of Brain Mass)	Development	**0.51**	0.05	**0.59**

* The Pearson correlation coefficients were calculated using 15 interpolated points across cubic spline curves per species, or among all species. Significant results are shown in bold (Pearson test $p<0.05$).

** The partial correlation analysis (Kim and Yi 2007) was used to calculate the correlation between age-related neurotransmitter concentration and the PFC M1 mean expression after removing the effect of brain growth. Significant correlation coefficients from the partial correlation analysis are shown in bold ($p<0.05$).

*** Here we used human samples with age < 20 years, chimpanzee < 10 years, macaque <5 years.

Table S10. Overlap of species-specific genes and genes response in neuronal activity.

1. Species-specific gene sets in PFC and CBC

Stimulus	Category	Number	PFC						CBC					
			human (702)		chimp. (55)		macaque (239)		human (260)		chimp. (82)		macaque (460)	
			num	p-value	num	p-value	num	p-value	num	p-value	num	p-value	num	p-value
BIC	up-regulated	336	31	3.16E-04	1	7.24E-01	6	6.33E-01	12	2.11E-02	1	8.63E-01	9	5.62E-01
KCl	up-regulated	947	75	2.58E-03	5	5.13E-01	17	6.83E-01	34	1.75E-03	3	9.37E-01	35	3.81E-01
BIC	down-regulated	117	8	1.33E-01	1	3.30E-01	6	1.47E-02	2	5.52E-01	0	1.00E+00	2	7.55E-01
KCl	down-regulated	769	31	9.46E-01	1	9.64E-01	11	7.56E-01	4	1.00E+00	4	6.09E-01	21	8.17E-01

2. Five human-specific expression Modules in PFC

Stimulus	Category	Number	M1 (184)		M2 (152)		M3 (117)		M4 (44)		M5 (43)	
			num	p-value	num	p-value	num	p-value	num	p-value	num	p-value
BIC	up-regulated	336	13	7.89E-05	2	9.19E-01	7	2.80E-02	0	1.00E+00	0	1.00E+00
KCl	up-regulated	947	24	1.05E-02	11	6.13E-01	19	3.71E-03	7	7.73E-02	1	9.66E-01
BIC	down-regulated	117	6	1.36E-03	0	1.00E+00	2	2.36E-01	0	1.00E+00	0	1.00E+00
KCl	down-regulated	769	7	9.13E-01	2	9.98E-01	7	6.13E-01	3	5.57E-01	3	4.06E-01

num: number of overlap genes between two gene sets
p-value: one-sided Fisher's exact test

Table S11. List of Module 1 genes that are up-regulated by neuronal activation.

Stimulus	Ensemble Gene ID	HGNC ID	Description
BIC	ENSG00000197991	*PCDH20*	Protocadherin-20 Precursor
BIC	ENSG00000198838	*RYR3*	Ryanodine receptor 3
BIC	ENSG00000168702	*LRP1B*	Low-density lipoprotein receptor-related protein 1B Precursor
BIC	ENSG00000169271	*HSPB3*	Heat shock protein beta-3
BIC	ENSG00000185053	*SGCZ*	Zeta-sarcoglycan
BIC	ENSG00000078725	*DBC1*	Deleted in bladder cancer protein 1 Precursor
BIC	ENSG00000133019	*CHRM3*	Muscarinic acetylcholine receptor M3
BIC	ENSG00000176697	*BDNF*	Brain-derived neurotrophic factor Precursor
BIC	ENSG00000058335	*RASGRF1*	Ras-specific guanine nucleotide-releasing factor 1
BIC	ENSG00000115896	*PLCL1*	Inactive phospholipase C-like protein 1
BIC	ENSG00000138411	*HECW2*	E3 ubiquitin-protein ligase HECW2
BIC	ENSG00000163285	*GABRG1*	Gamma-aminobutyric acid receptor subunit gamma-1 Precursor
BIC	ENSG00000147724	*FAM135B*	Protein FAM135B
KCl	ENSG00000060140	*STYK1*	Tyrosine-protein kinase STYK1
KCl	ENSG00000197991	*PCDH20*	Protocadherin-20 Precursor
KCl	ENSG00000198838	*RYR3*	Ryanodine receptor 3
KCl	ENSG00000138028	*CGREF1*	Cell growth regulator with EF hand domain protein 1
KCl	ENSG00000168702	*LRP1B*	Low-density lipoprotein receptor-related protein 1B Precursor
KCl	ENSG00000169271	*HSPB3*	Heat shock protein beta-3
KCl	ENSG00000152932	*RAB3C*	Ras-related protein Rab-3C
KCl	ENSG00000006128	*TAC1*	Protachykinin-1 Precursor
KCl	ENSG00000078725	*DBC1*	Deleted in bladder cancer protein 1 Precursor
KCl	ENSG00000162631	*NTNG1*	Netrin-G1 Precursor
KCl	ENSG00000133019	*CHRM3*	Muscarinic acetylcholine receptor M3
KCl	ENSG00000176697	*BDNF*	Brain-derived neurotrophic factor Precursor
KCl	ENSG00000139645	*ANKRD52*	Serine/threonine-protein phosphatase 6 regulatory ankyrin repeat subunit C
KCl	ENSG00000166068	*SPRED1*	Sprouty-related, EVH1 domain-containing protein 1
KCl	ENSG00000058335	*RASGRF1*	Ras-specific guanine nucleotide-releasing factor 1
KCl	ENSG00000131242	*RAB11FIP4*	Rab11 family-interacting protein 4
KCl	ENSG00000162975	*KCNF1*	Potassium voltage-gated channel subfamily F member 1
KCl	ENSG00000115896	*PLCL1*	Inactive phospholipase C-like protein 1
KCl	ENSG00000138411	*HECW2*	E3 ubiquitin-protein ligase HECW2
KCl	ENSG00000163285	*GABRG1*	Gamma-aminobutyric acid receptor subunit gamma-1 Precursor
KCl	ENSG00000151834	*GABRA2*	Gamma-aminobutyric acid receptor subunit alpha-2 Precursor
KCl	ENSG00000183775	*KCTD16*	BTB/POZ domain-containing protein KCTD16
KCl	ENSG00000185345	*PARK2*	E3 ubiquitin-protein ligase parkin
KCl	ENSG00000147724	*FAM135B*	Protein FAM135B

Table S12 Correlations between expression profiles of neuron-, synapse-, and MEF2A- related genes and PFC Module 1 genes.

		PFC		CBC	
Gene set	Description	PFC M1*	Others	PFC M1	Others
Neuron	Neuron-specific genes	0.039	-0.004	-0.022	-0.024
Neuron.exp	Genes highly expressed in neurons	-0.011	0.004	0.025	0.048
Synapse	Synapse-related genes	0.134	-0.004	0.021	0.034
MEF2A.exp	Activity-dependent targets of MEF2A	0.300	-0.035	0.002	0.098
MEF2A.pre	MEF2A predicted targets	0.138	-0.010	0.028	0.038

* The Pearson correlation coefficients were calculated using 15 interpolated points across cubic spline curves per species (Supplementary Information). The table shows the median correlation coefficient between each gene per gene set and each PFC Module 1 gene (PFC M1) or non-PFC Module 1 gene (Others).

Supplementary references

Ashburner M, Ball CA, Blake JA, Botstein D, Butler H, Cherry JM, Davis AP, Dolinski K, Dwight SS, Eppig JT et al. 2000. Gene Ontology: tool for the unification of biology. *Nat Genet* **25**(1): 25-29.

Cahoy JD, Emery B, Kaushal A, Foo LC, Zamanian JL, Christopherson KS, Xing Y, Lubischer JL, Krieg PA, Krupenko SA et al. 2008. A transcriptome database for astrocytes, neurons, and oligodendrocytes: a new resource for understanding brain development and function. *J Neurosci* **28**(1): 264-278.

Clancy B, Darlington RB, Finlay BL. 2001. Translating developmental time across mammalian species. *Neuroscience* **105**(1): 7-17.

de Magalhães J, Costa J. 2009. A database of vertebrate longevity records and their relation to other life-history traits. *J Evol Biol* **22**(8): 1770-1774.

Erraji-Benchekroun L, Underwood MD, Arango V, Galfalvy H, Pavlidis P, Smyrniotopoulos P, Mann JJ, Sibille E. 2005. Molecular aging in human prefrontal cortex is selective and continuous throughout adult life. *Biol Psychiatry* **57**(5): 549.

Faraway J. 2002. Practical Regression and ANOVA Using R. Available at: http://cran.rproject.org/doc/contrib/Faraway-PRA.pdf. .

Flavell SW, Kim TK, Gray JM, Harmin DA, Hemberg M, Hong EJ, Markenscoff-Papadimitriou E, Bear DM, Greenberg ME. 2008. Genome-wide analysis of MEF2 transcriptional program reveals synaptic target genes and neuronal activity-dependent polyadenylation site selection. *Neuron* **60**(6): 1022-1038.

Fu X, Fu N, Guo S, Yan Z, Xu Y, Hu H, Menzel C, Chen W, Li Y, Zeng R et al. 2009. Estimating accuracy of RNA-Seq and microarrays with proteomics. *BMC Genomics* **10**: 161.

Fu X, Giavalisco P, Liu X, Catchpole G, Fu N, Ning ZB, Guo S, Yan Z, Somel M, Pääbo S et al. 2011. Rapid metabolic evolution in human prefrontal cortex. *Proc Natl Acad Sci U S A* **108**(15): 6181-6186.

Gautier L, Cope L, Bolstad BM, Irizarry RA. 2004. affy--analysis of Affymetrix GeneChip data at the probe level. *Bioinformatics* **20**(3): 307-315.

Glantz LA, Gilmore JH, Hamer RM, Lieberman JA, Jarskog LF. 2007. Synaptophysin and postsynaptic density protein 95 in the human prefrontal cortex from mid-gestation into early adulthood. *Neuroscience* **149**(3): 582-591.

Green RE, Krause J, Briggs AW, Maricic T, Stenzel U, Kircher M, Patterson N, Li H, Zhai W, Fritz MH et al. 2010. A draft sequence of the Neandertal genome. *Science* **328**(5979): 710-722.

Haygood R, Fedrigo O, Hanson B, Yokoyama K, Wray GA. 2007. Promoter regions of many neural- and nutrition-related genes have experienced positive selection during human evolution. *Nat Genet* **39**(9): 1140-1144.

Hinds DA, Stuve LL, Nilsen GB, Halperin E, Eskin E, Ballinger DG, Frazer KA, Cox DR. 2005. Whole-genome patterns of common DNA variation in three human populations. *Science* **307**(5712): 1072-1079.

Hubbard TJP, Aken BL, Beal K, Ballester B, Caccamo M, Chen Y, Clarke L, Coates G, Cunningham F, Cutts T et al. 2007. Ensembl 2007. *Nucl Acids Res* **35**(suppl_1): D610-617.

Kanehisa M, Araki M, Goto S, Hattori M, Hirakawa M, Itoh M, Katayama T, Kawashima S, Okuda S, Tokimatsu T et al. 2008. KEGG for linking genomes to life and the environment. *Nucleic Acids Res* **36**(Database issue): D480-484.

Karolchik D, Kuhn RM, Baertsch R, Barber GP, Clawson H, Diekhans M, Giardine B, Harte RA, Hinrichs AS, Hsu F et al. 2008. The UCSC Genome Browser Database: 2008 update. *Nucleic Acids Res* **36**(Database issue): D773-779.

Kel AE, Gössling E, Reuter I, Cheremushkin E, Kel-Margoulis OV, Wingender E. 2003. MATCH: A tool for searching transcription factor binding sites in DNA sequences. *Nucleic Acids Res* **31**(13): 3576-3579.

Khaitovich P, Hellmann I, Enard W, Nowick K, Leinweber M, Franz H, Weiss G, Lachmann M, Pääbo S. 2005. Parallel Patterns of Evolution in the Genomes and Transcriptomes of Humans and Chimpanzees. *Science* **309**(5742): 1850-1854.

Kim SH, Yi SV. 2007. Understanding relationship between sequence and functional evolution in yeast proteins. *Genetica* **131**(2): 151-156.

Langmead B, Trapnell C, Pop M, Salzberg SL. 2009. Ultrafast and memory-efficient alignment of short DNA sequences to the human genome. *Genome Biol* **10**(3): R25.

Leigh S. 2004. Brain growth, life history, and cognition in primate and human evolution. *Am J Primatol* **62**(3): 139-164.

Lu L, Airey DC, Williams RW. 2001. Complex trait analysis of the hippocampus: mapping and biometric analysis of two novel gene loci with specific effects on hippocampal structure in mice. *J Neurosci* **21**(10): 3503-3514.

Mortazavi A, Williams BA, McCue K, Schaeffer L, Wold B. 2008. Mapping and quantifying mammalian transcriptomes by RNA-Seq. *Nat Meth* **5**(7): 621-628.

Shupe JM, Kristan DM, Austad SN, Stenkamp DL. 2006. The eye of the laboratory mouse remains anatomically adapted for natural conditions. *Brain Behav Evol* **67**(1): 39-52.

Siepel A, Bejerano G, Pedersen JS, Hinrichs AS, Hou M, Rosenbloom K, Clawson H, Spieth J, Hillier LW, Richards S et al. 2005. Evolutionarily conserved elements in vertebrate, insect, worm, and yeast genomes. *Genome Res* **15**(8): 1034-1050.

Smith BH, Crummett TL, Brandt KL. 1994. Ages of eruption of primate teeth: A compendium for aging individuals and comparing life histories. *Am J Phys Anthropol* **37**(S19): 177-231.

Sokal RR, Rohlf FJ. 1995. *Biometry*. Freeman, New York.

Somel M, Franz H, Yan Z, Lorenc A, Guo S, Giger T, Kelso J, Nickel B, Dannemann M, Bahn S et al. 2009. Transcriptional neoteny in the human brain. *Proc Natl Acad Sci U S A* **106**(14): 5743-5748.

Somel M, Guo S, Fu N, Yan Z, Hu HY, Xu Y, Yuan Y, Ning Z, Hu Y, Menzel C et al. 2010. MicroRNA, mRNA, and protein expression link development and aging in human and macaque brain. *Genome Res* **20**(9): 1207-1218.

Trapnell, Williams, Pertea, Mortazavi, Kwan, Baren v, Salzberg, Wold, Pachter. 2010. Transcript assembly and abundance estimation from RNA-Seq reveals thousands of new transcripts and switching among isoforms.

Trapnell C, Pachter L, Salzberg SL. 2009. TopHat: discovering splice junctions with RNA-Seq. *Bioinformatics* **25**(9): 1105-1111.

Xie X, Lu J, Kulbokas EJ, Golub TR, Mootha V, Lindblad-Toh K, Lander ES, Kellis M. 2005. Systematic discovery of regulatory motifs in human promoters and 3' UTRs by comparison of several mammals. *Nature* **434**(7031): 338.

Yuan Y, Chen YP, Ni S, Xu AG, Tang L, Vingron M, Somel M, Khaitovich P. 2011. Development and application of a modified dynamic time warping algorithm (DTW-S) to analyses of primate brain expression time series. *BMC Bioinformatics* **12**(1): 347.