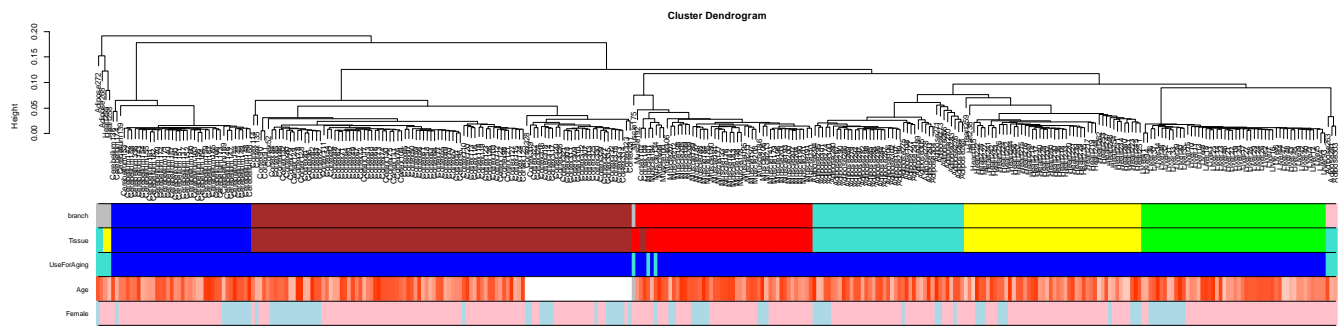
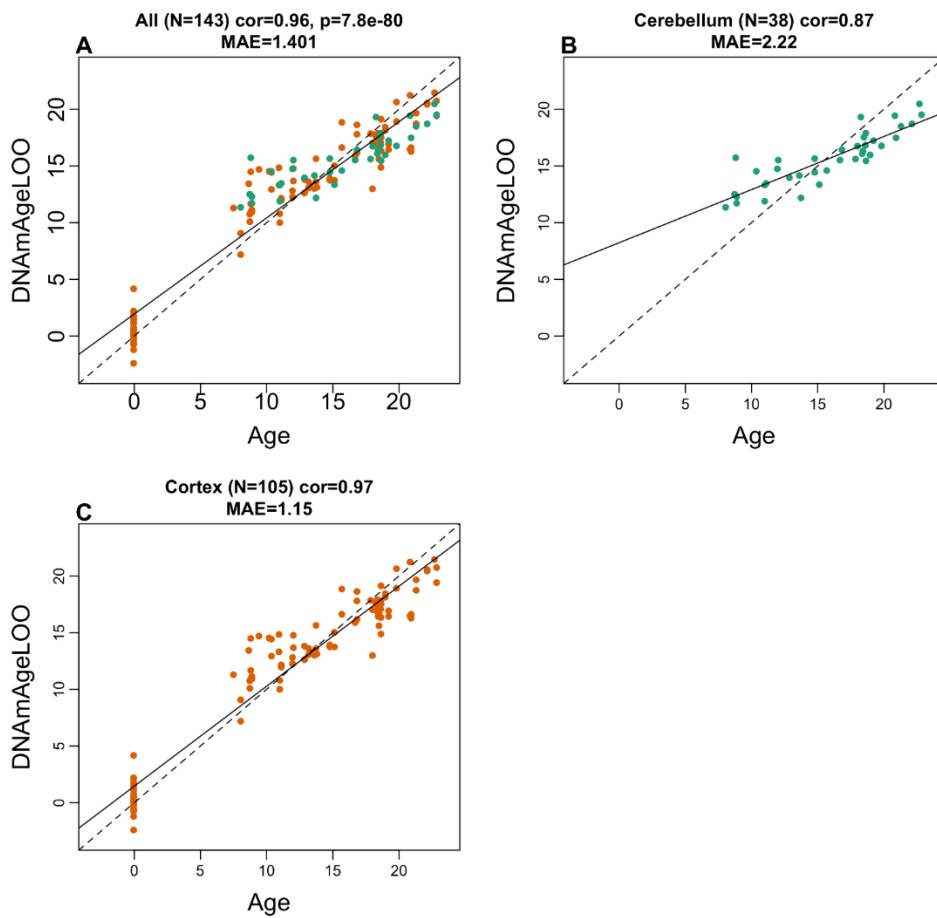


SUPPLEMENTARY MATERIAL



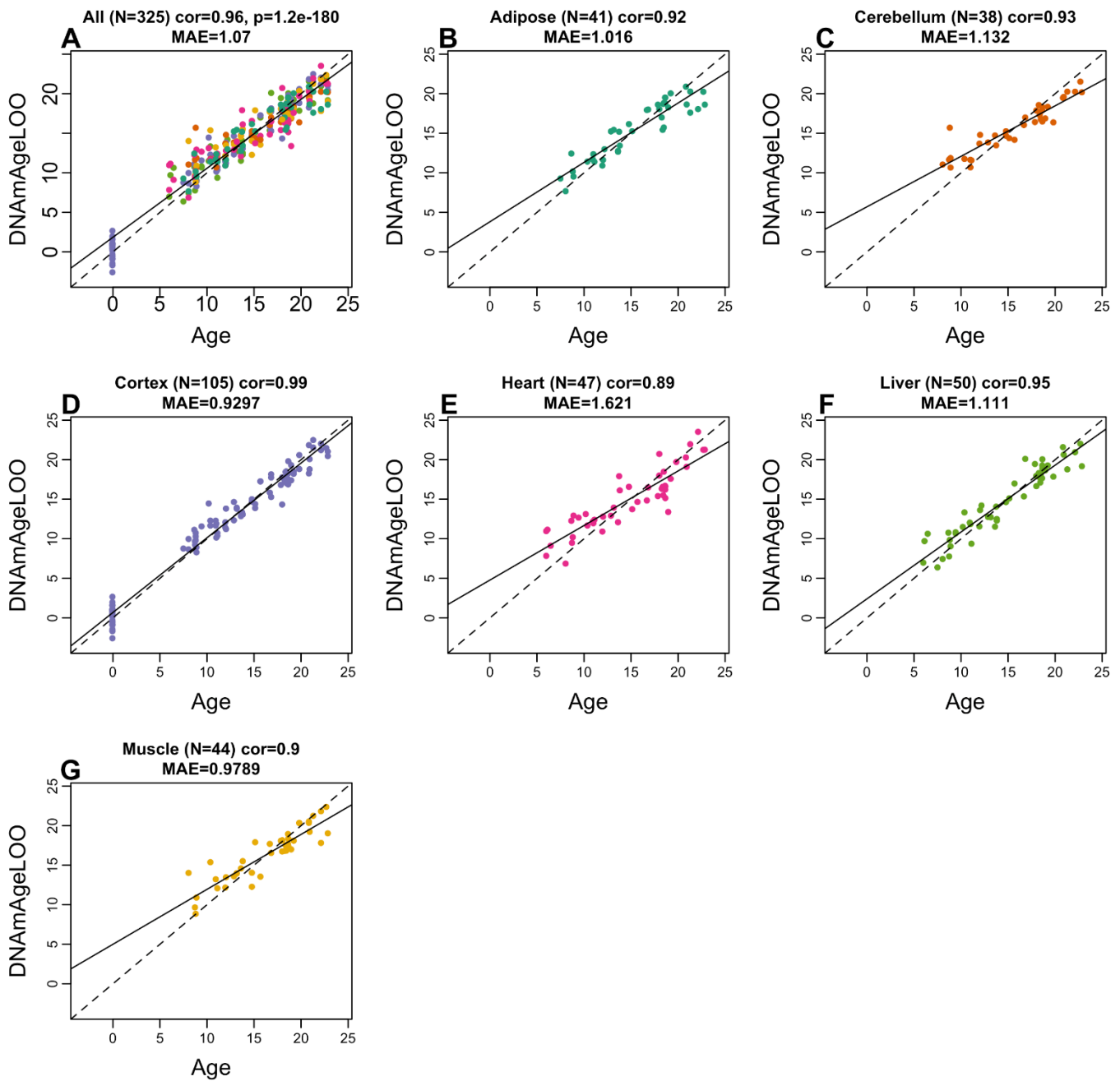
Supplementary Figure S1. Unsupervised hierarchical clustering of tissue samples from baboons. Average linkage hierarchical clustering based on the interarray correlation coefficient (Pearson correlation). A height cut-off of 0.07 led to branch colors that largely correspond to Tissue type (second panel): cerebral cortex=brown, muscle=red, heart=yellow, liver=green, adipose=turquoise, cerebellum=blue. A handful of outlying arrays were removed from the analysis (turquoise color in the third color band). Branches largely correspond to tissue type as one can see by comparing the first two color bands.

DNAmAgeLOO for Olive Baboon Brain, by Region



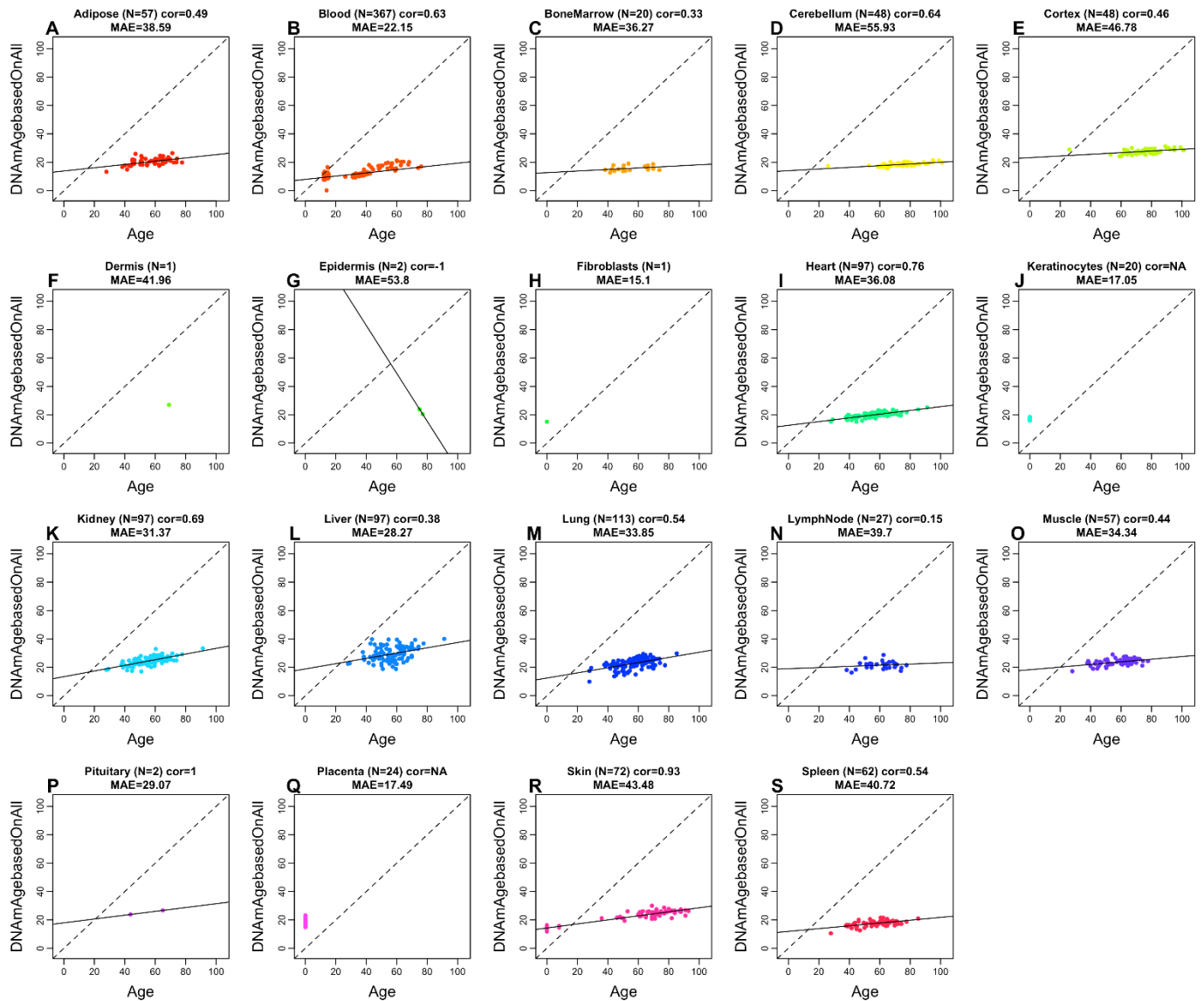
Supplementary Figure S2. Baboon brain clock Leave-one-sample-out estimate of age based on DNA methylation data (y-axis) versus chronological age (in units of years). A) The brain clock was developed using cerebellum, frontal cortex and temporal cortex samples. Results restricted to B) cerebellar samples and C) cortical samples. Each title reports the sample size, Pearson correlation coefficient and median absolute deviation (median error).

DNAmAgeLOO for Olive Baboon, by Tissue

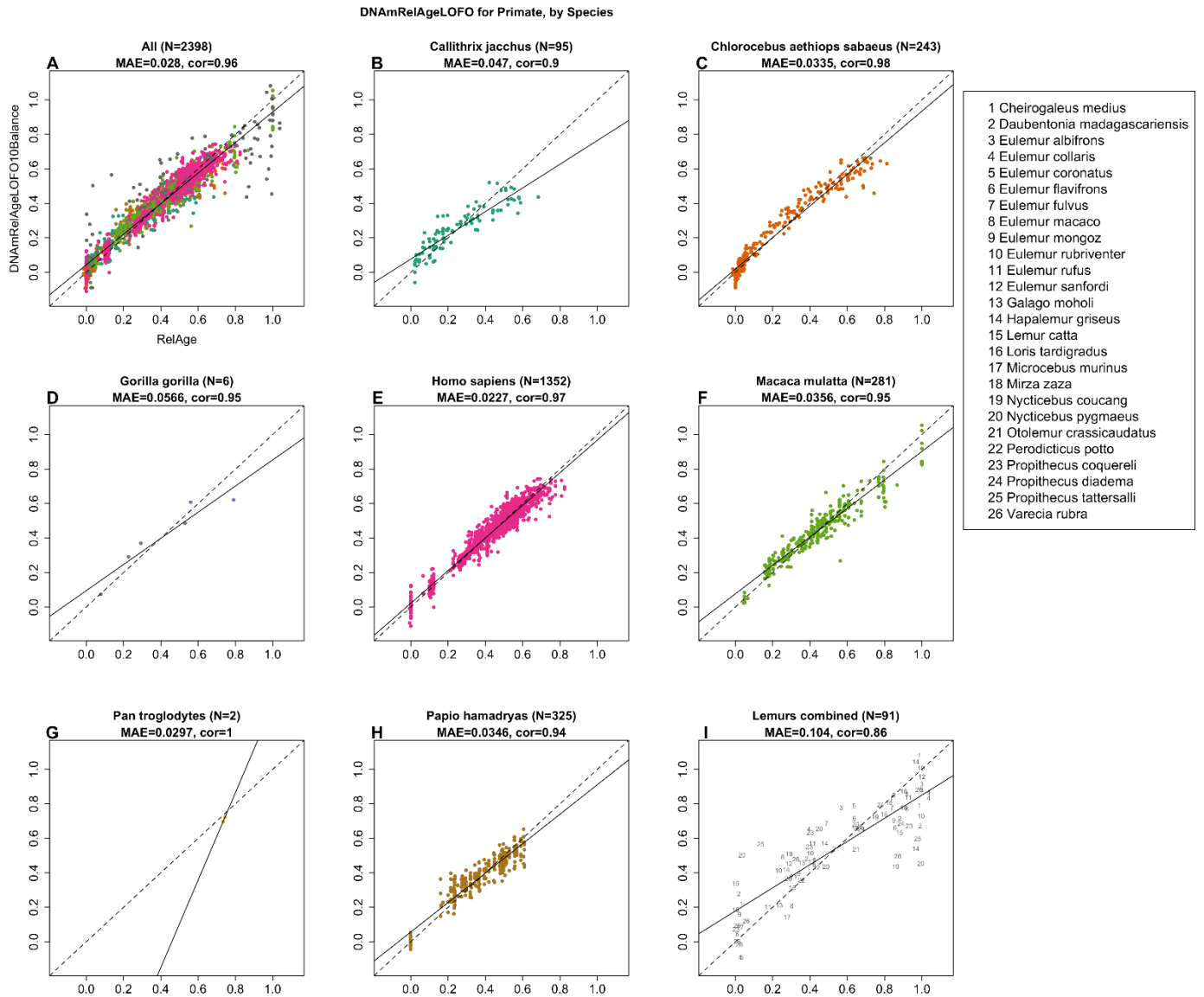


Supplementary Figure S3. Pan-tissue baboon epigenetic clock. Leave-one-sample-out estimate of age based on DNA methylation data (y-axis) versus chronological age (in units of years). Results for A) all tissues, B) adipose, C) brain cerebellum, D) cerebellar cortex, E) heart, F) liver, G) skeletal muscle. Each panel reports the sample size, Pearson correlation coefficient and median absolute deviation (median error).

Subset_Baboon_Clock_subCPGbaboon_basedOnAll_EpigeneticAge_toHuman

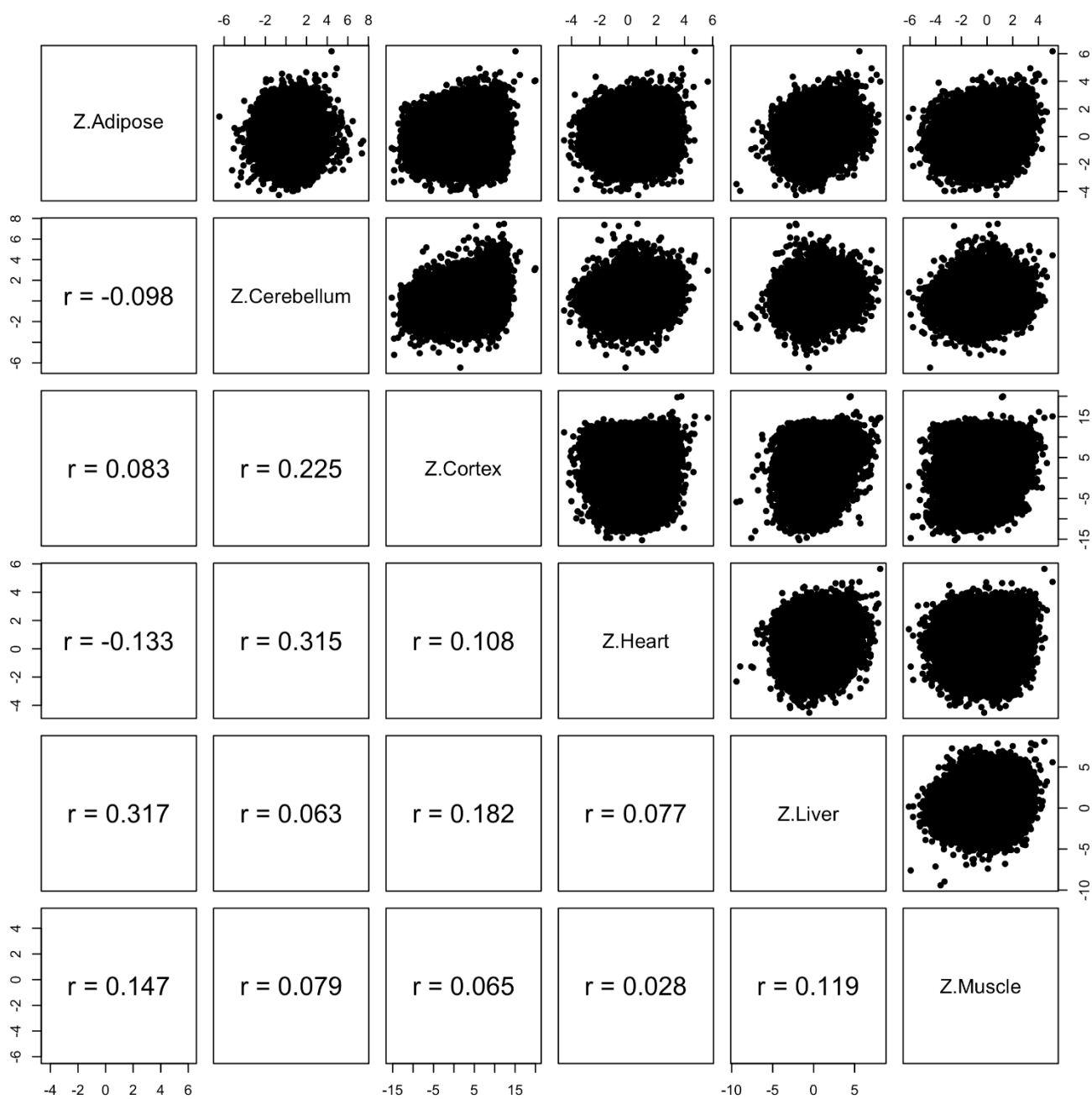


Supplementary Figure S4. Pan-tissue clock from baboons applied to human tissues. Baboon pan-tissue clock (trained on baboon tissues) applied to human A) adipose, B) blood, C) bone marrow, D) dermis, E) epidermis, F) fibroblasts G) heart, H) keratinocytes, I) kidney, J) liver, K) lung, L) lymph node, M) muscle, N) pituitary gland, O) skin, P) spleen. Estimate age based on the baboon pan tissue clock (y-axis) versus chronological age in humans (in units of years). Title: sample size, Pearson correlation coefficient and median absolute deviation (median error).

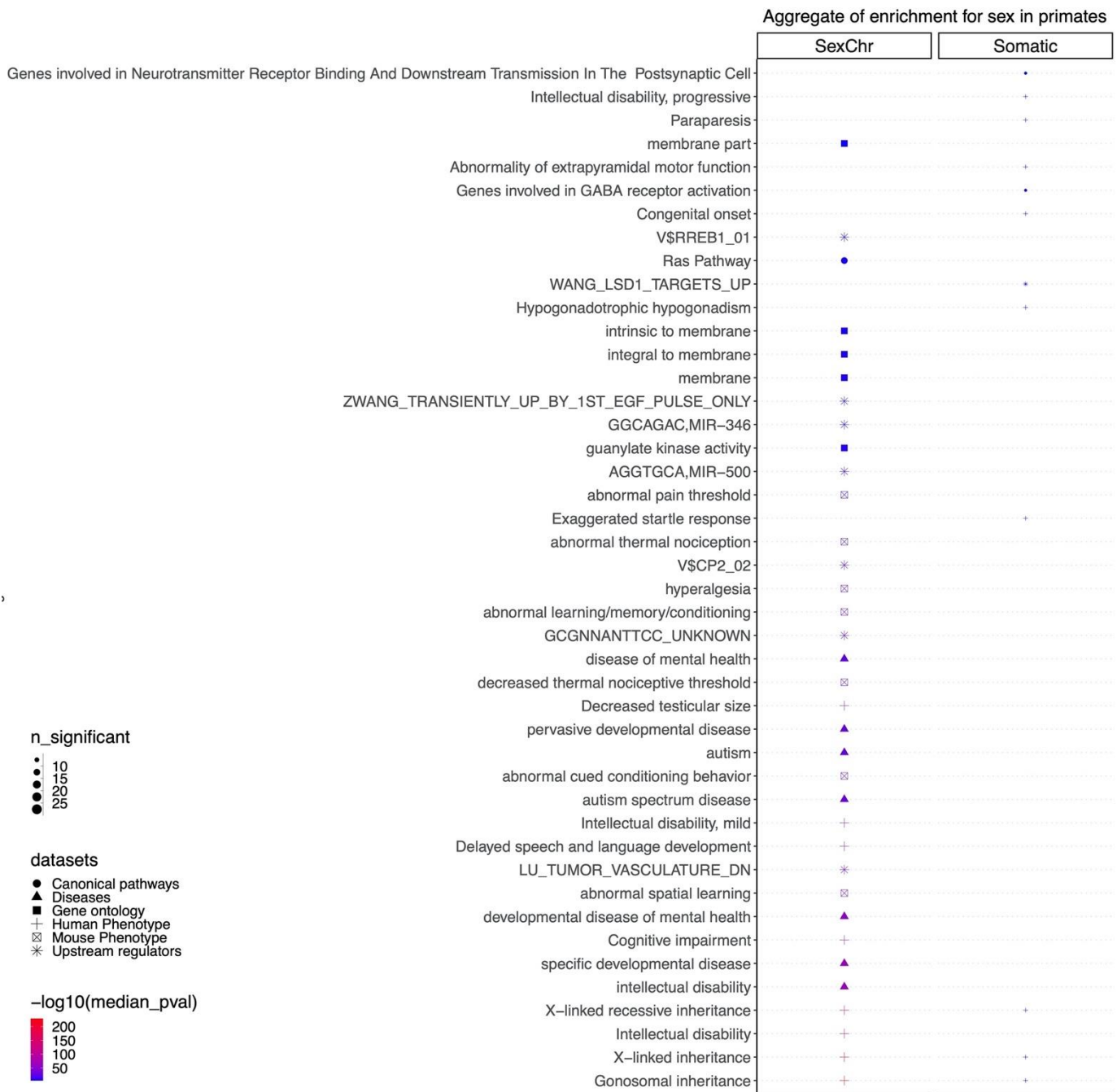


Supplementary Figure S5. Primate clock for relative age. A) Epigenetic clock based on tissues from all primate species (colored by species as indicated in the other panels). B-I) are excerpts from panel A but restricted to specific species mentioned in the title. I) Samples (dots) are blood and skin samples from 26 species of strepsirrhines as indicated in legend.

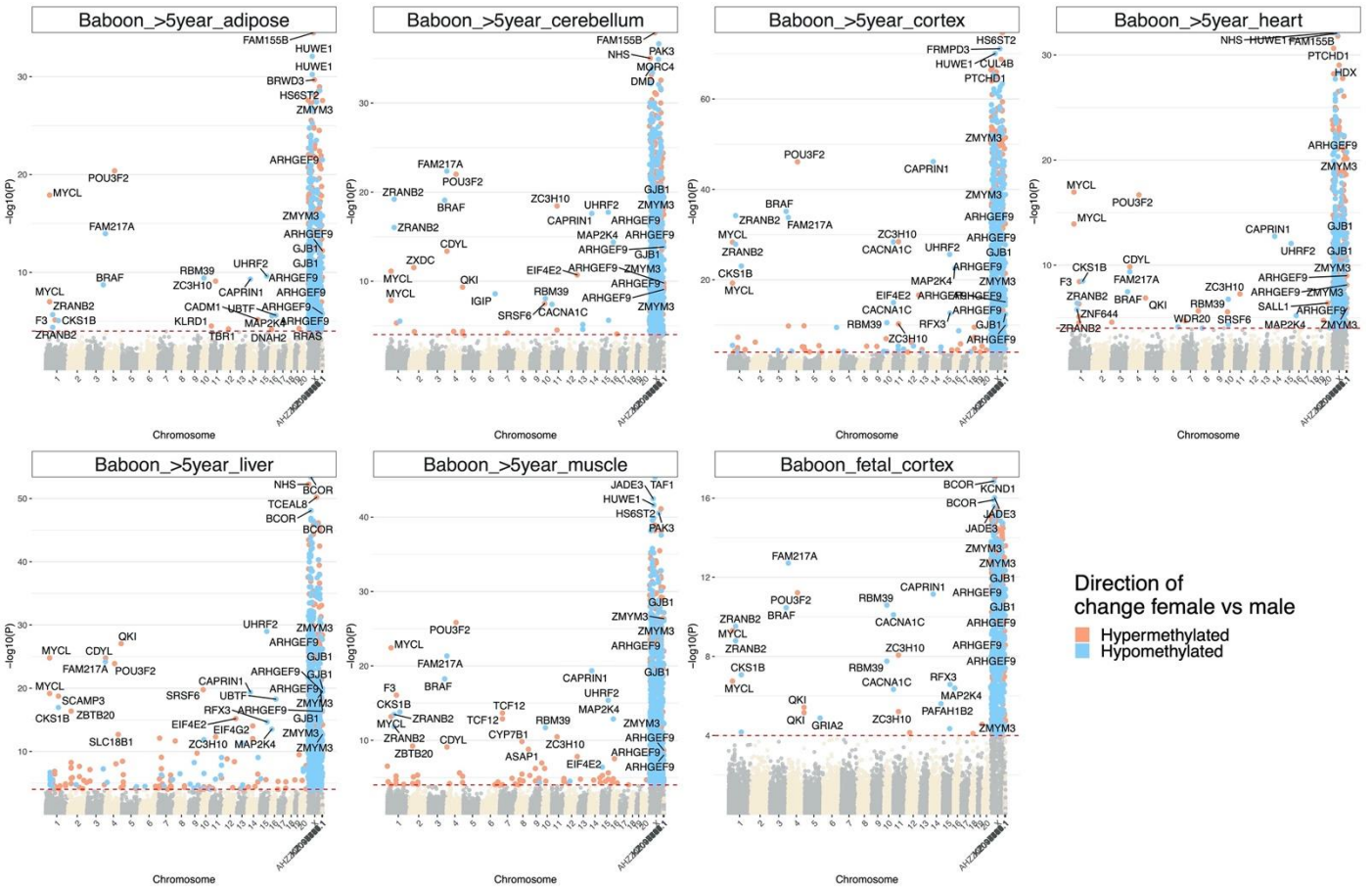
Relative age is defined as the ratio of chronological age with the maximum lifespan of the species. The maximum lifespan of each species is reported in a Supplementary Table. Relative age (x-axis) versus the ten-fold cross validation (balanced by species) of relative age based on methylation (y-axis). Each panel reports the sample size, correlation coefficient, median absolute error (MAE). Dots are colored by species. The primate clock was developed by regressing relative age on cytosines that map to baboons and humans. Details can be found in the Supplement.



Supplementary Figure S6. Epigenome wide association study of correlation in different baboon tissues. Each dot corresponds to a CpG. Z statistics for a correlation test of age in adipose, cerebellum, brain cortex, heart, liver, muscle, temporal cortex.



Supplementary Figure S7. Enrichment analysis of sex-related CpGs in primate tissues by sex chromosomes. The figure summarizes the results of 27 EWAS of sex corresponding to 27 different strata comprised by primate species and tissue type. For each term (y-axis) we obtained 27 enrichment p values (hypergeometric test) corresponding to the 27 strata. These 27 p values were summarized by their median value. This unusual meta analysis approach leads to a *descriptive* measure of significance as opposed to an inferential measure. The size of the symbol (n_significant) corresponds to the number of times that a term was significant ($p < 0.001$) across the 27 analyzed datasets. The top three enriched datasets from each category (Canonical pathways, diseases, gene ontology, human and mouse phenotypes, and upstream regulators) were selected and further filtered for significance at median pvalue $< 10^{-5}$. We excluded marmosets from the analysis for reasons mentioned in the text.

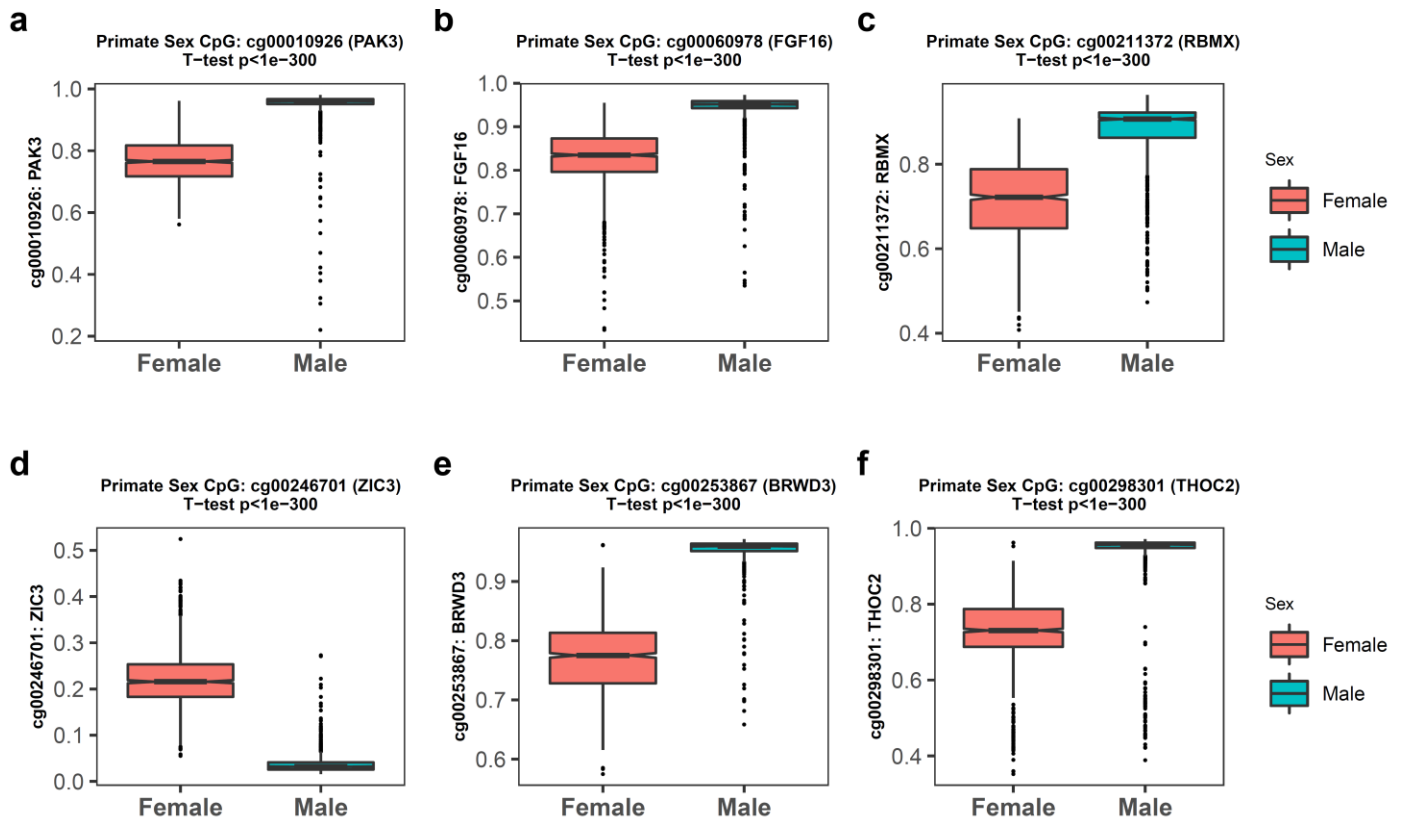


Supplementary Figure S8. Manhattan plots of sex difference in baboon samples. The coordinates are estimated based on the alignment of Mammalian array probes to Panu_3.0.100 genome assembly. The direction of change for female vs male with $p < 10^{-4}$ (red dotted line) is highlighted by red (increased methylation in females compared to males) and blue (decreased methylation in females) colors. The top 5 X chromosomal CpGs, and top 30 non-X chromosomal markers (i.e. autosomal) CpGs were labeled by neighboring genes.

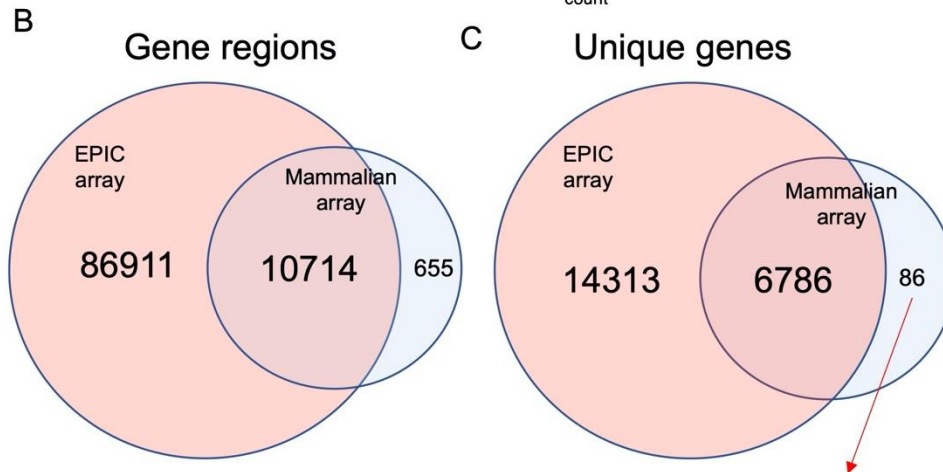
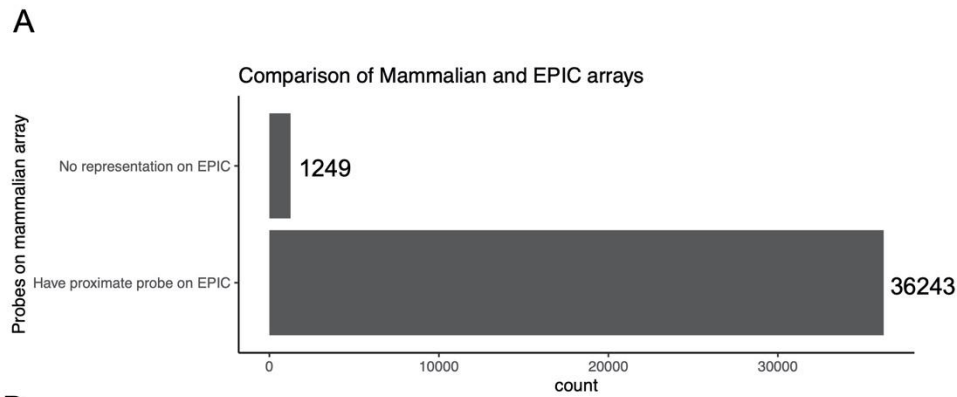
Enrichment for GO, Pathways, disease, phenotypes, upstream regulators



Supplementary Figure S9. Enrichment analysis of the top CpGs associated with sex in baboons. The gene level enrichment was done using GREAT analysis and human Hg19 background. The background probes were limited to probes that were mapped to the same gene in the olive baboon genome. The top two enriched datasets from each category (Canonical pathways, diseases, gene ontology, human and mouse phenotypes, and upstream regulators) were selected and further filtered for significance at $p < 10^{-10}$.

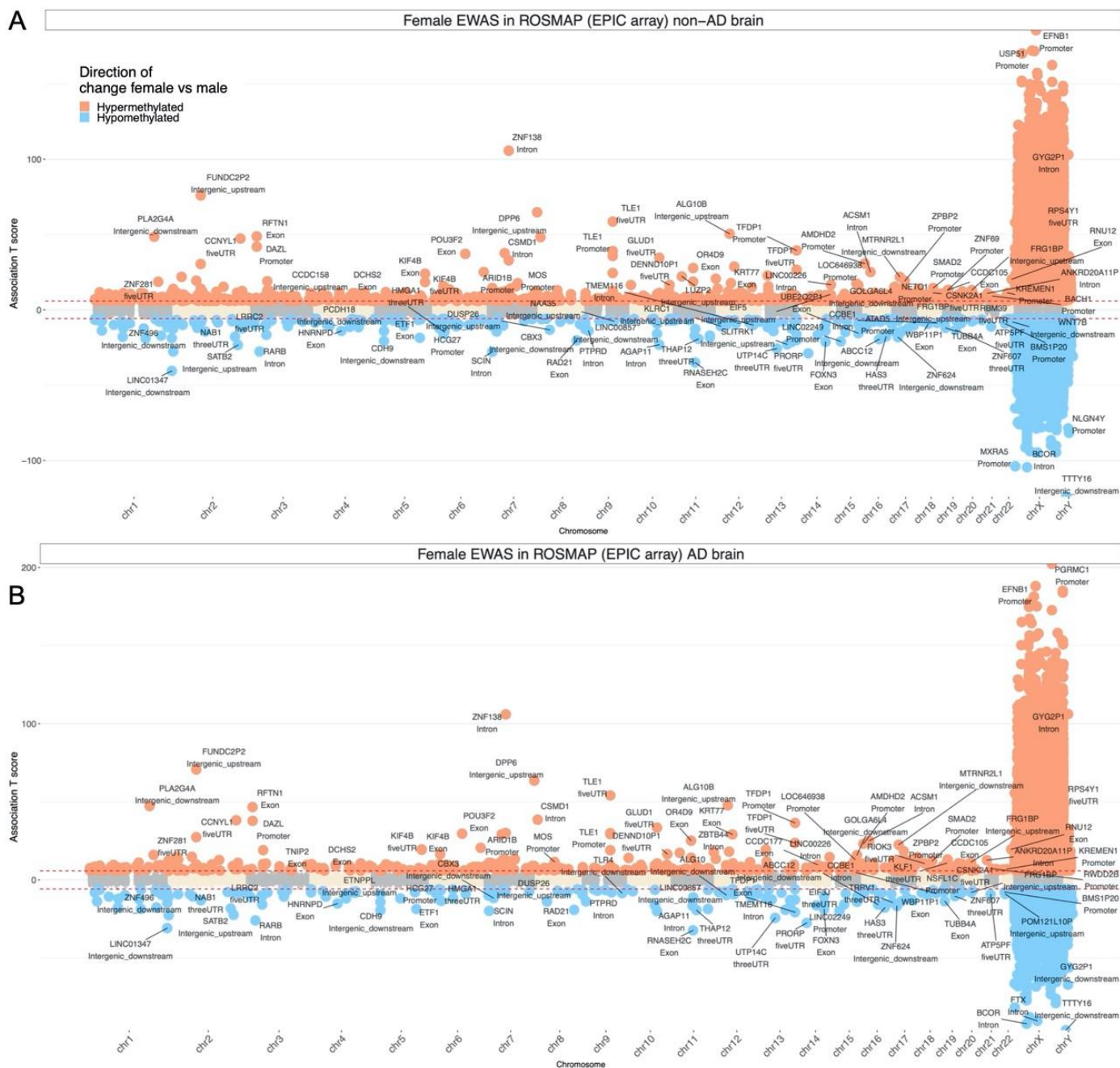


Supplementary Figure S10. Select CpGs that are highly associated with sex in primates. Each panel presents a CpG (and adjacent gene) that is highly associated with sex across all primate species. Student T-test p values.



PELO ; ZBTB12 ; MAB21L2 ; MIR181A1 ; FMC1-LUC7L2 ; EWSAT1 ; RBM12 ; HOXC6 ; MIRLETTG ; CHIC2 ; DKFZP434H168 ; ZNF551 ; MMP24 ; PAX6-AS1 ; ASPA ; MIR30E ; HOXB5 ; MIR618 ; MIR3184 ; MAZ ; CORO1A ; SNORA16A ; LOC100130872 ; HOXA6 ; ALDOA ; SENCN ; HOXB4 ; ZBED6CL ; DUSP8 ; DLX6 ; MIR181A2HG ; ITGB1BP2 ; MIR218-1 ; MIR1306 ; PDCD1LG2 ; OR51B5 ; STARD10 ; NONO ; GABPB1-IT1 ; CDSN ; KCNQ1OT1 ; MIR330 ; MIR628 ; MIR22 ; MIR301A ; MIR26A1 ; TBC1D10C ; MRPL38 ; CNKSR3 ; PRR34-AS1 ; PITPNM2-AS1 ; MIR217 ; MIR5047 ; LOC100126784 ; DNAL4 ; MIR142 ; MIR136 ; MIR133A1 ; MIR99A ; SDCBP2-AS1 ; PRRT2 ; UBE2F ; POC1B-GALNT4 ; LRRTM2 ; MIR423 ; MIR3064 ; LRTM2 ; MIR127 ; GSTM4 ; APOBEC2 ; MIR383 ; RFX4 ; MIR3652 ; ADORA2A ; HOXA5 ; SMG1P1 ; CHERP ; MIR499A ; MIR54814 ; SNORA50A ; MIR3618 ; MIR10A ; MIR3666 ; MIR5004 ; KCTD13 ; ASF1A

Supplementary Figure S11. Mammalian array compared to the human Illumina EPIC array. The EPIC array covers most of the genomic regions represented on mammalian array. A) Most of the mammalian array probes are located on gene regions that have at least one probe represented on the EPIC array. B) Venn Diagram visualizing the overlap between gene regions covered by the EPIC array and the mammalian array. Most of the gene regions on the mammalian array are also covered in EPIC array. C) Venn Diagram visualizing the overlap between genes covered by the EPIC array and the mammalian array. There are 86 genes that are specifically presented on mammalian but not the EPIC array.



Supplementary Figure S12. Sex differences in DNAm pattern in human postmortem prefrontal cortex samples. Results for individuals with (A) and without (B) Alzheimer’s disease (AD) neuropathology. Sex differences were adjusted for age in the model. The red lines represent T scores at $p < 10^{-8}$. The EWAS results of sex are based on human, baboon, Baboon, rhesus macaque.

Supplementary Tables

Row	Species	CommonName	N	N.Female	N.Blood	N.Skin	N.Liver	N.Cortex	Age.M in	Age.M ed	Age.M ax
1	Callithrix geoffroyi	White-fronted marmoset	1	1	1	0	0	0	18.2	18.2	18.2
2	Callithrix jacchus	Common marmoset	95	45	95	0	0	0	0.5	4.4	15.6
3	Cheirogaleus medius	Fat-tailed dwarf lemur	3	0	2	1	0	0	1.0	29.6	29.6
4	Chlorocebus aethiops sabaeus	Vervet monkey	243	152	144	0	48	48	-0.4	3.1	25.0
5	Daubentonia madagascariensis	Aye-aye	4	3	3	1	0	0	0.7	23.4	36.7
6	Eulemur albifrons	White-headed lemur	3	2	2	1	0	0	19.7	34.6	34.6
7	Eulemur collaris	Collared brown lemur	4	3	3	1	0	0	0.8	23.4	33.8
8	Eulemur coronatus	Crowned lemur	3	0	2	1	0	0	1.0	12.8	19.1
9	Eulemur flavifrons	Blue-eyed black lemur	4	0	3	1	0	0	0.3	17.0	27.4
10	Eulemur fulvus	Brown lemur	3	2	2	1	0	0	17.4	29.8	29.8
11	Eulemur macaco	Black lemur	4	1	3	1	0	0	9.5	22.9	34.5
12	Eulemur mongoz	Mongoose lemur	4	2	3	1	0	0	0.8	21.6	30.8
13	Eulemur rubriventer	Red-bellied lemur	4	3	3	1	0	0	7.9	23.7	33.8
14	Eulemur rufus	Red lemur	3	1	3	0	0	0	5.7	13.5	30.3
15	Eulemur sanfordi	Sanford's brown lemur	4	3	3	1	0	0	9.4	23.6	32.9
16	Galago moholi	South African galago	3	1	2	1	0	0	3.9	5.9	6.8
17	Gorilla gorilla	Gorilla	3	1	3	0	0	0	4.7	13.6	17.6
18	Gorilla gorilla	Western lowland gorilla	3	1	3	0	0	0	31.8	33.6	47.5
19	Hapalemur griseus	Bamboo lemur	4	3	3	1	0	0	7.4	19.5	26.1
20	Homo sapiens	Human	1352	655	511	74	97	46	-0.8	53.7	101.0
21	Lemur catta	Ring-tailed lemur	4	3	3	1	0	0	0.1	5.7	32.8

22	Loris tardigradus	Slender loris	2	1	1	1	0	0	17.2	17.5	17.8
23	Macaca mulatta	Rhesus macaque	281	99	199	51	5	6	1.8	18.5	42.0
24	Microcebus murinus	Gray mouse lemur	2	1	2	0	0	0	0.5	2.8	5.1
25	Mirza zaza	Northern giant mouse lemur	3	0	2	1	0	0	12.9	18.1	18.1
26	Nycticebus coucang	Slow loris	3	2	2	1	0	0	7.4	19.3	22.2
27	Nycticebus pygmaeus	Pygmy slow loris	4	2	3	1	0	0	0.7	9.3	19.9
28	Otolemur crassicaudatus	Greater galago	4	4	3	1	0	0	7.1	13.4	14.7
29	Pan troglodytes	Chimpanzee	2	2	2	0	0	0	43.6	43.9	44.2
30	Papio hamadryas	Olive baboon	325	248	0	0	50	105	-0.1	14.8	22.8
31	Perodicticus potto	Potto	1	0	1	0	0	0	11.5	11.5	11.5
32	Pongo pygmaeus	Orangutan	1	1	1	0	0	0	43.7	43.7	43.7
33	Propithecus coquereli	Potto	4	1	3	1	0	0	0.1	12.2	28.5
34	Propithecus diadema	Diademed sifaka	3	0	2	1	0	0	14.2	16.4	18.7
35	Propithecus tattersalli	Golden-crowned sifaka	3	0	3	0	0	0	3.5	17.3	25.4
36	Varecia rubra	Red ruffed lemur	8	1	6	2	0	0	0.4	6.9	39.4
37	Varecia variegata	Variiegated lemur	1	0	1	0	0	0	12.0	12.0	12.0

Supplementary Table S1. Data used for the primate clocks. Columns report the species (Latin Name, Common Name). Total sample size (N), i.e. the number of arrays/DNA samples per species. Number of samples from females. Number of samples from different tissues. Age: minimum, maximum, median.

Tissue	N	No. Female	Mean Age	Min. Age	Max. Age
Adipose	41	32	15.6	7.49	22.8
Cerebellum	38	29	15.8	8.04	22.8
Cortex	76	60	15.3	7.49	22.8

Fetal Cortex	29	16	0	0	0
Heart	48	38	14.5	5.98	22.8
Liver	50	40	14.6	5.98	22.8
Muscle	44	34	16.4	8.04	22.8

Table S2. Baboon samples.

Tissue type. N=Total number of samples per tissue. Number of females. Age: mean, minimum and maximum. The fetal brain cortex samples were collected at gestational age 165 days.

Latin Name	Common Name	Avg. Maturity	GestationTimeInYeares	max. Lifespan (Years)
Callithrix geoffroyi	White-fronted marmoset	1.375	0.407	19
Callithrix jacchus	Common marmoset	1.177	0.395	22.8
Cheirogaleus medius	Fat-tailed dwarf lemur	1.000	0.167	30
Chlorocebus aethiops sabaues	Vervet	3.916	0.444	30.8
Daubentonia madagascariensis	Aye-aye	2.416	0.452	37
Eulemur albifrons	White-headed lemur	8.234	0.329	34.59
Eulemur collaris	Collared brown lemur	12.137	0.337	32.61
Eulemur coronatus	Crowned lemur	1.666	0.345	30
Eulemur flavifrons	Blue-eyed black lemur	2.100	0.348	32
Eulemur fulvus	Brown lemur	1.564	0.323	35.5
Eulemur macaco	Black lemur	1.104	0.329	37.5
Eulemur mongoz	Mongoose lemur	2.349	0.329	36.2
Eulemur rubriventer	Red-bellied lemur	2.734	0.329	34
Eulemur rufus	Red lemur	12.426	0.329	32.67
Eulemur sanfordi	Sanford's brown lemur	7.836	0.329	32.94
Galago moholi	South African galago	0.710	0.340	16.6
Gorilla gorilla	Western lowland gorilla	9.375	0.701	60.1
Gorilla gorilla	Gorilla	9.375	0.701	60.1
Hapalemur griseus	Bamboo lemur	3.049	0.397	27
Homo sapiens	Human	13.500	0.767	122.5
Lemur catta	Ring-tailed lemur	2.064	0.370	37.3
Loris tardigradus	Slender loris	1.021	0.455	21.6
Macaca mulatta	Rhesus macaque	4.436	0.452	42
Microcebus murinus	Gray mouse lemur	0.666	0.167	18.2
Mirza zaza	Northern giant mouse lemur	1.100	0.245	20
Nycticebus coucang	Slow loris	1.584	0.515	25.8
Nycticebus pygmaeus	Pygmy slow loris	0.748	0.515	20
Otolemur crassicaudatus	Greater galago	1.553	0.356	22.7
Pan troglodytes	Chimpanzee	8.625	0.627	59.4
Papio hamadryas	Olive baboon	4.488	0.468	37.5

Perodicticus potto	Potto	1.499	0.466	32.4
Pongo pygmaeus	Orangutan	7.000	0.682	59
Propithecus coquereli	Potto	3.814	0.386	30.59
Propithecus diadema	Diademed sifaka	2.875	0.430	21
Propithecus tattersalli	Golden-crowned sifaka	4.499	0.404	26
Varecia rubra	Red ruffed lemur	1.725	0.268	40
Varecia variegata	Red ruffed lemur	1.718	0.268	39.4

Supplementary Table S3. Maximum lifespans of 37 primate species used in this article. Columns report the species common name, species Latin name, primate family, maximum observed lifespan (in years) and average age at sexual maturity (years, averaged across both sexes). These age estimates come from anAge [2] and were updated using the Duke Lemur Center Database - Duke Lemur Center <https://lemur.duke.edu/duke-lemur-center-database/> Since its establishment in 1966, the Duke Lemur Center has accumulated detailed records for over 4300 individuals from over 40 closely related yet biologically diverse prosimian primate taxa.

Supplementary Table S4, S5, S6, S7, S8, S9 can be found in the Excel file.

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