Supplementary Table 1. List of 25 genes found with the parallel mutation strategy together with their possible role in aging based on previous studies.

Gene	Organism in GenAge	Previous association to aging or related traits	References
AKAP9	-		
ATG7	*D. melanogaster* and *C. elegans*	Pro-longevity	
BRD8	-		
C1QTNF2	-	Weight loss	Hatoum et al. 2013
C9orf96/STKLD1	-		
DSC2	-	Dilated cardiomyopathy	
EFEMP2	-		
FCGBP	-		
FGA	-	Blood fibrinogen levels	
GP5	-		
HEMK1	-		
IQCK	-	Associated to BMI	Spelliotes et al. 2010
KIAA1614	-		
KLKB1	-	Blood pressure	
MNT	*D. melanogaster*	Pro-longevity	
MYO16	-	Age of onset in Alzheimer Disease Red blood cell count	Herold et al. 2016 Astle WJ et al. 2016
MYOF	-	Associated to muscle repair Epigenetically modified by aging	Demontis et al. 2013 Benton et al. 2017
PLTP	-	HDL levels	Global Lipids Genetics Consortium et al. 2013
PRL	-	Ames dwarf mice lacking *PRL*, *GH* and *TSH* live much longer than their normal siblings and exhibit many symptoms of delayed aging	Brown-Borg et al. 1996
RAD51AP1	-	double-strand break repair correlated to aging important player in the cellular senescence of yeast	Lorenzini et al. 2009 Park et al. 1999
RXFP4	-		
STK31	-	Age of onset in Alzheimer Disease	Mez et al. 2017
SUPV3L1	*S. cerevisae*	Anti-longevity	
WDR87	-		
ZNF233	-		

Supplementary Table 2. Each of the 25 amino-acid changes were assessed in three mammal long-lived species. The same change in the "*Increased Lifespan*" group was evaluated in these species and reported in the last column. NA: not available in the 100-way alignment. None: The long-lived species showed the reference amino-acid.

Gene	Reference	Parallel change	Long-lived not reference
AKAP9	V	I	N.A.
ATG7	A	T	N.A.
BRD8	R	Q	N.A.
C1QTNF2	A	T	N.A.
C9orf96	V	L	hetGla2, myoDav1
DSC2	V	I	hetGla2
EFEMP2	V	I	None
FCGBP	V	A	N.A.
FGA	A	V	myoDav2, myoLuc2
GP5	H	Q	hetGla2
HEMK1	Q	R	N.A.
IQCK	N	D	hetGla2*
KIAA1614	M	V	N.A.
KLKB1	T	A	myoDav2, myoLuc2
MNT	T	A	hetGla2*
MYO16	M	I	hetGla2, myoDav1, myoLuc2
MYOF	P	L	hetGla2
PLTP	P	T	None
PRL	I	M	myoDav2*, myoLuc2*
RAD51AP1	V	A	hetGla2*
RXFP4	V	A	N.A.
STK31	Y	C	myoDav2*, myoLuc2*
SUPV3L1	T	M	None
WDR87	V	I	None
ZNF233	R	Q	N.A.

* Shares the very same aminoacid change than "*Increased Lifespan*" group.

Supplementary Table 3. Top significant genes (p=9e-05) from the 5 life-history traits assessed. The genes marginally significant after FDR (q<0.1) are highlighted in bold. Last column shows whether the gene has been previously described in relation to aging in GenAge databases and in which one.

Trait	P-value	FDR corrected p-vaue (BH)	Gene	GenAge
MLS	**3.7e-06**	**0.06**	**STK17B**	**-**
MLS	4.6e-05	0.37	ITPR1	model org., human
Female Maturity	2.6e-05	0.30	HSPB6	model org.
Female Maturity	3.8e-05	0.30	COX5B	human, model.org
Female Maturity	6.7e-05	0.38	MYL2	-
Female Maturity	8.3e-05	0.38	SLC38A5	-
Gestation Length	**3e-06**	**0.04**	**IQCA1**	**-**
Gestation Length	3e-05	0.15	TRIB2	-
Gestation Length	3.7e-05	0.15	FBXO38	-
Gestation Length	3.8e-05	0.15	MEF2D	model org.
Gestation Length	6.1e-05	0.19	SLC10A1	-
Weaning Time	1e-05	0.14	TMEM182	-
Weaning Time	2.8e-05	0.14	JARID2	-
Weaning Time	3.6e-05	0.14	AP4M1	model org.
Weaning Time	4.8e-05	0.14	PRDX1	human, model org.
Weaning Time	5.6e-05	0.14	POLR1D	-
Weaning Time	5.5e-05	0.14	S100A2	-
Weaning Time	5.6e-05	0.14	GFAP	Longevity.Map
Weaning Time	6.2e-05	0.14	CHD4	model org.
Body Mass	**4.1e-06**	**0.06**	**CDC7**	**-**
Body Mass	**1.4e-05**	**0.09**	**PER3**	Longevity.Map
Body Mass	**1.8e-05**	**0.09**	**SPRRG2**	**-**
Body Mass	6.2e-05	0.2	KLHL9	-
Body Mass	6.5e-05	0.2	ENO3	-
Body Mass	8.17e-05	0.2	CD79A	-
Body Mass	9.3e-05	0.2	FANCD2OS	-

Supplementary Table 4. FDR corrected p-values (within mitochondrial genes) of PGLS association between each mitochondrial gene and each of the assessed life-history traits. Lower table represents PGLS p-values of gene root-to-tip omegas including mitochondrial-wide omegas as covariate. Results shown in the upper part of the table did not include mitochondrial-wide omegas as covariate in the PGLS.

Without mitocondrial-wide omegas

	MaximumLongevity	*AdultWeight*	*FemaleMaturity*	*Gestation*	*Weaning*
ATP6	0,040	4.72e-10	0,367	1,000	0,255
ATP8	0,905	0,242	0,389	1,000	0,939
COX1	0,374	NA	0,572	1,000	0,939
COX2	0,338	0,242	0,367	1,000	0,489
COX3	0,034	0,281	1,000	1,000	0,760
CYTB	0,006	0,242	0,236	1,000	0,105
ND1	0,034	0,047	0,980	1,000	0,358
ND2	0,338	0,242	NA	1,000	0,765
ND3	0,338	0,505	0,572	1,000	0,340
ND4	0,302	0,242	1,000	1,000	0,806
ND4L	0,338	0,242	NA	1,000	0,810
ND5	0,124	0,242	0,367	1,000	0,358
ND6	0,726	0,599	NA	1,000	0,939

With mitocondrial-wide omegas

	MaximumLongevity	*AdultWeight*	*FemaleMaturity*	*Gestation*	*Weaning*
ATP6	0,916	2,20E-06	0,800	0,477	0,893
ATP8	0,916	0,763	0,745	0,477	0,893
COX1	0,916	NA	0,836	0,477	0,893
COX2	0,916	0,980	0,800	0,949	0,893
COX3	0,916	0,980	0,800	0,611	0,893
CYTB	0,916	0,980	0,745	0,638	0,893
ND1	0,916	0,673	0,800	0,761	0,893
ND2	0,916	0,965	0,800	0,617	0,893
ND3	0,916	0,980	0,824	0,611	0,893
ND4	0,916	0,980	0,800	0,611	0,893
ND4L	0,916	0,980	0,745	0,477	0,893
ND5	0,916	0,980	0,800	0,623	0,893
ND6	0,932	0,980	0,800	0,477	0,893

Supplementary Table 5. Life history data used. In gray, species present in the UCSC alignment.

Species	UCSC version	Family	MLS (y)	LQ	Body weight (g)	Female maturity (d)	Gestation (d)	Weaning (d)
Homo sapiens	hg38	Hominidae	122.5	4.6	62035	4745	280	639
Pan troglodytes	panTro4	Hominidae	59.4	2.4	44983.5	3376	229	1111
Pan paniscus	panPan1	Hominidae	55	2.2	39925	3194	232	635
Gorilla gorilla	gorGor3	Hominidae	55.4	1.9	139842	2829	256	834
Pongo abelii	ponAbe2	Hominidae	58	2.2	55000	4380	227	1440
Nomascus leucogenys	nomLeu3	Hylobatidae	44.1	2.4	6000	2555	210	720
Macaca mulatta	rheMac3	Cercopithecidae	40	2.1	8235	1231	165	292
Macaca fascicularis	macFas5	Cercopithecidae	39	2.1	6362.5	1238	165	242
Papio anubis	papAnu2	Cercopithecidae	25.2	1.2	17730	2555	178.96	420
Chlorocebus sabaeus	chlSab2	Cercopithecidae	13	0.7	5620	730	165	365
Nasalis larvatus	nasLar1	Cercopithecidae	25.1	1.2	14617.5	1460	166	213
Rhinopithecus roxellana	rhiRox1	Cercopithecidae	29.5	1.4	14750	1642.5	195	365
Callithrix jacchus	calJac3	Callitrichidae	22.8	2	255.2	477	144	62
Saimiri boliviensis	saiBol1	Cebidae	30.3	2.3	615	1000.3	158	150
Tarsius syrichta	tarSyr2	Tarsiidae	16	1.6	119.2	547.5	179	83
Microcebus murinus	micMur1	Cheirogaleidae	18.2	2	64.8	243	61	37
Otolemur garnettii	otoGar3	Galagonidae	18.3	1.3	1300	600	132	140
Cercocebus atys	Caty	Cercopithecidae	26.8	1.4	8600	1650	167	300
Colobus angolensis	Cang	Cercopithecidae	35.3	1.8	8625	700	162.5	450
Macaca nemestrina	Mnem	Cercopithecidae	37.6	2	7912.5	1125	172	324
Mandrillus leucophaeus	Mleu	Cercopithecidae	39	1.8	18250	1277	179	487
Rhinopithecus bieti	Rbie	Cercopithecidae	NA	NA	9960	NA	NA	NA
Propithecus coquereli	Pcoq	Indridae	31	1.8	4190	1277	141	180.96
Aotus nancymaae	Anan	Cebidae	16	1.2	788	211	133	13
Cebus capucinus	Ccap	Cebidae	54	3.3	2655	1505	162	521

Supplementary Table 6. Number of genes and species per each gene alignment after applying the pipeline for including the new 8 primate species. In gray, the number of gene alignments that include more than 17 primate species.

Nº species	Nº of genes
2	37
3	64
4	87
5	107
6	133
7	204
8	263
9	380
10	458
11	673
12	800
13	938
14	1055
15	1269
16	1386
17	1255
18	1170
19	1329
20	1442
21	1418
22	1371
23	986
24	646
25	192

Supplementary Table 7. GO terms selected for each of the molecular hallmarks of aging (López-Otín, 2013).

Hallmark of Aging	GO terms included
Genomic Instability	DNA repair (GO:0006281) Nuclear lamina (GO:00005652)
Telomere Attrition	Telomere maintenance (GO:0000723) Telomere capping (GO:0016233)
Epigenetic Alterations	Histone modification (GO:0016570) DNA methylation (GO:0006306) Chromatine remodeling (GO:0006338)
Loss of Proteostasis	Chaperone-mediated protein folding (GO:0061077) Autophagy (GO:0006914) Ubiquitin-proteasome system (GO:0043161)
Deregulated Nutrient Sensing	Insulin receptor signaling Pathway (GO:0008286) TOR signaling (GO:0031929)
Mitochondrial Dysfunction	Response to ROS (GO:0000302) Mitochondrial genome maintenance (GO:0000002)
Cellular senescence	Cellular senescence (GO:0090398)
Stem Cell Exhaustion	Stem cell proliferation (GO:0072089)
Altered Intracellular Communication	Inflammatory response (GO:0006954) Inflammasome complex (GO:0061702)

Supplementary Figures Legends

Supplementary Figure 1. Spearman correlations between all life-history traits used in the study.

Supplementary Figure 2. Sequential threshold selection from 0 to 2 standard deviations from the family mean. In every interval from 0.6 to 1.4 standard deviations, the same 3 species were included in the *Increased Lifespan* group, suggesting that this grouping was the more consistent across several cut-offs (*Results*). Nonetheless, we performed the analyses selecting 0.5 (less stringent) and 1.5 standard deviations (more stringent) thresholds, which modified the number of included species in the *Increased Lifespan* group to 4 (addition of *Callythrix jacchus*) and 2 (drop of *Macaca fascicularis*), respectively. Using a soft cut-off of 0.5 SD, only one gene was found: a change in Q497R residue affecting the *CNTN5* gene. Interestingly, this gene is found in the LongevityMap database. Using a threshold of 1.5 SD, only 11 genes were found to harbor parallel changes within *Homo sapiens* and *Macaca mulatta* compared to the Control group. These genes were slightly enriched in musculoskeletal abnormalities and diseases (adjP=0.0126). Among them, one gene (*COL6A3*) was also present in the LongevityMap database.

Supplementary Figure 3. Multiple alignment of each gene discovered in the parallel mutation approach across the 17 primate species. White: non-conserved; purple: similar; blue:>50% conserved amino-acid.

Supplemental Figure 4. Distribution of parallel mutations in the test groups from a random sampling in the 17 species tree. Each column represent a different sampling protocol, described in methods. Red triangles show the empirical number of parallel differences observed between hg38, macFas5 and rheMac3.

Supplementary Figure 5. Venn diagram showing the number of overlapping genes between the list of 25 parallel mutated genes (Common), the list of human aging genes downloaded from GenAge (Human), the list of aging genes in model animals downloaded from GenAge (Models), the set corresponding to human genetic variants associated with longevity also downloaded from AnAge genes (Longevity), and the gene set from mortality/aging GO term (GO). All lists of genes were obtained on 06/14/2016. Note that three genes (ATG7, MNT and SUPV3L1) from the discovered gene set were present in another Aging gene list (Models).

Supplemental Figure 6. Phylogenetic regressions of primate life-history traits and genome-wide omega. P-values for the PGLS regression are displayed inside each plot. Note that only gestation length was significantly correlated to the genome-wide omega value.

Supplemental Figure 7. Correlation between p-values obtained in the PGLS regression using three different species trees. UCSC tree was downloaded from the 20-way alignment data (ucsc); chronogram (chrono) and phylogram (phylo) trees were downloaded from 10KTrees webpage. Notice that all the analyses in this study were performed using the chronogram tree from 10kTrees.

Supplemental Figure 8. The number of overlapping occurrences between MLS, weaning time, gestation and female maturity (in red) and body mass (in blue) are plotted together with a random distribution of 4/5 bootstrapped phenotypes 1000 times. The number of overlapping significant genes is much higher than expected in the studied phenotypes.

Supplementary Figure 9. A) Heat map of GO, KEGG, Pathway Commons and diseases enrichment created using the enrichment analysis of overlapping significant genes between the 4 phenotypes (first column), genes showing a p-value < 0.01in at least three life-history traits (2nd column) and genes showing a p-value < 0.01 in MLS, weaning time, female maturity and gestation length. **B)** Venn diagram of the genes with a p-value < 0.01 in the assessed life-history traits. **C)** Venn Diagram of significant genes (p-value<0.05) excluding body mass.

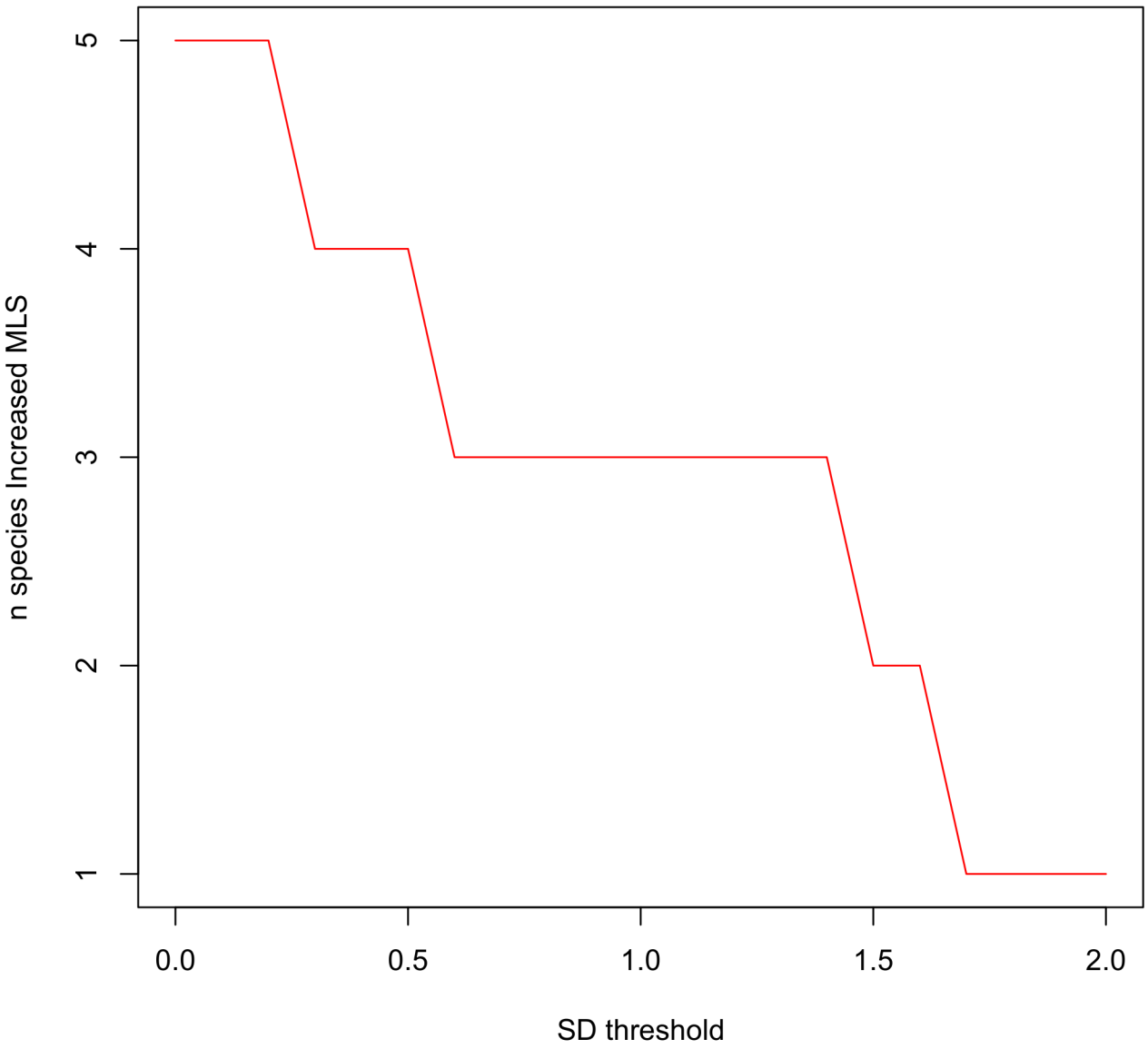
Supplementary Figure 10. Correlation plots between phenotype data from AnAge and ADW databases regarding four representative traits.

Supplementary Figure 11. A) Species included in the *Increased Lifespan* group are shown in red in the phylogenetic tree. Illustrations of the four levels of bootstrap to evaluate the significance in the number of parallel mutations are displayed in the figures: **B)** In the first level, shared mutations were evaluated within any possible grouping of 3 primate species (in yellow). **C)** In the second level, combinations of two Cercopithecidade (yellow) and one outgrup (green) were assessed for shared mutations. **D)** Third resampling consisted in combinations of two Cercopithecidae (yellow) and one Hominidae (green). **E)** Finally, combinations of two Cercopithecidae species (in yellow) plus Homo sapiens (in red) were evaluated. **F)** Phylogenetic tree including the new primates used. Species that were included in the *Increased Lifespan* group are shown in red.

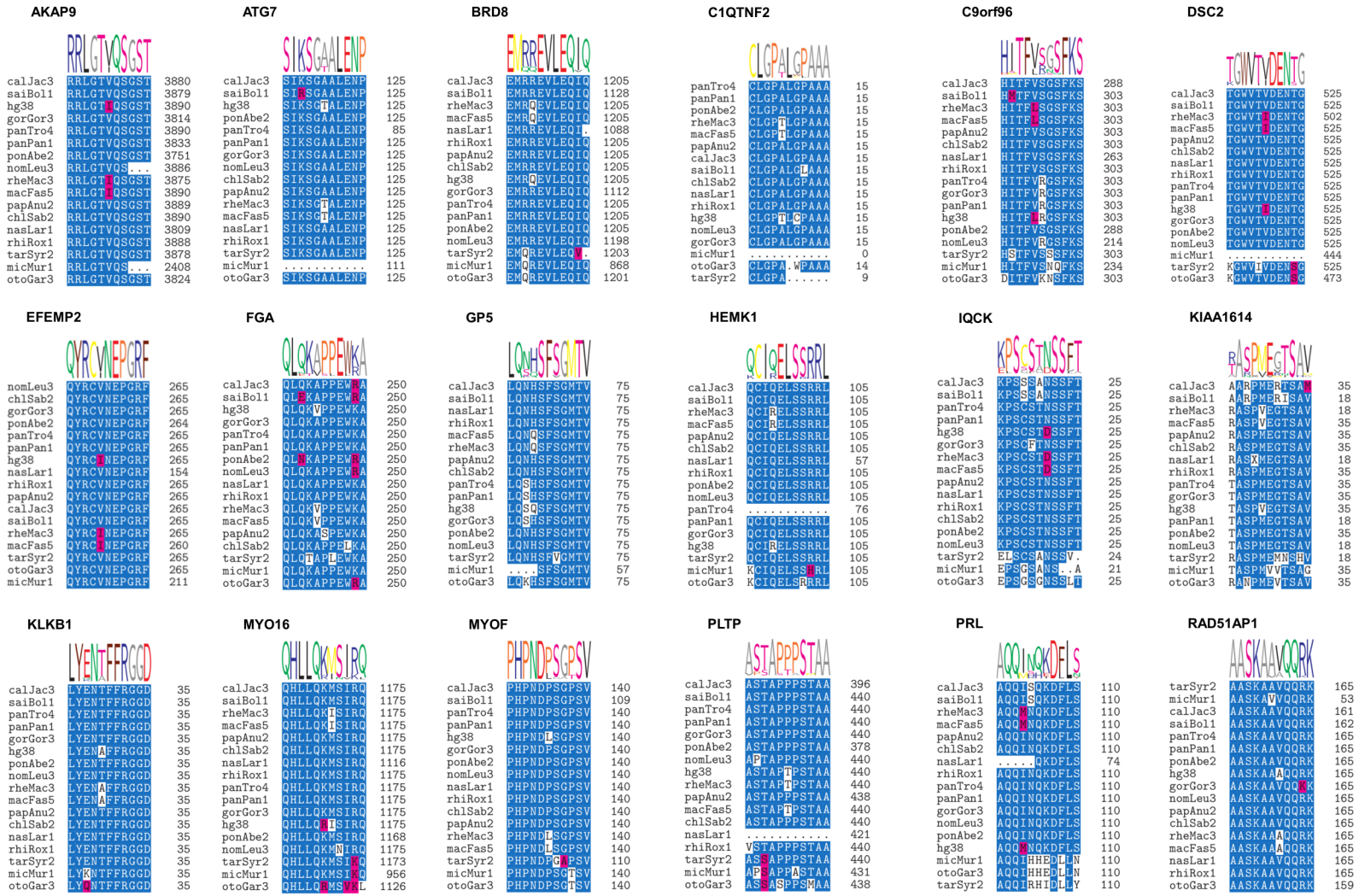
Supplementary Figure 12. Violin plots showing the minimum number of species every mitochondrial gene needed to calculate λ correctly using the Pagel's λ method from *nlme* package. Distributions represent the maximum number of species used before an error appeared in calculating lambda (100 bootstraps of random subtraction of one specie without replacement). Roughly, when having less than 40 species it is not adequate to use Pagel's λ method and then, Brownian motion method should be prioritized.

Suppl. Figure 1

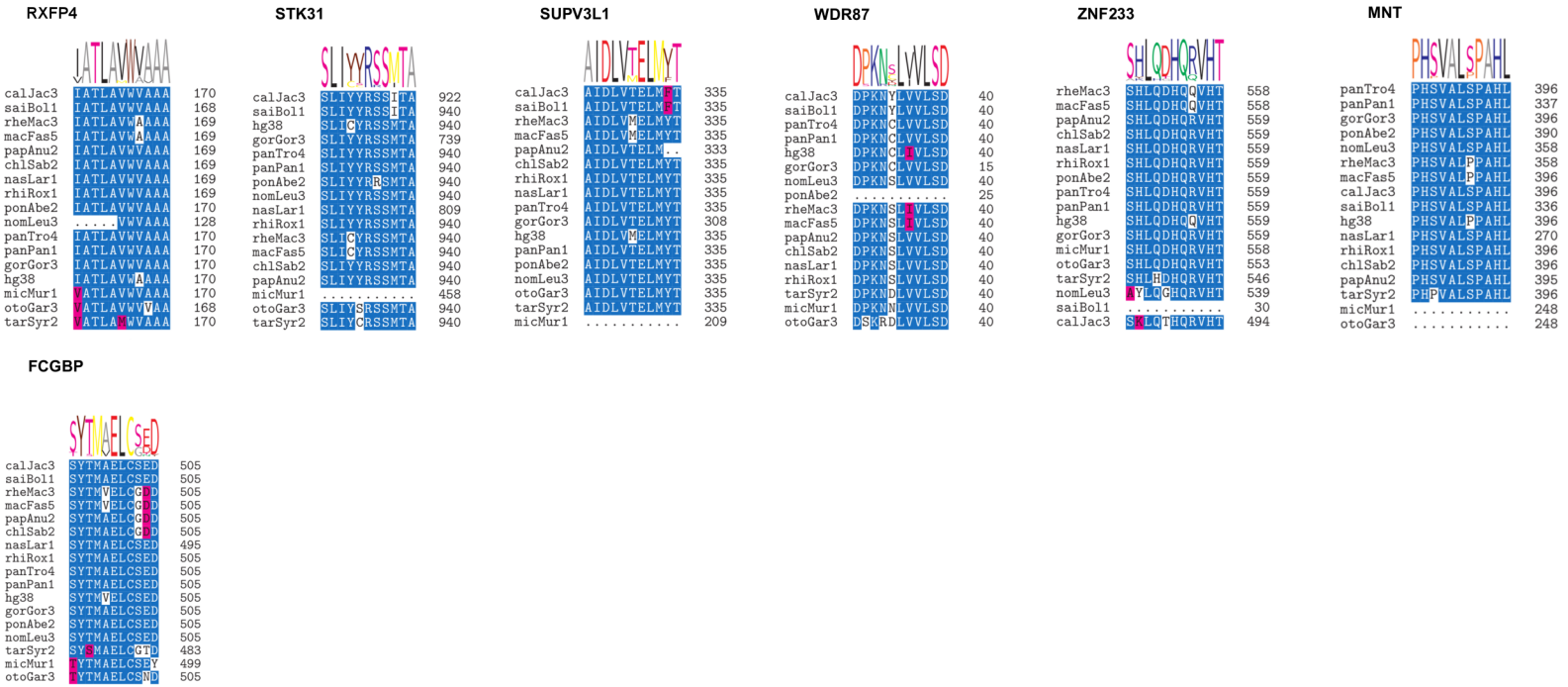
Suppl. Figure 2



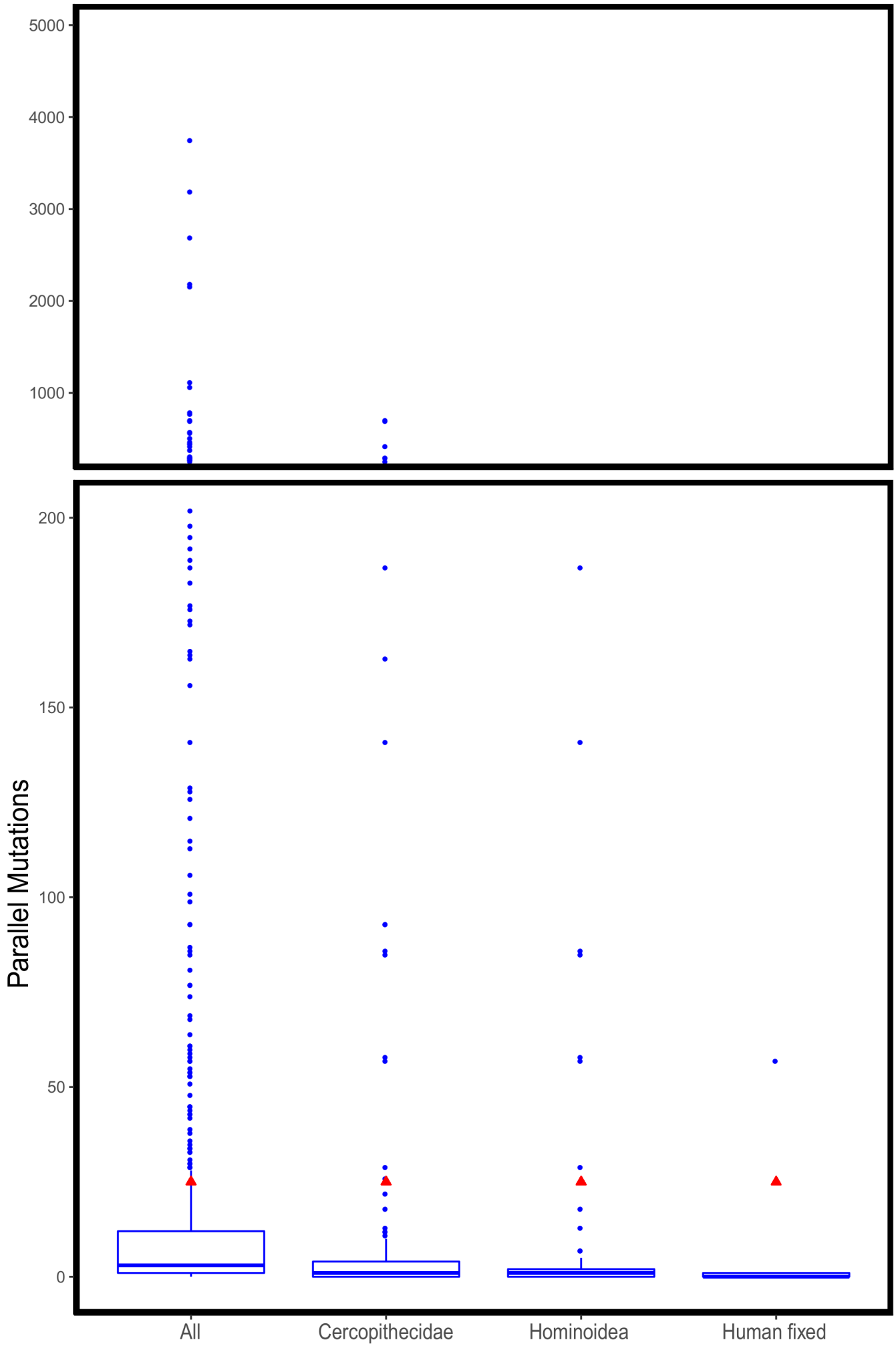
Suppl. Figure 3



Suppl. Figure 3 (contd)



Suppl. Figure 4



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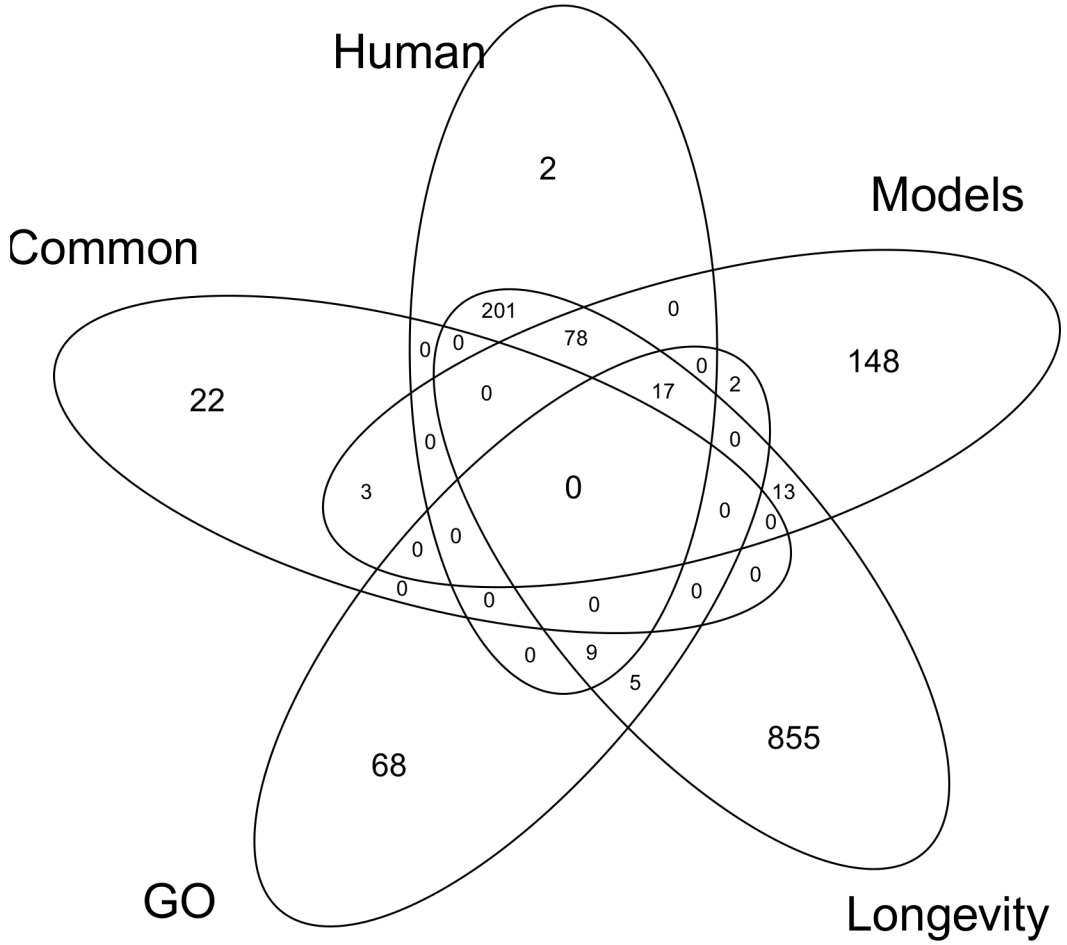

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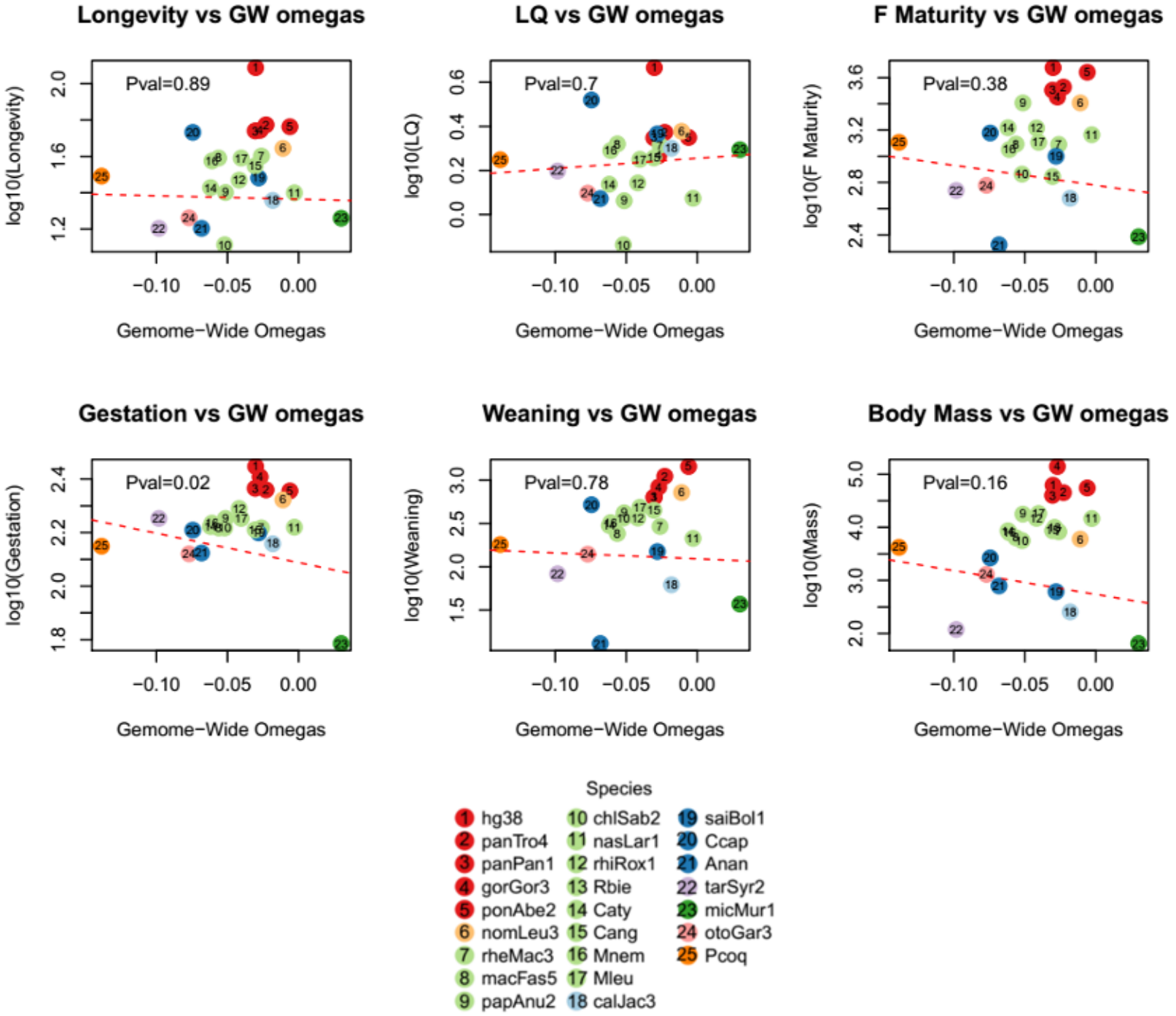

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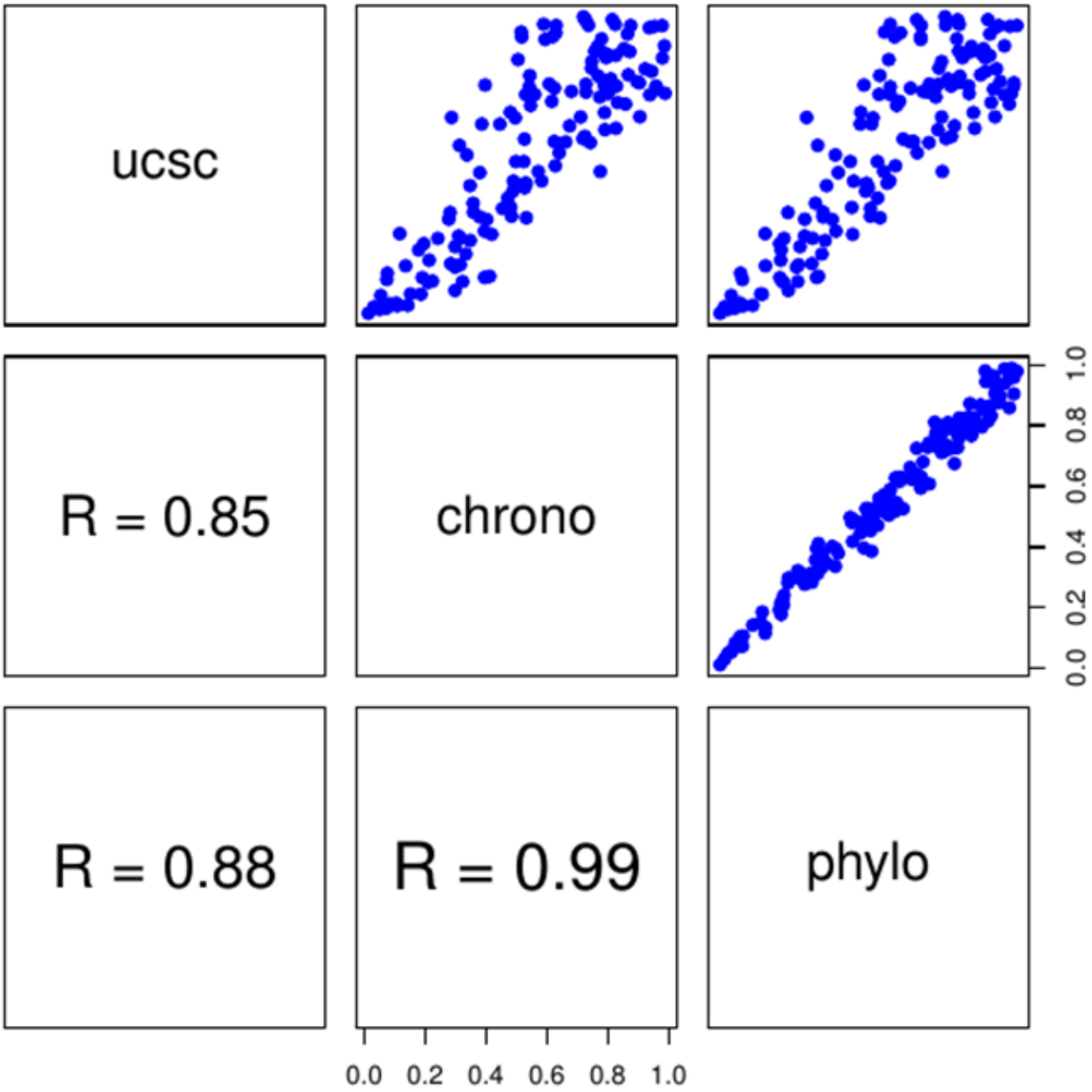

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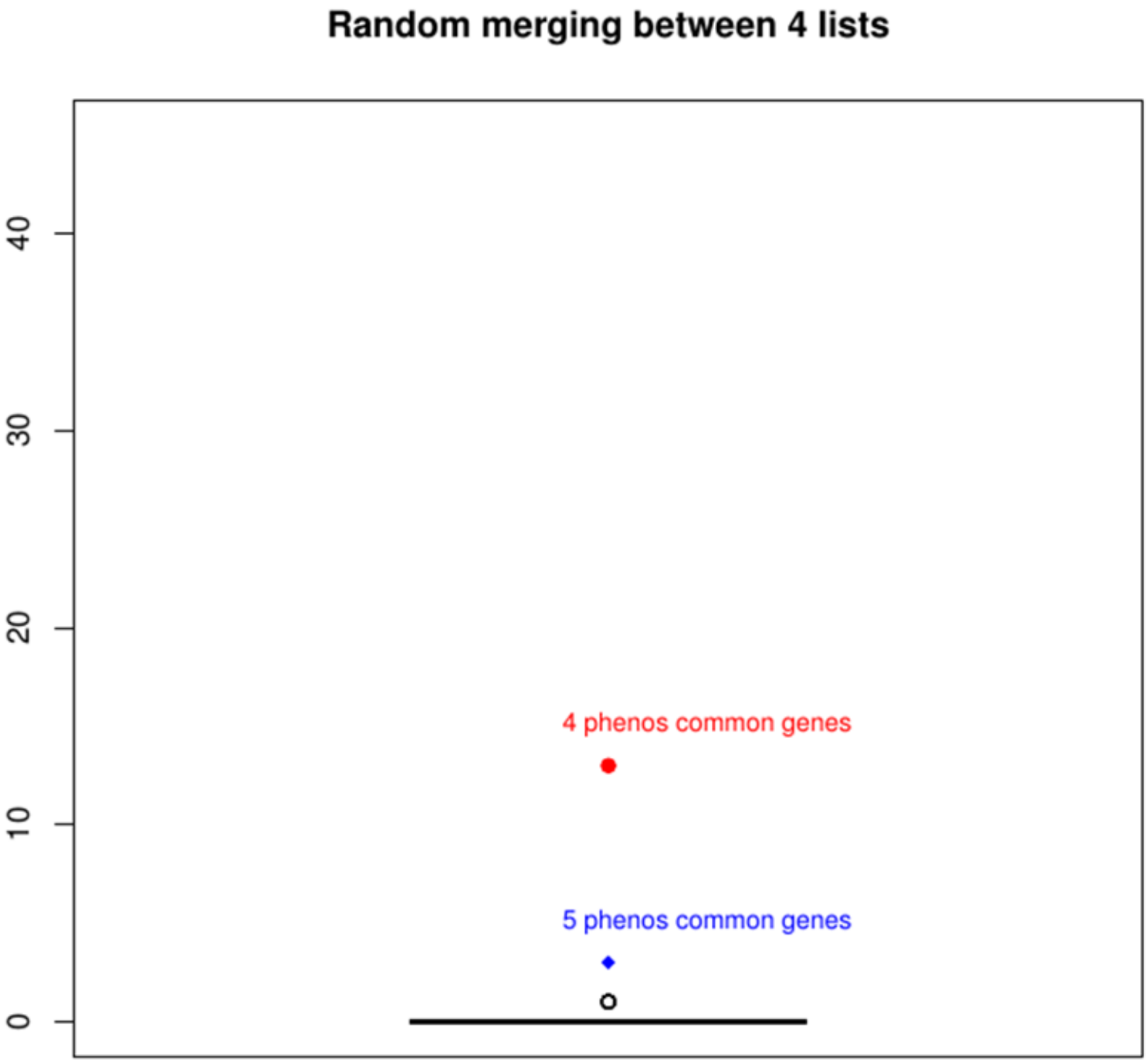

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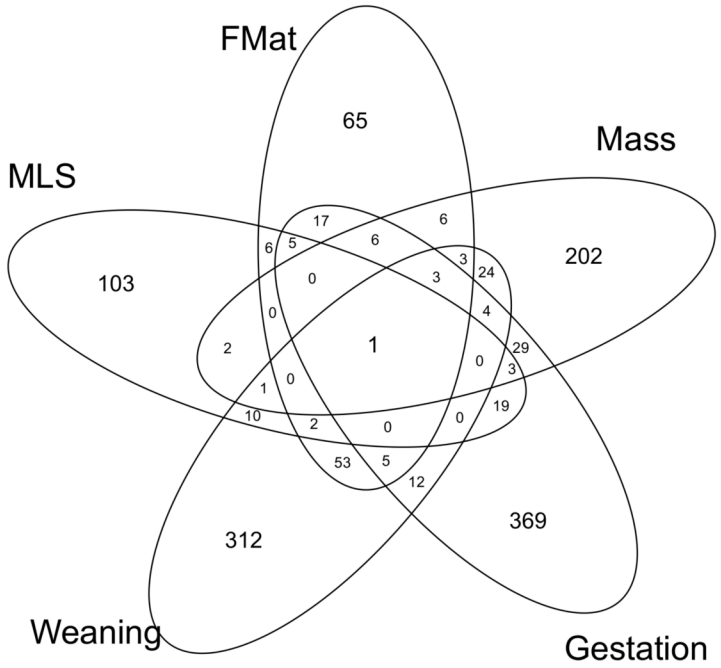
B



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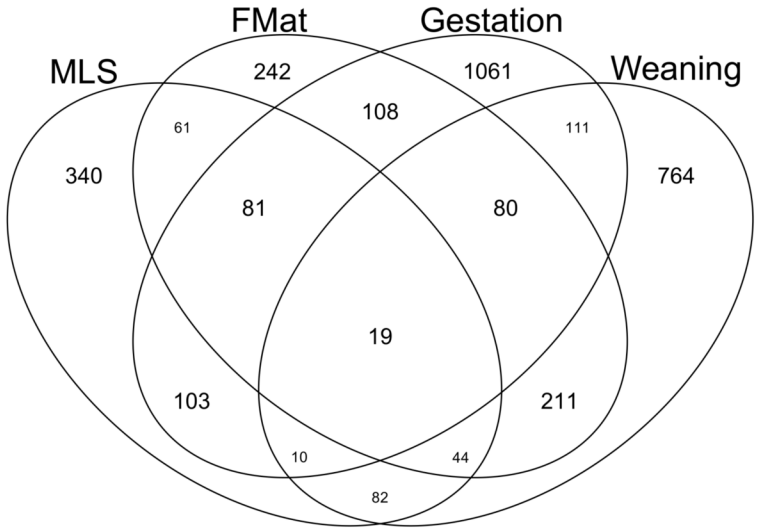

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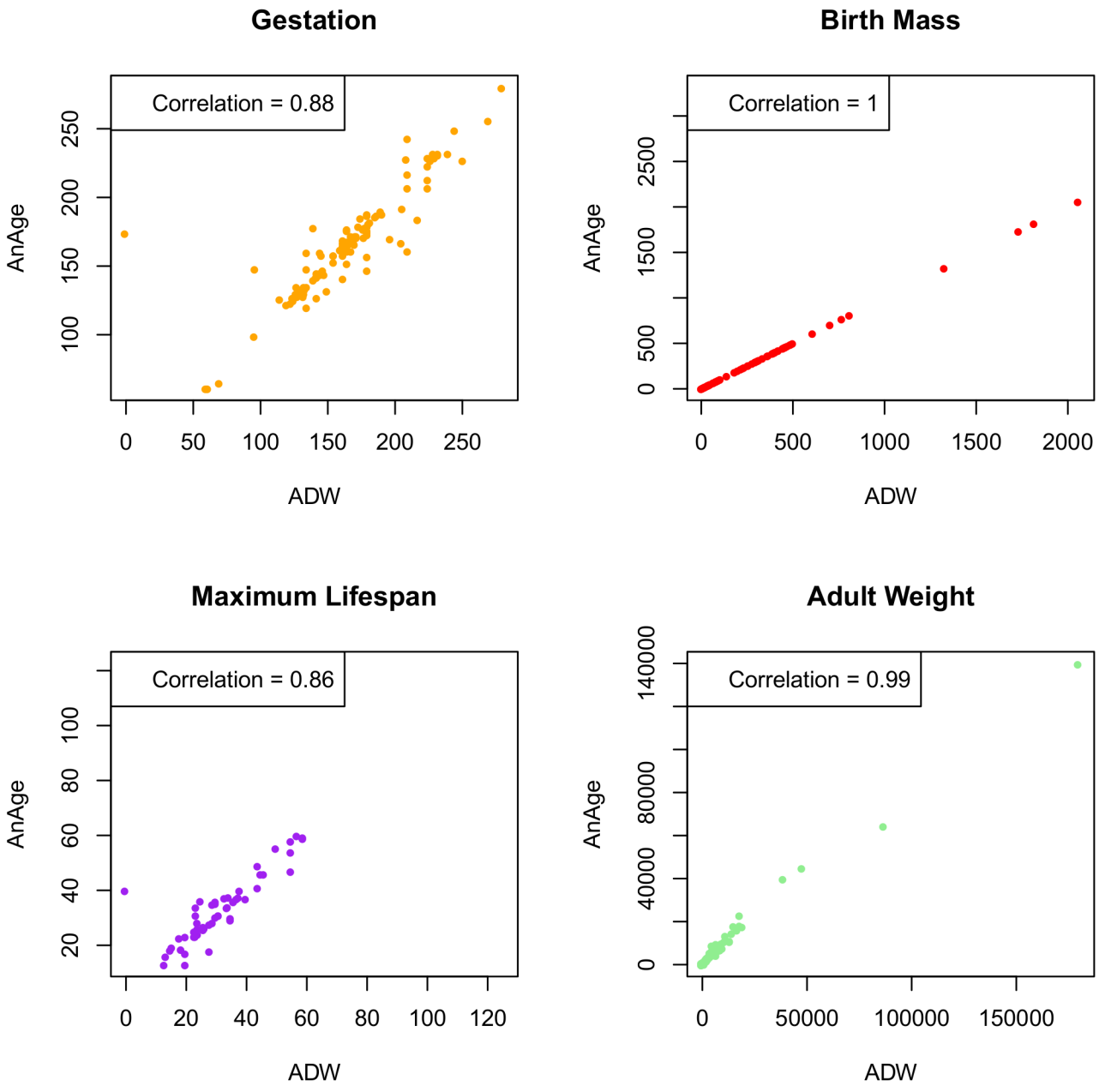
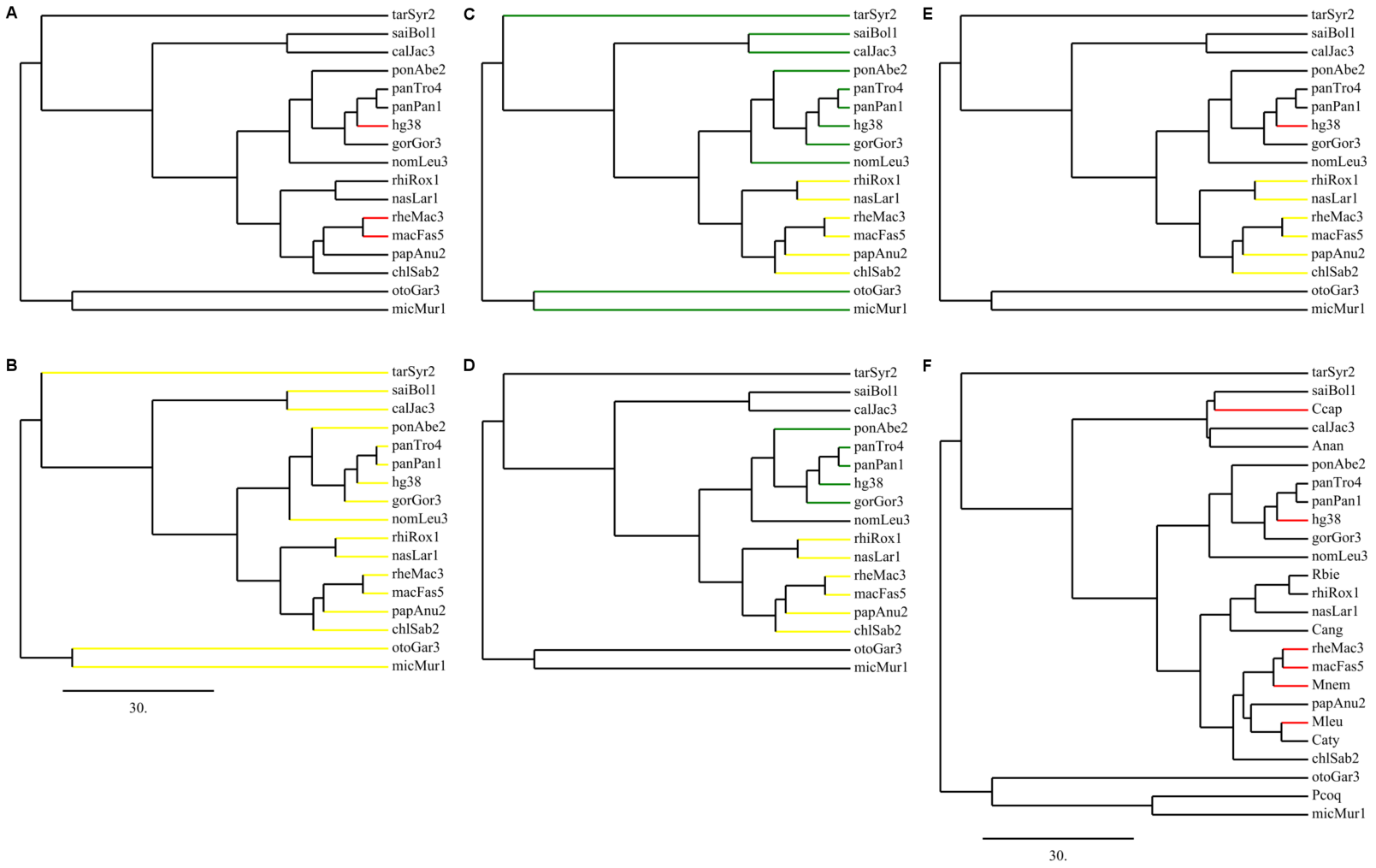


Suppl. Figure 11



Suppl. Figure 12