Supplementary Material for:

Title: **Broad phylogenetic comparisons of the pheromone receptor Class 1 family (V1R) in novel primate genomes reveal extreme complexity in mouse lemurs (genus, *Microcebus*) and genomic hotspots across mammals**

Authors: Kelsie E. Hunnicutt[1,8]†, George P. Tiley[1]†, Rachel C. Williams[1,2], Peter A. Larsen[1,9], Marina B. Blanco[2], Rodin M. Rasoloarison[3,4], C. Ryan Campbell[1], Kevin Zhu[5], David W. Weisrock[6], Hiroaki Matsunami[5,7] & Anne D. Yoder[1*]

Affiliations:

[1]Department of Biology, Duke University, Durham, NC 27708, USA

[2]Duke Lemur Center, Duke University, Durham, NC 27705

[3]Behavioral Ecology and Sociobiology Unit, German Primate Centre, 37077 Göttingen, Germany

[4]Département de Biologie Animale, Université d'Antananarivo, BP 906, Antananarivo 101, Madagascar

[5]Department of Molecular Genetics and Microbiology, Duke University Medical Center, Durham, NC 27710

[6]Department of Biology, University of Kentucky, Lexington, KY 40506

[7]Department of Neurobiology, Duke Institute for Brain Sciences, Duke University Medical Center, Durham, NC 27710

[8]Current address: Department of Biological Sciences, University of Denver, Denver, CO 80208

[9]Current address: Department of Veterinary and Biomedical Sciences, University of Minnesota, Saint Paul, MN 55108

†Equal contributors

*Author for Correspondence: Anne D. Yoder, Department of Biology, Duke University, Durham, USA, 919-660-7366, anne.yoder@duke.edu

Supplementary Methods

Genome Annotation

Although *de novo* gene annotations were not used in this study, gene annotations are provided with genomes available through NCBI. RNAseq data (Peng et al. 2014) was used to train gene prediction models with the grey mouse lemur genome. RNAseq libraries from multiple tissues and replicates (Table S15) were used to assemble a single transcriptome with TRINITY v2.2.0 (Haas et al. 2013). Assembled transcripts and homologous protein evidence from closely-related species were used as direct evidence for gene annotations as well as for training the *ab initio* gene predictor SNAP (Korf 2004) with MAKER v2.31.9 (Cantarel et al. 2008) for the *Microcebus murinus* 3.0 assembly (https://www.ncbi.nlm.nih.gov/genome/?term=Microcebus+murinus; last accessed 8 November 2017). For an independently trained gene predictor, we optimized the AUGUSTUS v3.3 (Stanke et al. 2006) human parameters with the *M. murinus* 3.0 assembly using BUSCO v3.0.2 (Simão et al. 2015). Final annotations for all five genomes were estimated with a single MAKER run using a combination of transcriptome and homologous protein alignment as well as gene predictions. Genomes of related species used for homologous protein evidence are as follow:

- Norway Rat 6.0 (https://www.ncbi.nlm.nih.gov/genome/?term=rattus; last accessed 8 November 2017)
- House Mouse GRCm38.6 (https://www.ncbi.nlm.nih.gov/genome/?term=Mus+musculus; last accessed 8 November 2017)
- Chimpanzee 3.0 (https://www.ncbi.nlm.nih.gov/genome/?term=Pan+troglodytes; last accessed 8 November 2017)
- Gorilla 4.0 (https://www.ncbi.nlm.nih.gov/genome/?term=Gorilla; last accessed 8 November 2017)
- Sumatran orangutan 2.0.2 (https://www.ncbi.nlm.nih.gov/genome/?term=Pongo+abelii; last accessed 8 November 2017)
- Human GRCh38.p11 (https://www.ncbi.nlm.nih.gov/genome/?term=Homo+sapiens; last accessed 8 November 2017)

The transcriptome was assembled with 15 paired-end 100bp Illumina libraries representing 9 tissues. Reads were trimmed with trimmomatic. A single transcriptome was then assembled by pooling all libraries, using *in silico* normalization of each library to avoid unnecessarily large RAM requirements. We then estimated the fragments per kilobase million (FPKM) per locus using RSEM (Li and Dewey 2011) as called from TRINITY.

For training our *in silico* gene predictors, we first trained SNAP (Korf 2004) from within MAKER. We first ran MAKER on the *Microcebus murinus* 3.0 assembly only using evidence-based annotations from our *de novo* transcriptome assembly and homologous proteins of related species. A single GFF file was merged from the resulting annotations and MAKER was run again only using SNAP with hints supplied from the previous GFF. A new GFF file was made from SNAP's predications and we repeated gene finding once more to refine the HMM used by SNAP.

Enrichment of LINES in V1R clusters

We assessed the molecular environment of vomeronasal receptors with the newly improved *Microcebus murinus* genome compared to mouse (Larsen et al. 2017). We used bedtools closest to determine average distance separating V1Rs. We assigned receptors within 500kb of other receptors to clusters then calculated repeat element density and analyzed surrounding annotations for the V1R-containing subset of the genome. We generated 100 randomly distributed subsets of each genome of similar size and base pair composition to the V1R-containing subsets for each species. We estimated repeat element density in the random and V1R-containing subsets using RepeatMasker version open-4.0.6 with the RepBase database (Chen 2004; Jurka et al. 2005).

Supplementary Results

Subfamily-Specific Patterns in Sites Under Pervasive Positive Selection

Sites under positive selection were biased towards transmembrane domains in subfamilies *Strep*/I, II, V, VI, and VIII, although not consistently across taxonomic filters (Supplementary Table S8). Increased numbers of sites under selection in transmembrane domains were only evident when analyzing Lemuriformes, Cheirogaleidae, or *Microcebus*, which suggests that selection on these structurally conserved domains may be occurring at more shallow time scales or specifically in dwarf and mouse lemurs. Subfamily III was enriched for sites under positive selection in loop domains (Supplementary Table S8). Some individual transmembrane domains showed decreased or increased levels of positive selection depending on the subfamily (Supplementary Figure S5; Table S9). For instance, transmembrane domain three was conserved, showing less evidence of positive selection with respect to all other transmembrane domains, across all taxonomic filters in subfamilies *Strep*/I and IX (Figure 5; Figure S5). Some loop domains appeared to experience more positive selection in specific subfamilies too; loop three was particularly enriched for sites under positive selection in subfamilies II and VII; loop five in subfamilies II, IV, V, and VI while loop seven was enriched for positive selection in subfamily IX.

Lemur Subfamily IX and Uncertainty in Detecting Episodic Positive Selection

Approximately 10% of sites are estimated to be under selection along the basal cheirogaleid branch and were identified in transmembrane domain three as well as in loops three and five (Supplementary Table S12). However, signatures of episodic positive selection in subfamily IX are typically downstream or upstream of domains comprising the ligand-binding pocket (Supplementary Table S12). Otherwise episodic positive selection was detected in 5% or less of sites among branches with many sites mapping downstream of transmembrane domain seven where alignment can be less reliable. However, incorrectly identified sites under positive selection due to alignment or topological errors were likely minimal. For each lemur subfamily, the topological relationships based on the ML analysis of the entire repertoire could not be rejected when compared to arguably more correct trees based on realigned data (Supplementary Table S3). Bootstrap trees from the entire repertoire and realigned subtree analyses found only one false branch, which occurred in subfamily IX (Supplementary Figure S6).

Supplementary Figures

Figure S1 – Comparing Benchmarking Universal Single-Copy Orthologs (BUSCO) results across publicly available Strepsirrhine genomes. Bars depict percentage of orthologs recovered from assemblies that were complete (Single), more than once but were still complete (Duplicate), recovered but were fragmented (Fragment), or that were not recovered from the genome (Missing). Orthologs were from the mammalian BUSCO gene set.

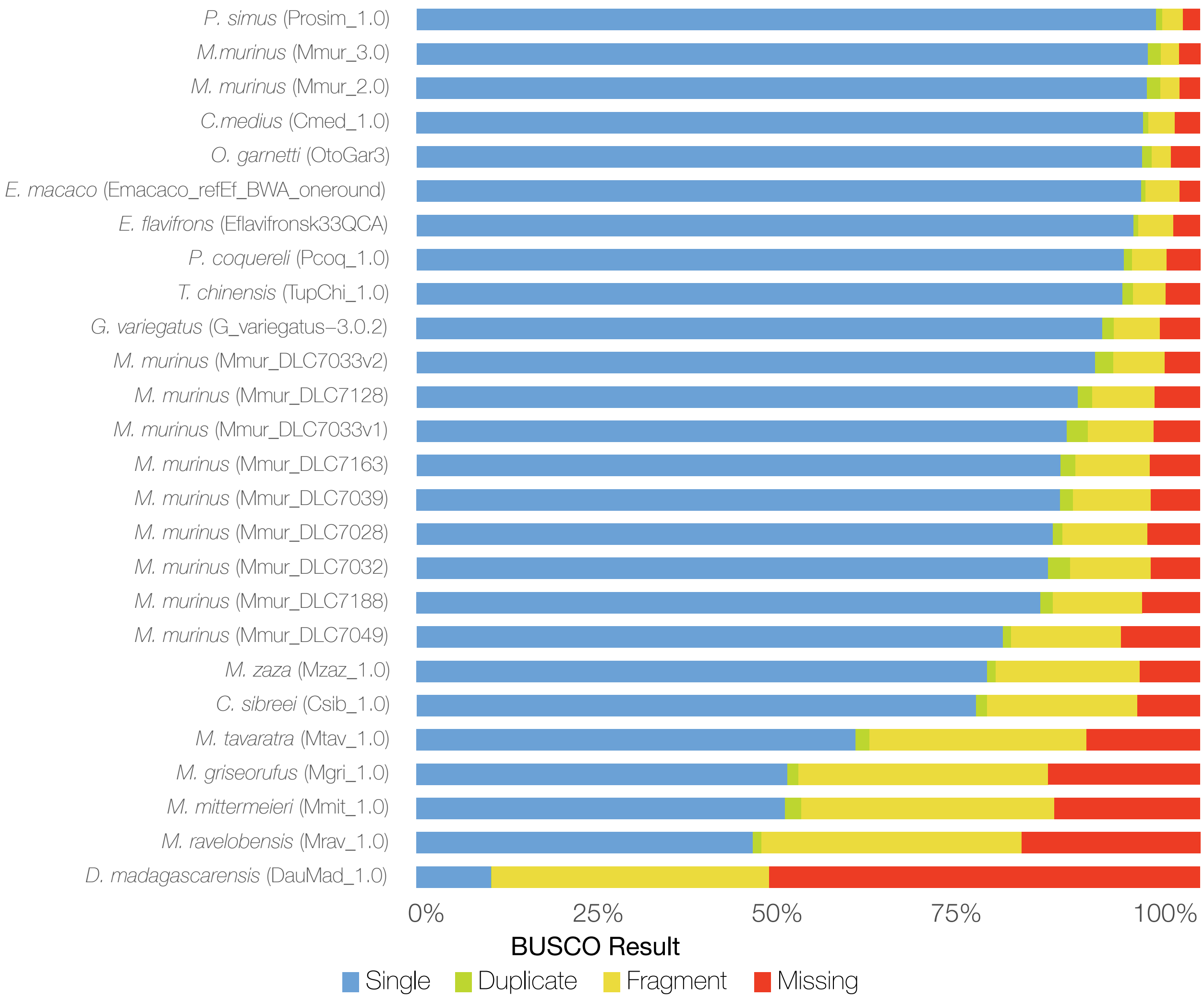


Figure S2 – Changes in subfamily counts given increasing alignment stringency. The number of gene copies per subfamily per species is largely insensitive to removal of sequences introducing that require multiple gap openings in transmembrane domains. Alignment version 1 (v1) represents the least conservative alignment while v17 represents the most conservative alignment.

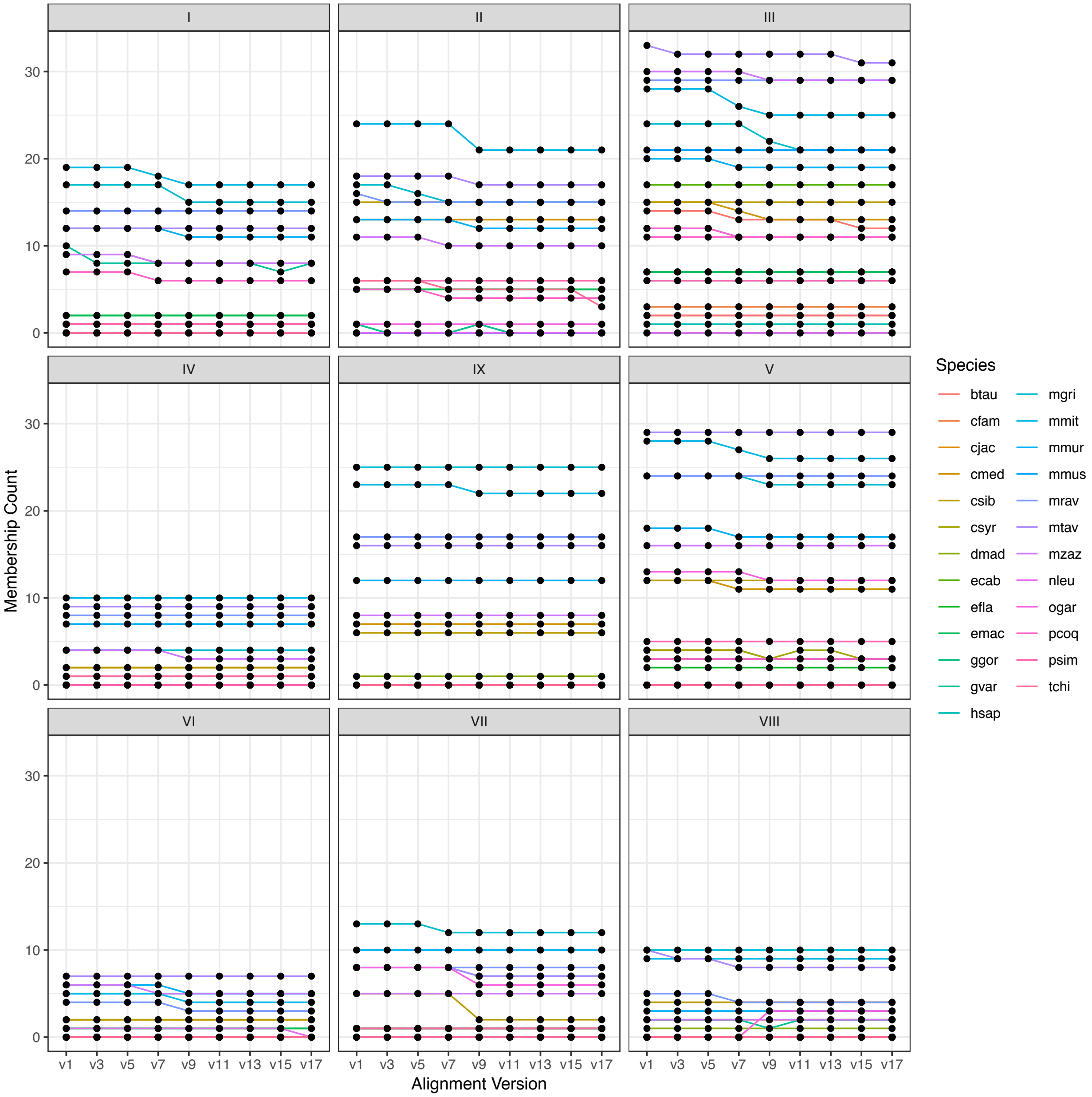


Figure S3 – Sites under pervasive positive selection shared across subfamilies. Although many sites under positive selection are unique to one subfamily, most sites are under selection in two or more subfamilies. Shared sites may be found in at least one taxonomic filter.

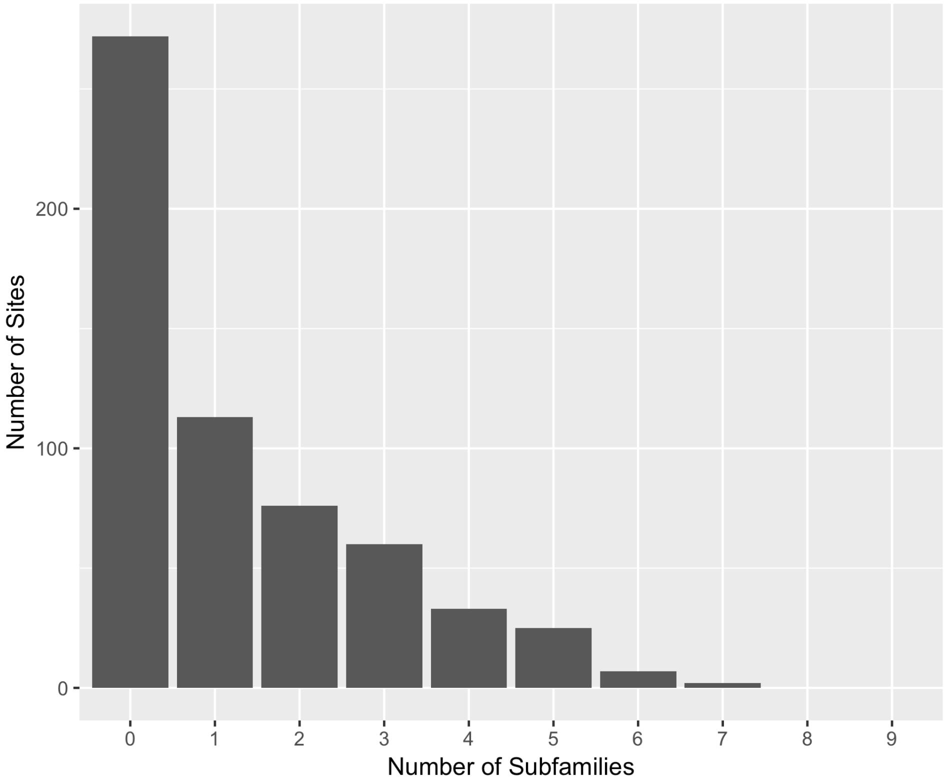


Figure S4 – Transmembrane domain predictions in *Microcebus murinus* sequences from subfamilies I-IX. Each line is a an aligned and putatively intact V1R sequence from the *M. murinus* genome. Pink lines are extracellular loops, blue lines are inside, and thickened gray lines represent predicted transmembrane domains. Black vertical dashed lines are the average start and stop positions for transmembrane domains one through seven when mapped to the codon alignment. Only models with seven predicted transmembrane domains were used for obtaining alignment-wide start and stop sites.

Figure S5 – Over- or under-representation of sites under selection among V1R domains. Red boxes represent more than expected and blue boxes represent fewer than expected sites under selection for loop (L) and transmembrane (T) domains. Subfamilies are given on the y-axis and multiple rows represent different taxonomic filters.

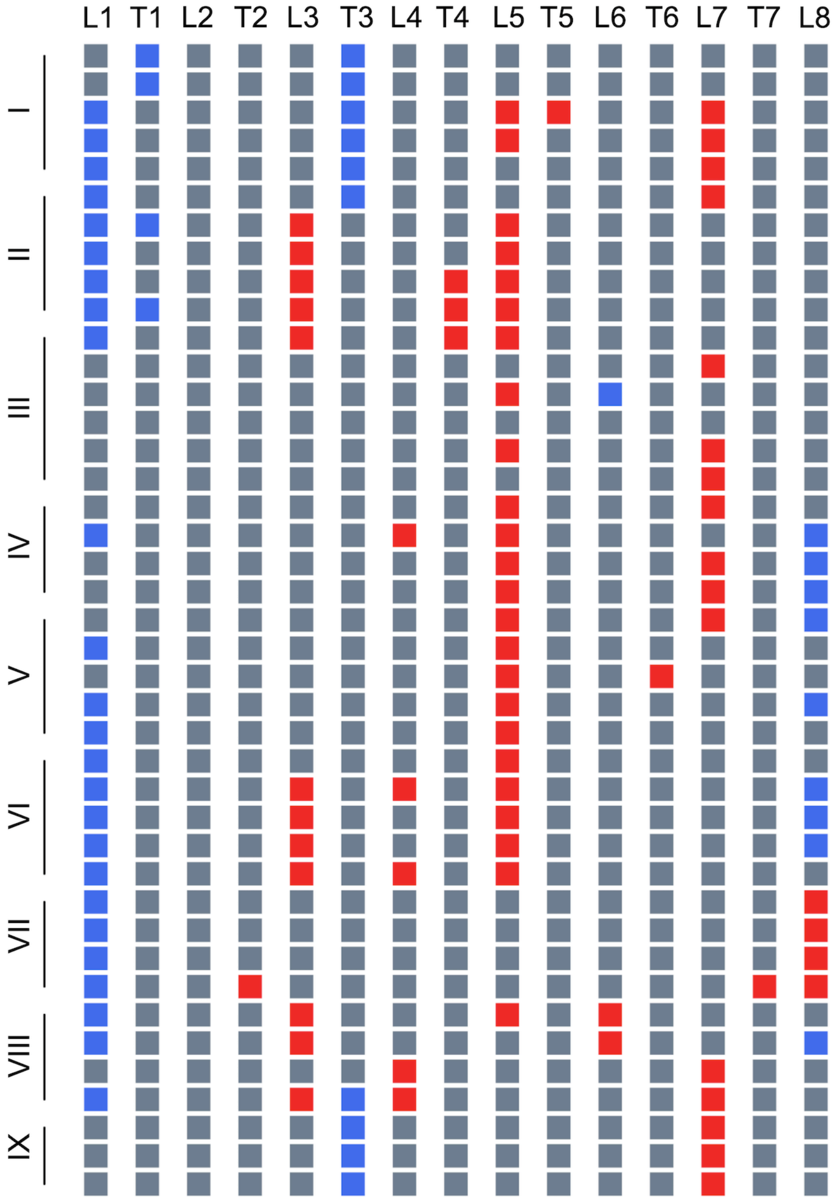


Figure S6 – Branches with evidence of episodic positive selection across subfamilies. The subtrees are parsed from the ML topology of the entire V1R repertoire. Blue diamonds at nodes represent evidence of episodic positive selection occurring during the subtending branch. Solid lines are taxa within Cheirogaleidae while dashed lines may represent other primates or *Tupaia*. Circles at internal nodes represent the ratio of bootstrap support between the realigned data and alignment from the entire repertoire. Red circles indicate bipartitions supported in the whole repertoire ML analysis that were not supported in the realigned ML trees. No episodic positive selection was detected in subfamily VIII; subfamily III was too large for computationally efficient estimation of likelihoods. Node numbers correspond to Supplementary Table S12 for identifying individual sites under selection along branches.

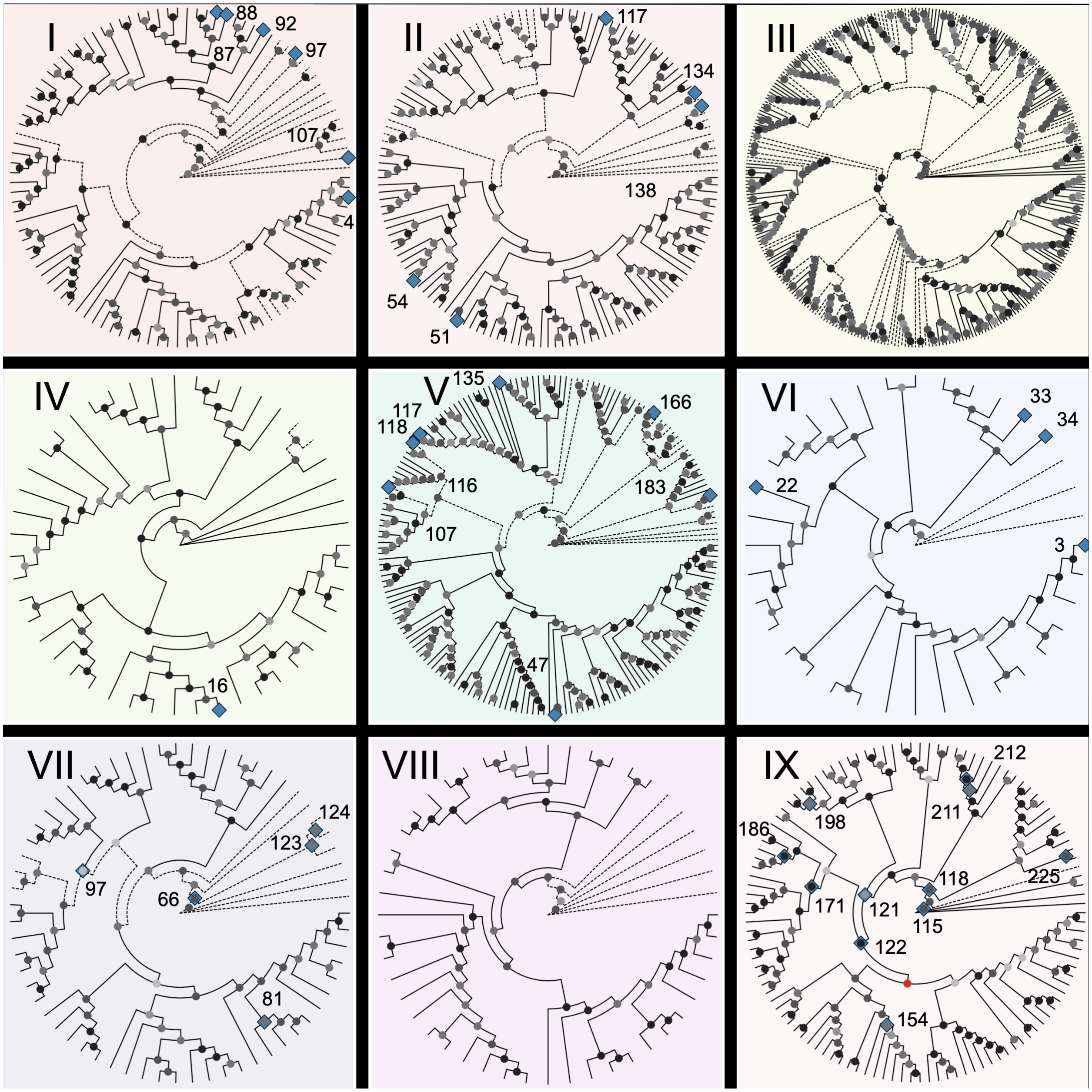


Figure S7 – Repeat element density of V1R-containing and non-V1R-containing regions. Regions of the genome containing V1Rs were analyzed for repeat element density and compared with random non-V1R containing regions to test for element enrichment in the cow, horse, mouse, and mouse lemur genomes. We estimated the percentage of the regions analyzed that are comprised of SINEs, LINEs, LTRs, and DNA transposons. Significance denoted by * for p<0.05 and *** for p<0.001.

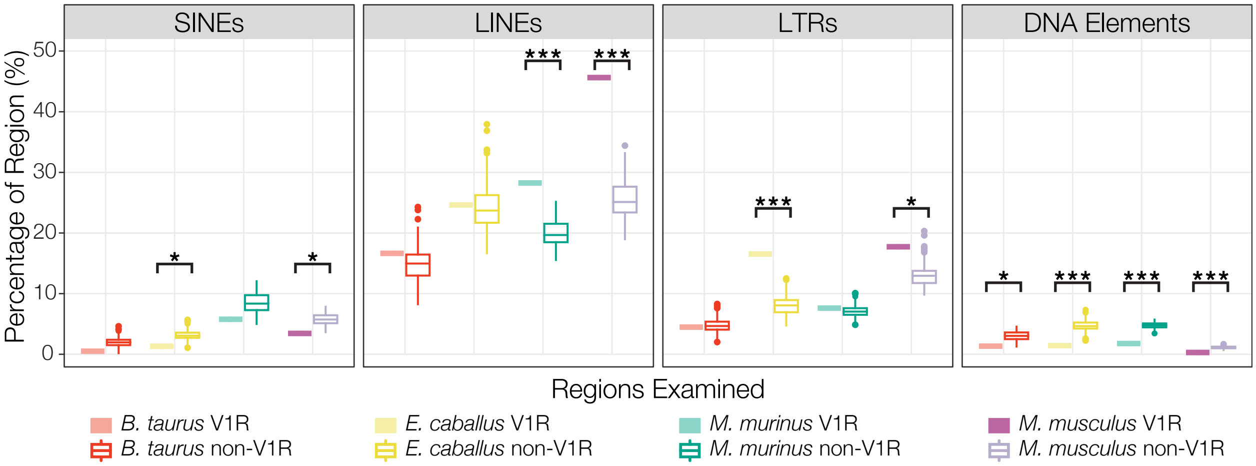


Figure S8 – Syntenic relationships between mouse and dog. Dog chromosomes are painted based on syntenic relationships with mouse. Locations of V1R genes are denoted in red.

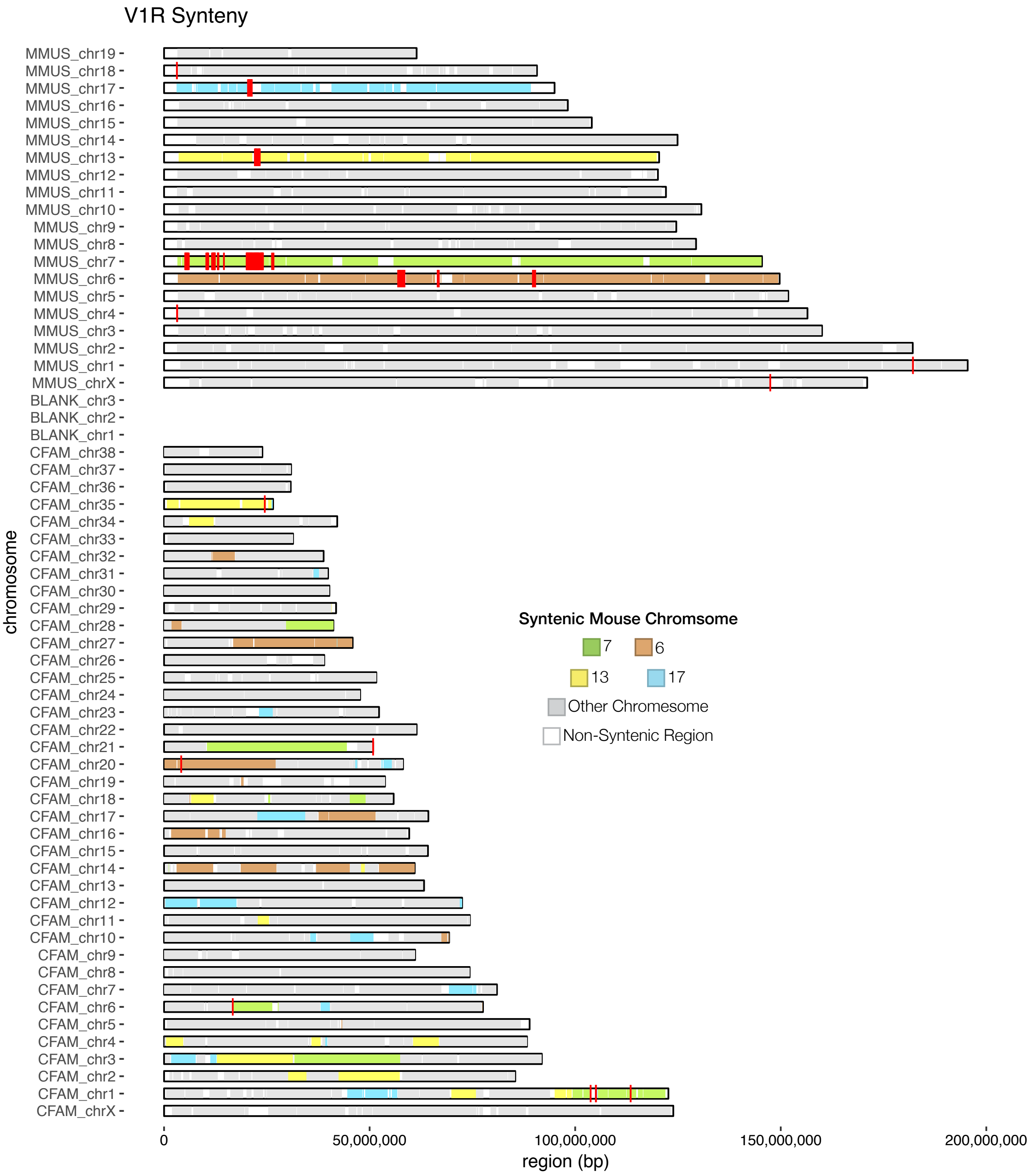


Figure S9 – Syntenic relationships between mouse and horse. Horse chromosomes are painted based on syntenic relationships with mouse. Locations of V1R genes are denoted in red.

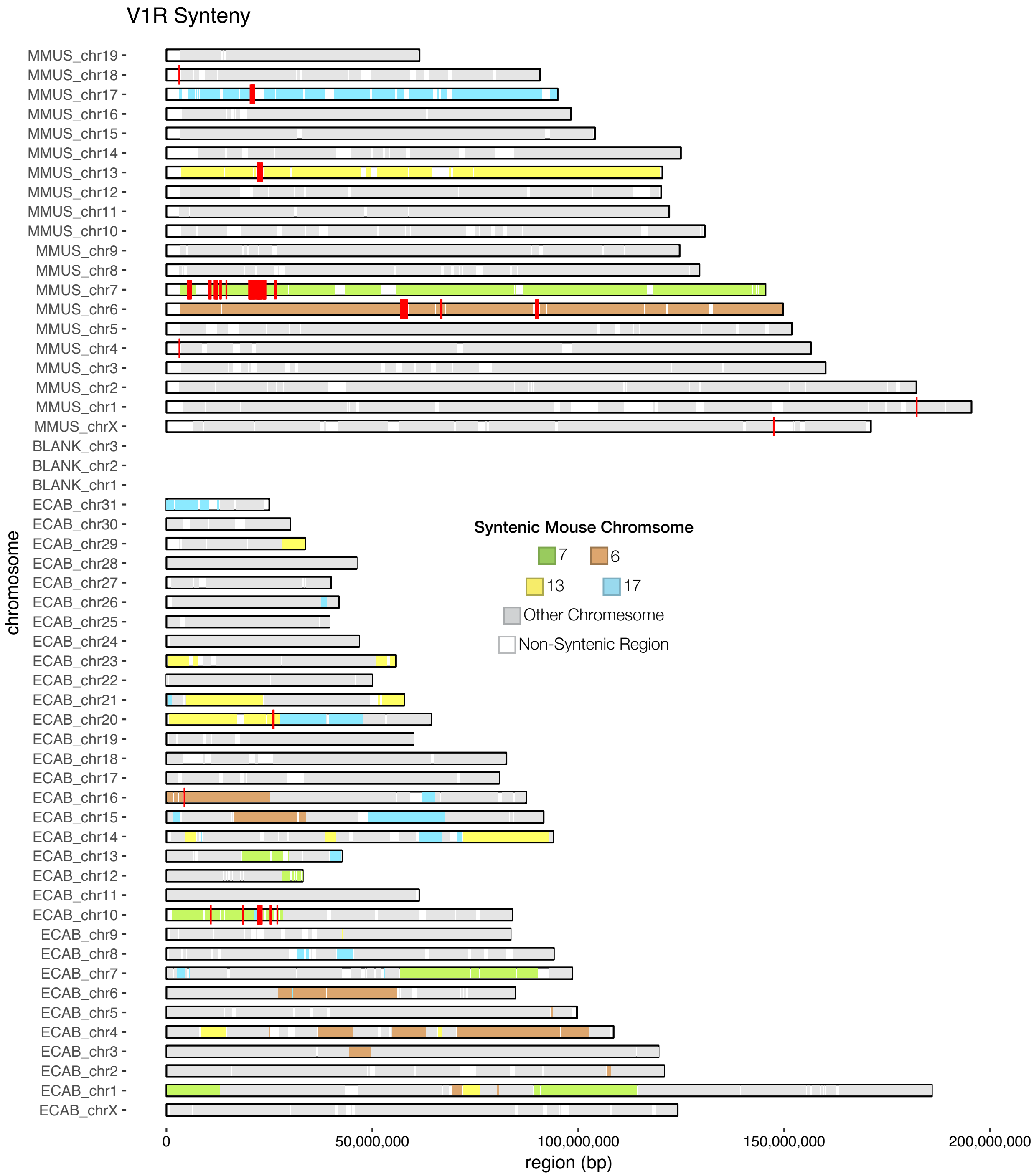


Figure S10 – Syntenic relationships between mouse and human. Human chromosomes are painted based on syntenic relationships with mouse. Locations of V1R genes are denoted in red.

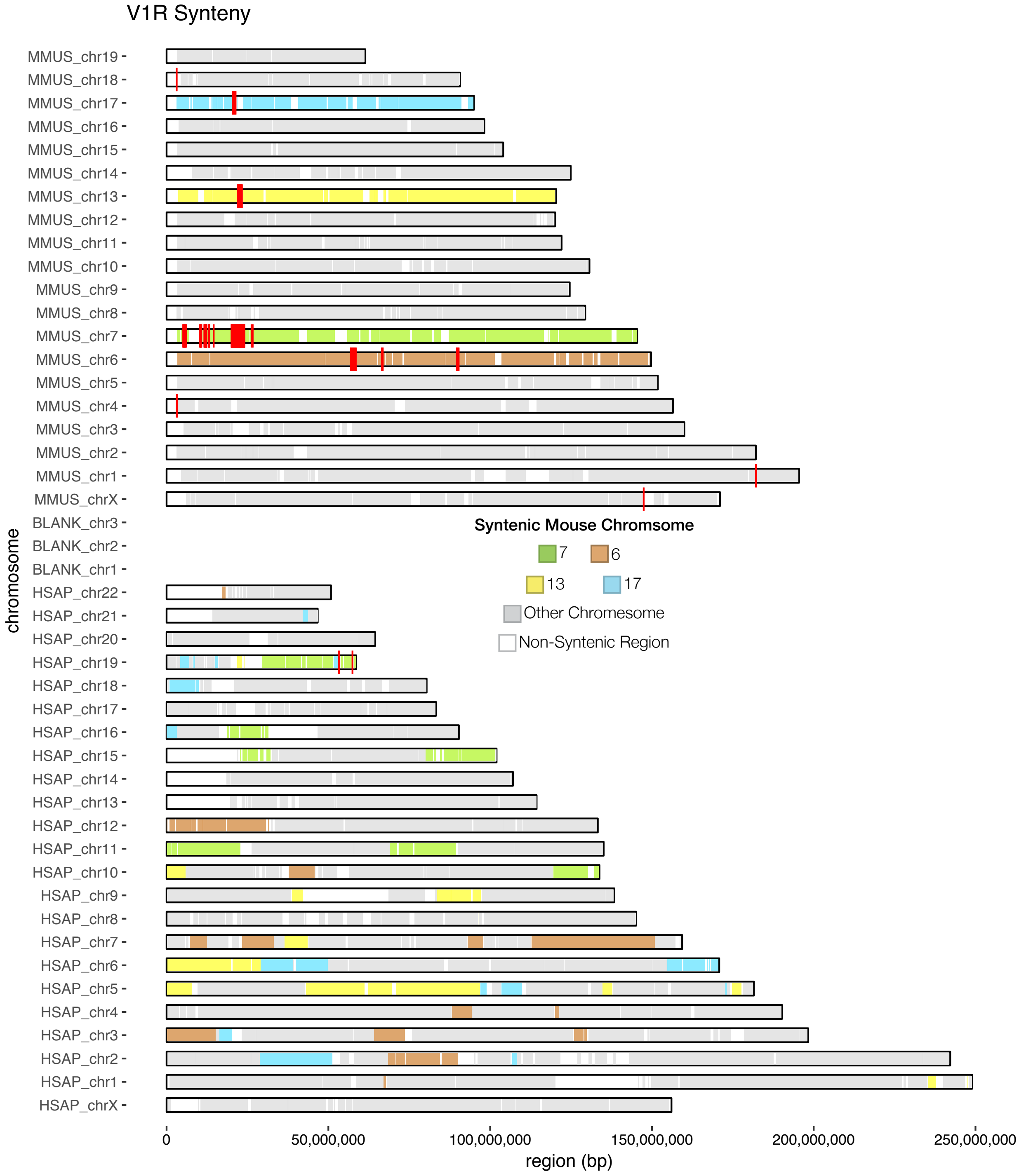


Figure S11 – Syntenic relationships between mouse lemur and human. Human chromosomes are painted based on syntenic relationships with mouse lemur. Locations of V1R genes are denoted in red. Putatively intact human V1Rs are labelled with gene names; VN1R1 and VN1R4 are the most likely V1Rs to have retained function in humans. Dashed box corresponds to "hotspot" chromosome in Figure 7.

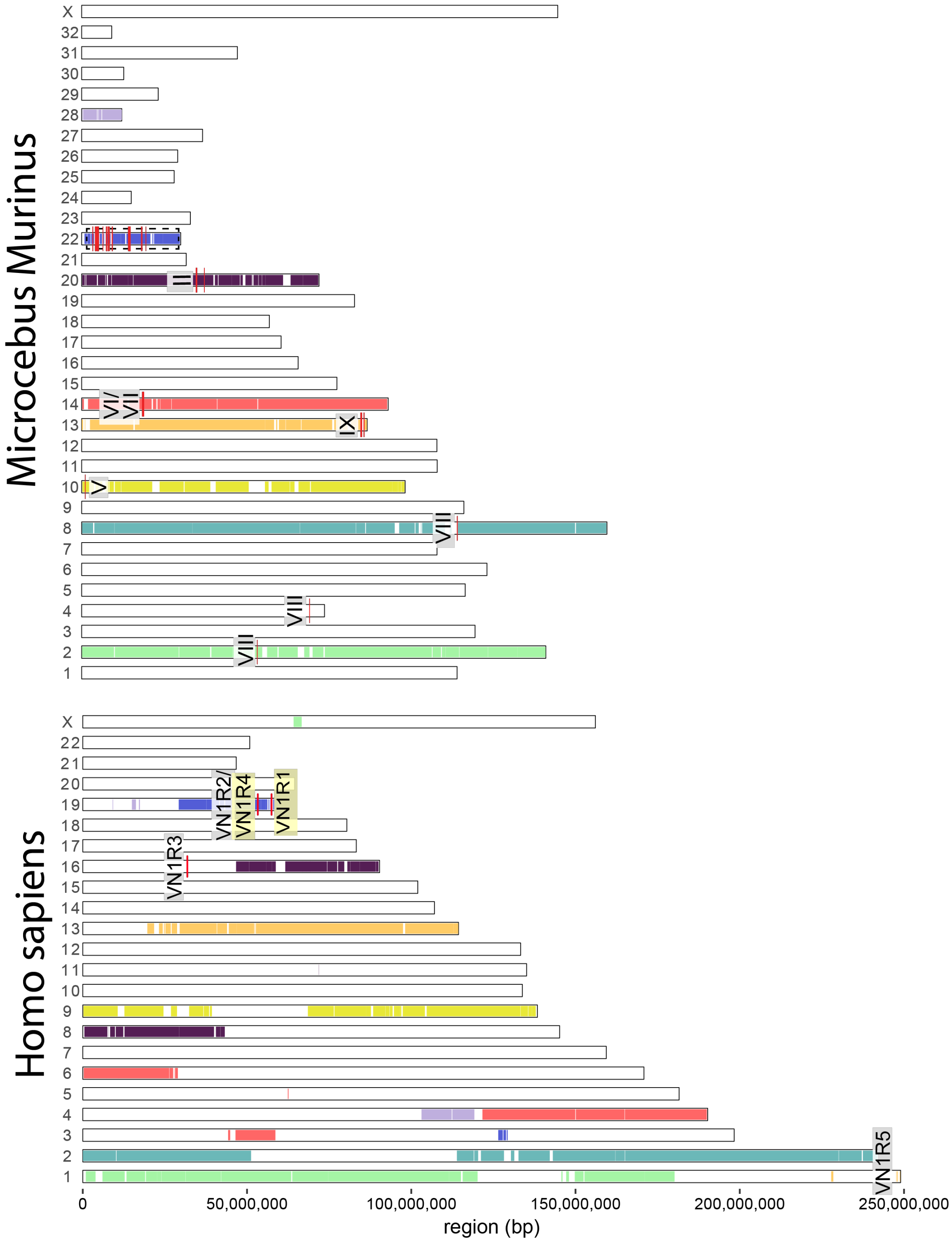
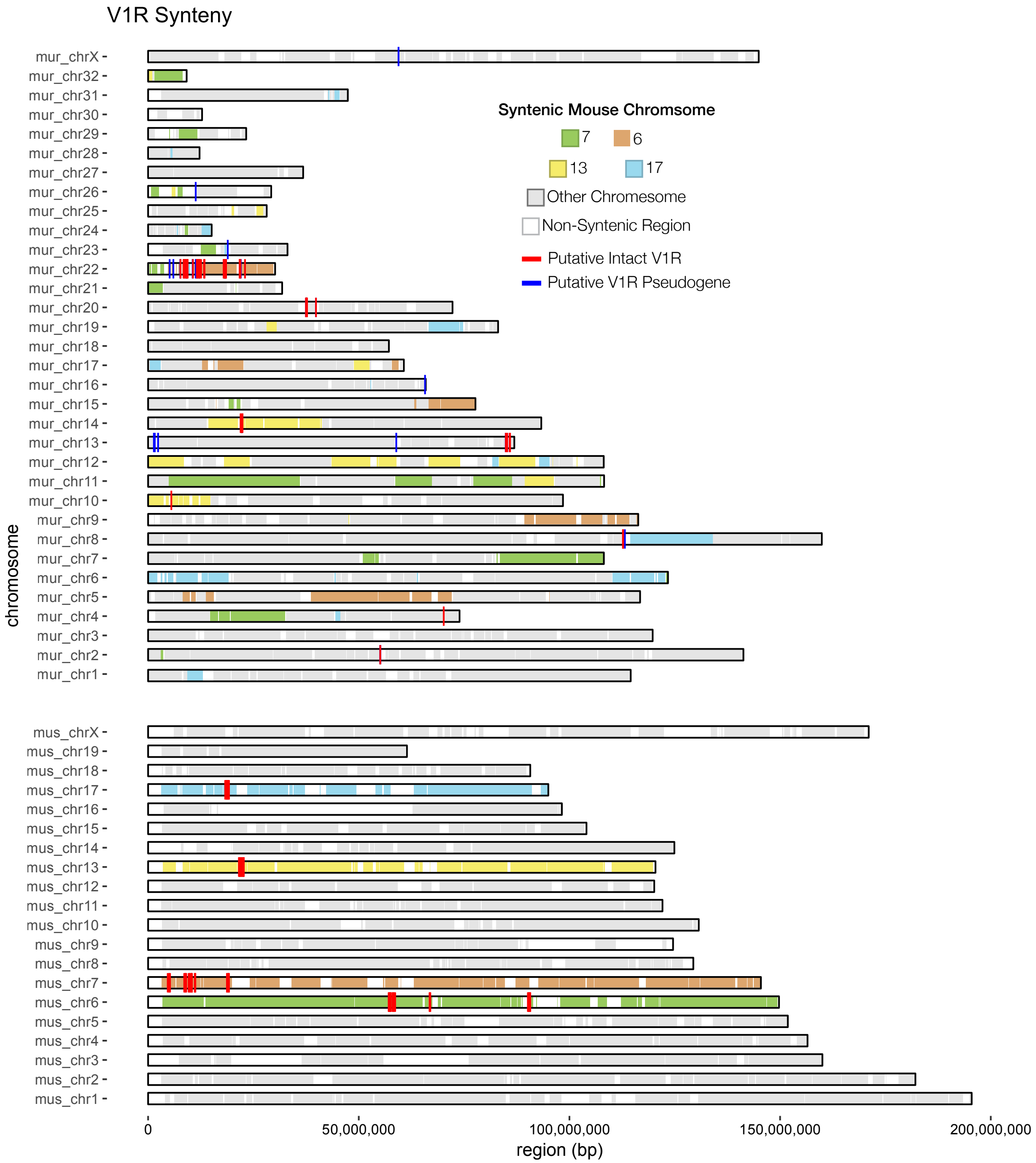


Figure S12 – Intact and pseudogenized V1Rs in mouse and mouse lemur. Mouse lemur chromosomes are painted based on syntenic relationships with mouse. Intact V1Rs indicated in red and pseudogenes in blue.



Supplementary Tables

Table S1 –Genome assemblies used for analyses. Gray rows indicate new dwarf or mouse lemur genomes.

Species	Assembly Name	Assembly Accession	Total Sequence Length (Gb)	Contig N50 (bp)	Scaffold N50 (bp)	Coverage
Bos taurus	Bos_taurus_UMD_3.1.1	GCF_000003055.6	2.67	98406	105708250*	9x
Callithrix jacchus	Callithrix jacchus-3.2	GCF_000004665.1	2.91	37523	132174527*	6.6x
Canis Familiaris	CanFam3.1	GCF_000002285.3	2.41	411364	63241923*	>7x
Carlito syrichta	Tarsius_syrichta_2.0.1	GCF_164805.1	3.45	59907	401181	48x
Cheirogaleus medius	Cmed_1.0	Pending	2.22	36308	50625866	110x
Cheirogaleus sibreei	Csib_1.0	Pending	2.4	53909	54899	39x
Daubentonia madagascariensis	DauMad_1.0	GCA_241425.1	2.86	3594	3653	38x
Equus Caballus	EquCab3.0	GCF_002863925.1	2.51	4715787	87230776*	88x
Eulemur flavifrons	Eflavifronsk33QCA	GCA_001262665.1	2.12	28371	413352	52.0x
Eulemur macaco	Emacaco_refEf_BWA_oneround	GCA_1262655.1	2.12	29783	405987	21.0x
Galeopterus variegatus	G_variegatus-3.0.2	GCF_000696425.1	3.19	22275	245189	55x
Gorilla gorilla	gorGor4	GCF_000151905.2	3.06	73808	146757320*	80x
Homo sapiens	GRCh38.p12	GCF_000001405.38	3.26	56413054	145138636*	NA
Microcebus griseorufus	Mgri_1.0	Pending	2.84	16706	16814	40x
Microcebus mittermeieri	Mmit_1.0	Pending	3.01	15313	15313	35x
Microcebus murinus	Mmur_2.0	GCF_165445.1	2.44	182929	3711085	221.6x
Microcebus murinus	Mmur_3.0	GCF_165445.2	2.49	234371	108171978*	221.6x
Microcebus murinus	Mmur_DLC7028	Pending	2.48	40992	7199757	29x
Microcebus murinus	Mmur_DLC7032	Pending	2.4	52099	9443435	28x
Microcebus murinus	Mmur_DLC7033v1	Pending	2.4	43653	10213316	25x
Microcebus murinus	Mmur_DLC7033v2	Pending	2.4	50994	12158062	27x
Microcebus murinus	Mmur_DLC7039	Pending	2.34	51699	4172979	26x
Microcebus murinus	Mmur_DLC7049	Pending	2.26	24431	631600	21x
Microcebus murinus	Mmur_DLC7128	Pending	2.37	40965	7271319	24x
Microcebus murinus	Mmur_DLC7163	Pending	2.3	38087	1220679	24x
Microcebus murinus	Mmur_DLC7188	Pending	2.3	32375	973440	22x
Microcebus ravelobensis	Mrav_1.0	Pending	2.42	21470	21489	26x
Microcebus tavaratra	Mtav_1.0	Pending	2.58	29674	30035	41x
Mirza zaza	Mzaz_1.0	Pending	2.36	74231	75828	44x
Mus musculus	GRCm38.p6	GCF_000001635.26	2.82	32273079	130694993*	NA
Nomascus leucogenys	Nleu_3.0	GCA_000146795.3	2.96	35148	117381234	5.6x
Otolemur garnetti	OtoGar3	GCF_181295.1	2.52	30487	13852661	137x
Prolemur simus	Prosim_1.0	GCA_003258685.1	2.41	47760	2710671	153x
Propithecus coquereli	Pcoq_1.0	GCF_000956105.1	2.8	28129	5604909	104.7x
Tupaia chinensis	TupChi_1.0	GCF_000334495.1	2.85	30015	3670124	80x

Table S2 – Allele counts by lemur V1R subfamily. Strepsirrhine primates shown in blue; haplorrhine primates in orange; outgroups in gray. Larsen et al. (2014) evaluated V1Rs for subfamily I and IX only.

Species	**I**	**II**	**III**	**IV**	**V**	**VI**	**VII**	**VIII**	**IX**	**Sum**
Otolemur garnetti	1	1	10	1	12	6	0	3	0	54
Daubentonia madagascariensis	0	0	6	0	0	1	0	1	1	17
Propithecus coquereli	6	4	10	0	3	1	0	0	0	27
Prolemur simus	1	6	6	0	5	1	0	0	0	22
Eulemur flavifrons	2	5	7	0	2	1	1	0	0	23
Eulemur macaco	2	5	7	0	3	1	1	0	0	25
Cheirogaleus medius	1	13	10	2	11	1	2	2	7	58
Cheirogaleus sibreei	8	15	14	2	12	2	2	4	6	70
Mirza zaza	8	10	26	3	16	5	5	2	8	95
Microcebus ravelobensis	14	15	25	8	24	8	3	4	17	129
Microcebus tavaratra	12	17	27	9	29	7	7	8	16	143
Microcebus griseus	15	15	17	4	23	12	5	10	25	137
Microcebus mittermeieri	17	21	22	10	26	7	4	9	22	146
Microcebus murinus 3.0 (reference)	11	12	17	7	17	10	5	3	12	102
Microcebus murinus (Larsen et al., 2014)	34-36	-	-	-	-	-	-	-	28-32	-
Microcebus murinus (Young et al., 2010)	29	7	13	4	14	9	4	5	19	105
Homo sapiens	0	0	1	0	0	0	0	0	0	2
Gorilla gorilla	0	0	0	0	0	0	0	0	0	2
Nomascus leucogenys	0	0	0	0	0	0	1	0	0	1
Callithrix jacchus	0	0	2	0	3	0	0	0	0	7
Carlito syrichta	1	0	10	0	4	0	0	0	0	28
Galeopterus variegatus	8	0	4	0	0	0	0	2	0	32
Tupaia chinensis	0	5	1	1	0	0	0	0	0	15

Table S3 – AU p-values for three competing topological hypotheses for each lemur subfamily. The three hypotheses are the topology estimated from the entire repertoire (Parsed Subtree), the topology estimated by ML from the original alignment when only analyzing taxa in each respective subfamily separately (MLE Subtree), and the MLE topology from the re-aligned data for each subfamily (Re-aligned Subtree). P-values < 0.0.5 should be interpreted as rejecting a topology from the plausible set.

	Subfamily	Parsed Subtree	MLE Subtree	Re-aligned Subtree
Original Alignment	I	0.194	0.688	0.524
	II	0.195	0.604	0.611
	III	0.398	0.622	0.428
	IV	0.433	0.525	0.511
	V	0.317	0.472	0.644
	VI	0.347	0.551	0.574
	VII	0.399	0.696	0.309
	VIII	0.465	0.447	0.535
	IX	0.217	0.569	0.605
Subfamily Re-Alignment	I	0.184	0.682	0.532
	II	0.149	0.614	0.618
	III	0.363	0.509	0.571
	IV	0.401	0.522	0.548
	V	0.347	0.171	0.783
	VI	0.374	0.533	0.562
	VII	0.269	0.45	0.667
	VIII	0.47	0.467	0.517
	IX	0.209	0.581	0.597

Table S4 – Site model results for M2a and M1a comparisons. Proportions of sites (p) and dN/dS for each proportion (ω) are given for each subfamily analysis across taxonomic filters. Missing rows mean that a taxonomic filter was equivalent the next-rank filter.

		Model M1a				Model M2a							
Subfamily	**Filter**	**p_1**	**p_2**	**ω_1**	**ω_2**	**p_1**	**p_2**	**p_3**	**ω_1**	**ω_2**	**ω_3**	**LRT**	**p-value**
I	Microcebus	0.60	0.40	0.10	1	0.57	0.31	0.12	0.12	1	2.82	111.805934	3.9405E-26
I	Cheirogaleidae	0.57	0.43	0.11	1	0.54	0.33	0.12	0.12	1	2.67	137.943934	7.4964E-32
I	Lemuriformes	0.58	0.42	0.13	1	0.56	0.29	0.15	0.15	1	2.45	160.95441	7.0004E-37
I	Strepsirrhini	0.58	0.42	0.13	1	0.55	0.31	0.14	0.15	1	2.48	165.751974	6.2668E-38
I	Primates	0.59	0.41	0.14	1	0.56	0.30	0.14	0.16	1	2.42	157.485958	4.0083E-36
I	Euarchontoglires	0.58	0.42	0.17	1	0.53	0.33	0.13	0.18	1	2.41	165.310042	7.8268E-38
II	Microcebus	0.51	0.49	0.12	1	0.46	0.39	0.15	0.13	1	2.55	116.820924	3.1419E-27
II	Cheirogaleidae	0.55	0.45	0.17	1	0.46	0.41	0.14	0.16	1	2.65	242.259782	1.2647E-54
II	Lemuriformes	0.54	0.46	0.17	1	0.49	0.35	0.16	0.19	1	2.38	255.74758	1.4503E-57
II	Strepsirrhini	0.52	0.48	0.16	1	0.46	0.38	0.16	0.17	1	2.41	262.997026	3.8129E-59
II	Primates	-	-	-	-	-	-	-	-	-	-	-	-
II	Euarchontoglires	0.50	0.50	0.17	1	0.45	0.38	0.16	0.18	1	2.33	261.758322	7.0998E-59
III	Microcebus	0.47	0.53	0.27	1	0.45	0.46	0.09	0.29	1	2.09	30.298634	3.7039E-08
III	Cheirogaleidae	0.47	0.53	0.29	1	0.44	0.47	0.08	0.30	1	2.05	36.328468	1.6671E-09
III	Lemuriformes	0.42	0.58	0.29	1	0.38	0.51	0.11	0.29	1	2.21	86.534884	1.3729E-20
III	Strepsirrhini	0.44	0.56	0.31	1	0.39	0.50	0.11	0.31	1	2.27	136.735624	1.3776E-31
III	Primates	0.42	0.58	0.31	1	0.38	0.51	0.11	0.32	1	2.18	156.325702	7.1861E-36
III	Euarchontoglires	0.41	0.59	0.31	1	0.36	0.48	0.16	0.31	1	1.94	176.839356	2.3744E-40
IV	Microcebus	0.59	0.41	0.10	1	0.56	0.40	0.03	0.10	1	4.95	53.482136	2.6096E-13
IV	Cheirogaleidae	0.61	0.39	0.10	1	0.59	0.36	0.06	0.10	1	3.32	47.768638	4.796E-12
IV	Lemuriformes	-	-	-	-	-	-	-	-	-	-	-	-
IV	Strepsirrhini	0.62	0.38	0.14	1	0.60	0.35	0.06	0.15	1	3.38	59.238676	1.3966E-14
IV	Primates	-	-	-	-	-	-	-	-	-	-	-	-
IV	Euarchontoglires	0.60	0.40	0.15	1	0.58	0.37	0.05	0.16	1	3.26	54.28628	1.7331E-13
V	Microcebus	0.53	0.47	0.18	1	0.49	0.41	0.10	0.19	1	2.46	90.854152	1.5466E-21
V	Cheirogaleidae	0.56	0.44	0.21	1	0.52	0.36	0.12	0.22	1	2.32	158.032934	3.044E-36
V	Lemuriformes	0.56	0.44	0.23	1	0.53	0.35	0.12	0.25	1	2.24	171.736126	3.0902E-39
V	Strepsirrhini	0.54	0.46	0.24	1	0.50	0.34	0.16	0.27	1	2.20	233.18608	1.2037E-52
V	Primates	0.53	0.47	0.25	1	0.48	0.37	0.16	0.27	1	2.24	274.17196	1.3985E-61
V	Euarchontoglires	-	-	-	-	-	-	-	-	-	-	-	-
VI	Microcebus	0.41	0.59	0.00	1	0.39	0.50	0.11	0.00	1	3.51	19.380746	0.000010708
VI	Cheirogaleidae	0.49	0.51	0.12	1	0.44	0.51	0.04	0.12	1	4.61	42.972056	5.5527E-11
VI	Lemuriformes	0.47	0.53	0.14	1	0.42	0.54	0.04	0.14	1	4.70	39.72317	2.9263E-10
VI	Strepsirrhini	-	-	-	-	-	-	-	-	-	-	-	-
VI	Primates	0.48	0.52	0.16	1	0.43	0.54	0.03	0.16	1	5.45	46.81382	7.8061E-12
VI	Euarchontoglires	-	-	-	-	-	-	-	-	-	-	-	-
VII	Microcebus	0.64	0.36	0.13	1	0.70	0.17	0.13	0.20	1	2.50	29.510204	5.5623E-08
VII	Cheirogaleidae	0.65	0.35	0.16	1	0.66	0.28	0.06	0.19	1	2.85	28.2485	1.067E-07
VII	Lemuriformes	0.63	0.37	0.15	1	0.62	0.35	0.04	0.16	1	3.21	24.418524	7.752E-07
VII	Strepsirrhini	0.49	0.51	0.16	1	0.47	0.45	0.08	0.16	1	2.54	33.064448	8.9154E-09
VII	Primates	-	-	-	-	-	-	-	-	-	-	-	-
VII	Euarchontoglires	-	-	-	-	-	-	-	-	-	-	-	-
VIII	Microcebus	0.51	0.49	0.02	1	0.62	0.19	0.19	0.13	1	2.87	34.796766	3.6598E-09
VIII	Cheirogaleidae	0.51	0.49	0.11	1	0.51	0.35	0.14	0.16	1	2.91	40.058136	2.4652E-10
VIII	Lemuriformes	-	-	-	-	-	-	-	-	-	-	-	-
VIII	Strepsirrhini	0.52	0.48	0.20	1	0.49	0.37	0.14	0.26	1	2.99	64.793112	8.3189E-16
VIII	Primates	-	-	-	-	-	-	-	-	-	-	-	-
VIII	Euarchontoglires	0.51	0.49	0.25	1	0.49	0.35	0.15	0.31	1	2.62	57.357012	3.6347E-14
IX	Microcebus	0.61	0.39	0.11	1	0.57	0.26	0.16	0.12	1	2.99	245.664162	2.2894E-55
IX	Cheirogaleidae	0.60	0.40	0.13	1	0.54	0.29	0.17	0.15	1	2.94	329.572516	1.191E-73
IX	Lemuriformes	-	-	-	-	-	-	-	-	-	-	-	-
IX	Strepsirrhini	0.60	0.40	0.14	1	0.55	0.28	0.18	0.16	1	2.87	329.832496	1.0454E-73
IX	Primates	-	-	-	-	-	-	-	-	-	-	-	-
IX	Euarchontoglires	-	-	-	-	-	-	-	-	-	-	-	-

Table S5 – Site model results for M8 and M7 comparisons. Proportions of sites (p) and dN/dS for each proportion (ω) are given for each subfamily analysis across taxonomic filters. Missing rows mean that a taxonomic filter was equivalent the next-rank filter.

		Model M7		**Model M8**						
Subfamily	**Filter**	**α**	**β**	**$p_{<=1}$**	**$p_{>1}$**	**α**	**β**	**ω> 1**	**LRT**	**p-value**
I	Microcebus	0.26	0.31	0.84	0.16	0.4	0.71	2.47	137.392636	9.90E-32
I	Cheirogaleidae	0.27	0.31	0.85	0.15	0.36	0.57	2.37	157.565802	3.85E-36
I	Lemuriformes	0.33	0.37	0.81	0.19	0.51	0.9	2.17	197.675886	6.71E-45
I	Strepsirrhini	0.34	0.38	0.82	0.18	0.5	0.84	2.18	196.47499	1.23E-44
I	Primates	0.37	0.41	0.82	0.18	0.56	0.97	2.1	192.406904	9.48E-44
I	Euarchontoglires	0.45	0.47	0.83	0.17	0.64	0.96	2.05	193.734876	4.87E-44
II	Microcebus	0.3	0.27	0.82	0.18	0.43	0.55	2.28	137.184348	1.10E-31
II	Cheirogaleidae	0.38	0.37	0.83	0.17	0.51	0.64	2.27	251.543584	1.20E-56
II	Lemuriformes	0.42	0.37	0.8	0.2	0.59	0.72	2.14	287.17727	2.05E-64
II	Strepsirrhini	0.43	0.36	0.81	0.19	0.58	0.68	2.13	280.149164	6.97E-63
II	Primates	-	-	-	-	-	-	-	-	-
II	Euarchontoglires	0.47	0.38	0.81	0.19	0.62	0.69	2.07	274.870922	9.85E-62
III	Microcebus	0.82	0.52	0.81	0.19	1.15	1.04	1.63	53.054524	3.24E-13
III	Cheirogaleidae	0.87	0.56	0.84	0.16	1.1	0.93	1.6	56.213286	6.50E-14
III	Lemuriformes	0.81	0.48	0.86	0.14	0.96	0.7	1.79	95.212948	1.71E-22
III	Strepsirrhini	0.81	0.48	0.86	0.14	0.95	0.67	1.84	138.378504	6.023E-32
III	Primates	0.84	0.49	0.84	0.16	1	0.71	1.73	152.993582	3.84E-35
III	Euarchontoglires	0.82	0.49	0.82	0.18	1.01	0.76	1.66	172.539424	2.06E-39
IV	Microcebus	0.18	0.2	0.92	0.08	0.31	0.44	3.29	60.529864	7.25E-15
IV	Cheirogaleidae	0.22	0.28	0.92	0.08	0.31	0.5	2.8	58.369812	2.17E-14
IV	Lemuriformes	-	-	-	-	-	-	-	-	-
IV	Strepsirrhini	0.34	0.4	0.91	0.09	0.52	0.77	2.74	76.188962	2.58E-18
IV	Primates	-	-	-	-	-	-	-	-	-
IV	Euarchontoglires	0.41	0.45	0.91	0.09	0.58	0.81	2.59	71.923442	2.24E-17
V	Microcebus	0.47	0.4	0.81	0.19	0.7	0.87	1.93	113.537168	1.65E-26
V	Cheirogaleidae	0.57	0.51	0.85	0.15	0.78	0.91	2.04	186.14484	2.21E-42
V	Lemuriformes	0.64	0.54	0.84	0.16	0.93	1.03	1.96	210.413496	1.12E-47
V	Strepsirrhini	0.66	0.51	0.81	0.19	0.94	0.99	1.96	269.719446	1.31E-60
V	Primates	0.71	0.54	0.82	0.18	1	1	1.96	295.790652	2.72E-66
V	Euarchontoglires	-	-	-	-	-	-	-	-	-
VI	Microcebus	0.01	0.01	0.87	0.13	0.03	0.03	3.32	19.33141	0.000010988
VI	Cheirogaleidae	0.21	0.15	0.94	0.06	0.27	0.2	4.21	47.128876	6.65E-12
VI	Lemuriformes	0.25	0.17	0.95	0.05	0.32	0.21	4.17	43.464826	4.32E-11
VI	Strepsirrhini	-	-	-	-	-	-	-	-	-
VI	Primates	0.33	0.21	0.96	0.04	0.35	0.22	5.08	51.081888	8.86E-13
VI	Euarchontoglires	-	-	-	-	-	-	-	-	-
VII	Microcebus	0.26	0.29	0.81	0.19	2.7	7.43	2.18	43.343834	4.59E-11
VII	Cheirogaleidae	0.42	0.48	0.88	0.12	1.08	1.98	2.26	45.243112	1.74E-11
VII	Lemuriformes	0.39	0.46	0.9	0.1	0.68	1.07	2.24	36.053678	1.92E-09
VII	Strepsirrhini	0.43	0.35	0.86	0.14	0.62	0.7	2.07	47.219908	6.35E-12
VII	Primates	-	-	-	-	-	-	-	-	-
VII	Euarchontoglires	-	-	-	-	-	-	-	-	-
VIII	Microcebus	0.02	0.02	0.76	0.24	0.75	2.24	2.67	34.656634	3.93E-09
VIII	Cheirogaleidae	0.16	0.11	0.82	0.18	0.56	0.69	2.65	48.01802	4.22E-12
VIII	Lemuriformes	-	-	-	-	-	-	-	-	-
VIII	Strepsirrhini	0.54	0.36	0.83	0.17	1.09	1.04	2.7	89.677224	2.80E-21
VIII	Primates	-	-	-	-	-	-	-	-	-
VIII	Euarchontoglires	0.63	0.37	0.82	0.18	1.2	1	2.43	80.584932	2.78E-19
IX	Microcebus	0.29	0.37	0.82	0.18	0.45	0.93	2.65	280.7036	5.28E-63
IX	Cheirogaleidae	0.32	0.36	0.81	0.19	0.46	0.76	2.63	356.988518	1.27E-79
IX	Lemuriformes	-	-	-	-	-	-	-	-	-
IX	Strepsirrhini	0.35	0.38	0.81	0.19	0.51	0.83	2.6	365.349952	1.93E-81
IX	Primates	-	-	-	-	-	-	-	-	-
IX	Euarchontoglires	-	-	-	-	-	-	-	-	-

Table S6 – Site model results for M2a and M1a comparisons with realigned subfamilies. Proportions of sites (p) and dN/dS for each proportion (ω) are given for each subfamily analysis across taxonomic filters. Missing rows mean that a taxonomic filter was equivalent the next-rank filter.

		Model M1a				Model M2a							
Subfamily	**Filter**	p_1	p_2	ω_1	ω_2	p_1	p_2	p_3	ω_1	ω_2	ω_3	**LRT**	**p-value**
I	Microcebus	0.60	0.40	0.10	1.00	0.57	0.31	0.12	0.12	1.00	2.86	122.50463	1.79E-28
I	Cheirogaleidae	0.57	0.43	0.12	1.00	0.54	0.33	0.13	0.13	1.00	2.68	147.000558	7.85E-34
I	Lemuriformes	0.59	0.41	0.13	1.00	0.56	0.29	0.16	0.15	1.00	2.50	173.567412	1.23E-39
I	Strepsirrhini	0.58	0.42	0.13	1.00	0.54	0.31	0.15	0.15	1.00	2.54	179.88805	5.13E-41
I	Primates	0.59	0.41	0.14	1.00	0.55	0.30	0.14	0.16	1.00	2.47	170.458462	5.88E-39
I	Euarchontoglires	0.58	0.42	0.17	1.00	0.53	0.33	0.14	0.18	1.00	2.44	173.354098	1.37E-39
II	Microcebus	0.51	0.49	0.13	1.00	0.46	0.39	0.15	0.13	1.00	2.54	116.795128	3.18E-27
II	Cheirogaleidae	0.55	0.45	0.17	1.00	0.46	0.41	0.13	0.16	1.00	2.66	247.423316	9.47E-56
II	Lemuriformes	0.54	0.46	0.17	1.00	0.49	0.34	0.17	0.19	1.00	2.41	267.714142	3.57E-60
II	Strepsirrhini	0.52	0.48	0.17	1.00	0.47	0.37	0.16	0.18	1.00	2.44	274.394682	1.25E-61
II	Primates	-	-	-	-	-	-	-	-	-	-	-	-
II	Euarchontoglires	0.50	0.50	0.17	1.00	0.46	0.38	0.16	0.18	1.00	2.36	274.093382	1.45E-61
III	Microcebus	0.48	0.52	0.27	1.00	0.45	0.47	0.08	0.28	1.00	2.26	39.516662	3.25E-10
III	Cheirogaleidae	0.48	0.52	0.29	1.00	0.46	0.50	0.04	0.29	1.00	3.27	55.03314	1.19E-13
III	Lemuriformes	0.44	0.56	0.29	1.00	0.40	0.50	0.10	0.29	1.00	2.23	105.810392	8.11E-25
III	Strepsirrhini	0.46	0.54	0.31	1.00	0.42	0.48	0.10	0.31	1.00	2.29	154.07496	2.23E-35
III	Primates	0.45	0.55	0.32	1.00	0.40	0.49	0.11	0.32	1.00	2.21	179.411586	6.51E-41
III	Euarchontoglires	0.43	0.57	0.31	1.00	0.38	0.46	0.16	0.32	1.00	1.96	198.090052	5.45E-45
IV	Microcebus	0.60	0.40	0.10	1.00	0.58	0.38	0.04	0.11	1.00	4.32	53.61382	2.44E-13
IV	Cheirogaleidae	0.61	0.39	0.10	1.00	0.59	0.35	0.06	0.11	1.00	3.42	54.955884	1.23E-13
IV	Lemuriformes	-	-	-	-	-	-	-	-	-	-	-	-
IV	Strepsirrhini	0.62	0.38	0.14	1.00	0.59	0.35	0.06	0.15	1.00	3.52	64.523152	9.54E-16
IV	Primates	-	-	-	-	-	-	-	-	-	-	-	-
IV	Euarchontoglires	0.60	0.40	0.15	1.00	0.58	0.36	0.06	0.16	1.00	3.41	63.486246	1.61E-15
V	Microcebus	0.52	0.48	0.18	1.00	0.49	0.42	0.09	0.19	1.00	2.43	84.930738	3.09E-20
V	Cheirogaleidae	0.54	0.46	0.20	1.00	0.50	0.37	0.13	0.22	1.00	2.30	151.910276	6.63E-35
V	Lemuriformes	0.55	0.45	0.23	1.00	0.51	0.36	0.13	0.25	1.00	2.24	167.123622	3.14E-38
V	Strepsirrhini	0.53	0.47	0.24	1.00	0.50	0.35	0.15	0.27	1.00	2.21	230.308924	5.10E-52
V	Primates	0.51	0.49	0.25	1.00	0.47	0.37	0.15	0.27	1.00	2.27	280.939722	4.69E-63
V	Euarchontoglires	-	-	-	-	-	-	-	-	-	-	-	-
VI	Microcebus	0.40	0.60	0.00	1.00	0.39	0.52	0.10	0.00	1.00	3.53	16.811742	0.000041277
VI	Cheirogaleidae	0.48	0.52	0.12	1.00	0.44	0.51	0.05	0.12	1.00	4.23	32.927292	9.57E-09
VI	Lemuriformes	0.46	0.54	0.13	1.00	0.42	0.53	0.04	0.13	1.00	4.25	32.307594	1.32E-08
VI	Strepsirrhini	-	-	-	-	-	-	-	-	-	-	-	-
VI	Primates	0.46	0.54	0.15	1.00	0.42	0.55	0.03	0.15	1.00	4.84	37.918052	7.38E-10
VI	Euarchontoglires	-	-	-	-	-	-	-	-	-	-	-	-
VII	Microcebus	0.65	0.35	0.12	1.00	0.75	0.07	0.18	0.21	1.00	2.29	34.254512	4.84E-09
VII	Cheirogaleidae	0.65	0.35	0.15	1.00	0.68	0.23	0.10	0.19	1.00	2.36	23.969488	9.79E-07
VII	Lemuriformes	0.63	0.37	0.14	1.00	0.63	0.33	0.04	0.16	1.00	2.86	19.910532	8.12E-06
VII	Strepsirrhini	0.50	0.50	0.15	1.00	0.48	0.44	0.08	0.16	1.00	2.54	30.027	4.26E-08
VII	Primates	-	-	-	-	-	-	-	-	-	-	-	-
VII	Euarchontoglires	-	-	-	-	-	-	-	-	-	-	-	-
VIII	Microcebus	0.51	0.49	0.02	1.00	0.62	0.19	0.19	0.13	1.00	2.87	34.796754	3.66E-09
VIII	Cheirogaleidae	0.51	0.49	0.11	1.00	0.51	0.35	0.14	0.16	1.00	2.91	40.058122	2.47E-10
VIII	Lemuriformes	-	-	-	-	-	-	-	-	-	-	-	-
VIII	Strepsirrhini	0.53	0.47	0.21	1.00	0.50	0.37	0.13	0.26	1.00	2.96	63.007258	2.06E-15
VIII	Primates	-	-	-	-	-	-	-	-	-	-	-	-
VIII	Euarchontoglires	0.51	0.49	0.25	1.00	0.50	0.35	0.15	0.31	1.00	2.59	55.772076	8.14E-14
IX	Microcebus	0.61	0.39	0.10	1.00	0.57	0.26	0.16	0.12	1.00	3.06	255.83814	1.39E-57
IX	Cheirogaleidae	0.60	0.40	0.13	1.00	0.55	0.28	0.17	0.15	1.00	2.95	333.087086	2.04E-74
IX	Lemuriformes	-	-	-	-	-	-	-	-	-	-	-	-
IX	Strepsirrhini	0.60	0.40	0.14	1.00	0.55	0.27	0.18	0.16	1.00	2.91	342.395736	1.92E-76
IX	Primates	-	-	-	-	-	-	-	-	-	-	-	-
IX	Euarchontoglires	-	-	-	-	-	-	-	-	-	-	-	-

Table S7 – Site model results for M8 and M7 comparisons with realigned subfamilies. Proportions of sites (p) and dN/dS for each proportion (ω) are given for each subfamily analysis across taxonomic filters. Missing rows mean that a taxonomic filter was equivalent the next-rank filter.

		Model M7		Model M8						
Subfamily	**Filter**	**α**	**β**	**$p_{<=1}$**	**$p_{>1}$**	**α**	**β**	**$\omega > 1$**	**LRT**	**p-value**
I	Microcebus	0.26	0.31	0.83	0.17	0.41	0.74	2.53	150.170338	1.59E-34
I	Cheirogaleidae	0.27	0.31	0.84	0.16	0.37	0.60	2.39	167.935146	2.09E-38
I	Lemuriformes	0.33	0.37	0.81	0.19	0.52	0.94	2.22	212.262326	4.41E-48
I	Strepsirrhini	0.34	0.38	0.82	0.18	0.51	0.84	2.24	210.760468	9.37E-48
I	Primates	0.37	0.42	0.82	0.18	0.57	0.98	2.15	205.612676	1.24E-46
I	Euarchontoglires	0.45	0.47	0.82	0.18	0.66	1.00	2.06	202.948876	4.75E-46
II	Microcebus	0.30	0.27	0.82	0.18	0.44	0.56	2.28	137.529682	9.24E-32
II	Cheirogaleidae	0.38	0.37	0.82	0.18	0.53	0.66	2.27	259.714792	1.98E-58
II	Lemuriformes	0.42	0.36	0.80	0.20	0.60	0.72	2.17	300.977164	2.02E-67
II	Strepsirrhini	0.43	0.36	0.80	0.20	0.59	0.69	2.15	294.108412	6.33E-66
II	Primates	-	-	-	-	-	-	-	-	-
II	Euarchontoglires	0.47	0.38	0.81	0.19	0.63	0.69	2.11	288.757602	9.27E-65
III	Microcebus	0.81	0.52	0.84	0.16	1.09	0.94	1.74	60.595118	7.01E-15
III	Cheirogaleidae	0.86	0.57	0.87	0.13	1.06	0.87	1.72	69.257938	8.64E-17
III	Lemuriformes	0.81	0.50	0.87	0.13	0.96	0.71	1.85	113.20616	1.94E-26
III	Strepsirrhini	0.82	0.50	0.86	0.14	0.96	0.70	1.84	157.63547	3.7179E-36
III	Primates	0.84	0.50	0.85	0.15	0.99	0.72	1.79	176.906024	2.30E-40
III	Euarchontoglires	0.81	0.50	0.82	0.18	1.01	0.78	1.69	193.914718	4.45E-44
IV	Microcebus	0.19	0.22	0.92	0.08	0.34	0.50	3.27	61.911974	3.59E-15
IV	Cheirogaleidae	0.22	0.29	0.91	0.09	0.33	0.54	2.88	66.474776	3.54E-16
IV	Lemuriformes	-	-	-	-	-	-	-	-	-
IV	Strepsirrhini	0.35	0.41	0.91	0.09	0.52	0.76	2.91	81.651228	1.62E-19
IV	Primates	-	-	-	-	-	-	-	-	-
IV	Euarchontoglires	0.39	0.44	0.90	0.10	0.55	0.77	2.79	82.09013	1.30E-19
V	Microcebus	0.47	0.39	0.81	0.19	0.68	0.82	1.90	105.453038	9.72E-25
V	Cheirogaleidae	0.56	0.49	0.84	0.16	0.76	0.86	2.03	177.625352	1.60E-40
V	Lemuriformes	0.64	0.52	0.83	0.17	0.91	0.99	1.95	202.804436	5.10E-46
V	Strepsirrhini	0.66	0.50	0.81	0.19	0.93	0.97	1.95	263.943558	2.37E-59
V	Primates	0.71	0.53	0.82	0.18	0.97	0.93	2.00	296.61835	1.80E-66
V	Euarchontoglires	-	-	-	-	-	-	-	-	-
VI	Microcebus	0.01	0.01	0.89	0.11	0.02	0.02	3.37	16.584434	0.000046531
VI	Cheirogaleidae	0.21	0.15	0.94	0.06	0.28	0.20	3.88	36.764068	1.33E-09
VI	Lemuriformes	0.25	0.16	0.95	0.05	0.32	0.22	3.86	35.786758	2.20E-09
VI	Strepsirrhini	-	-	-	-	-	-	-	-	-
VI	Primates	0.32	0.21	0.96	0.04	0.36	0.23	4.42	41.867654	9.77E-11
VI	Euarchontoglires	-	-	-	-	-	-	-	-	-
VII	Microcebus	0.23	0.27	0.79	0.21	29.05	99.00	2.14	51.540866	7.01E-13
VII	Cheirogaleidae	0.38	0.45	0.78	0.22	3.50	10.37	1.78	44.981404	1.99E-11
VII	Lemuriformes	0.37	0.43	0.76	0.24	1.90	5.96	1.59	35.581718	2.45E-09
VII	Strepsirrhini	0.41	0.35	0.85	0.15	0.62	0.75	2.00	44.861122	2.12E-11
VII	Primates	-	-	-	-	-	-	-	-	-
VII	Euarchontoglires	-	-	-	-	-	-	-	-	-
VIII	Microcebus	0.02	0.02	0.76	0.24	0.75	2.24	2.67	34.657132	3.93E-09
VIII	Cheirogaleidae	0.04	0.02	0.82	0.18	0.56	0.69	2.65	47.580534	5.28E-12
VIII	Lemuriformes	-	-	-	-	-	-	-	-	-
VIII	Strepsirrhini	0.53	0.37	0.83	0.17	1.09	1.03	2.67	87.56152	8.17E-21
VIII	Primates	-	-	-	-	-	-	-	-	-
VIII	Euarchontoglires	0.63	0.38	0.82	0.18	1.20	1.03	2.39	79.258242	5.45E-19
IX	Microcebus	0.28	0.36	0.82	0.18	0.43	0.87	2.73	289.51926	6.33E-65
IX	Cheirogaleidae	0.32	0.36	0.81	0.19	0.46	0.79	2.63	360.772864	1.91E-80
IX	Lemuriformes	-	-	-	-	-	-	-	-	-
IX	Strepsirrhini	0.34	0.38	0.80	0.20	0.51	0.85	2.62	376.86275	6.00E-84
IX	Primates	-	-	-	-	-	-	-	-	-
IX	Euarchontoglires	-	-	-	-	-	-	-	-	-

Table S8 – P-values from chi-square tests for biases of pervasive selection occurring in transmembrane or loop domains across subfamilies. Asterisks (*) indicate a p-value less than 0.05 given a null distribution of X^2_1.

Subfamily	Filter	Chi Square	p-value	significant	Proportion TM	Proportion Loop	Expected Proportion
I	Microcebus	1.61	0.20455	NS	0.129	0.094	0.104
I	Cheirogaleidae	7.03	0.0080016	*	0.158	0.084	0.105
I	Lemuriformes	4.59	0.032105	*	0.164	0.101	0.119
I	Strepsirrhini	2.20	0.13794	NS	0.146	0.103	0.116
I	Primates	3.83	0.050241	NS	0.152	0.096	0.112
I	Euarchontoglires	2.78	0.095474	NS	0.140	0.094	0.107
II	Microcebus	4.28	0.038654	*	0.140	0.084	0.100
II	Cheirogaleidae	4.59	0.032105	*	0.164	0.101	0.119
II	Lemuriformes	0.75	0.38538	NS	0.146	0.120	0.128
II	Strepsirrhini	0.38	0.53519	NS	0.146	0.127	0.133
II	Euarchontoglires	1.76	0.18491	NS	0.158	0.118	0.129
III	Microcebus	0.00	0.99873	NS	0.094	0.094	0.094
III	Cheirogaleidae	1.96	0.16169	NS	0.064	0.101	0.090
III	Lemuriformes	1.36	0.24414	NS	0.070	0.101	0.092
III	Strepsirrhini	2.21	0.13691	NS	0.076	0.118	0.105
III	Primates	5.49	0.01911	*	0.070	0.139	0.119
III	Euarchontoglires	3.44	0.063462	NS	0.070	0.122	0.107
IV	Microcebus	0.30	0.58325	NS	0.088	0.074	0.078
IV	Cheirogaleidae	1.73	0.18881	NS	0.041	0.070	0.061
IV	Strepsirrhini	1.07	0.30198	NS	0.047	0.070	0.063
IV	Euarchontoglires	2.87	0.090478	NS	0.035	0.072	0.061
V	Microcebus	8.55	0.0034553	*	0.170	0.086	0.111
V	Cheirogaleidae	2.14	0.14336	NS	0.129	0.089	0.100
V	Lemuriformes	3.12	0.077566	NS	0.140	0.091	0.105
V	Strepsirrhini	3.48	0.062259	NS	0.164	0.108	0.124
V	Primates	2.25	0.13356	NS	0.158	0.113	0.126
VI	Microcebus	12.37	0.00043689	*	0.199	0.094	0.124
VI	Cheirogaleidae	10.74	0.0010499	*	0.164	0.074	0.100
VI	Lemuriformes	6.49	0.010834	*	0.158	0.086	0.107
VI	Primates	0.79	0.37518	NS	0.094	0.072	0.078
VII	Microcebus	0.91	0.33983	NS	0.082	0.108	0.100
VII	Cheirogaleidae	2.74	0.097887	NS	0.047	0.086	0.075
VII	Lemuriformes	1.26	0.26123	NS	0.041	0.065	0.058
VII	Strepsirrhini	1.27	0.2601	NS	0.105	0.077	0.085
VIII	Microcebus	18.49	0.000017052	*	0.240	0.103	0.143
VIII	Cheirogaleidae	3.48	0.062278	NS	0.140	0.089	0.104
VIII	Strepsirrhini	0.06	0.79916	NS	0.105	0.098	0.100
VIII	Euarchontoglires	3.83	0.050361	NS	0.170	0.110	0.128
IX	Microcebus	1.23	0.26704	NS	0.140	0.108	0.117
IX	Cheirogaleidae	1.54	0.21492	NS	0.158	0.120	0.131
IX	Strepsirrhini	2.55	0.11038	NS	0.164	0.115	0.129

Table S9 – P-values from Fisher exact tests for biases of pervasive selection occurring within individual transmembrane domains with respect to the other six. Asterisks (*) indicate a p-value less than 0.05 given a null distribution of X^2_1.

Subfamily	Filter	TM Domain	p-value	Odds Ratio	Significant
I	Microcebus	TM1	0.047081412	0	*
I	Microcebus	TM2	0.327206822	1.888790677	NS
I	Microcebus	TM3	0.046370661	0	*
I	Microcebus	TM4	0.350786439	1.691888237	NS
I	Microcebus	TM5	0.168022974	2.270072172	NS
I	Microcebus	TM6	1	0.962604963	NS
I	Microcebus	TM7	0.518523455	1.430020846	NS
I	Cheirogaleidae	TM1	0.015437577	0	*
I	Cheirogaleidae	TM2	0.238366712	1.871747847	NS
I	Cheirogaleidae	TM3	0.015853999	0	*
I	Cheirogaleidae	TM4	0.773305955	1.258532828	NS
I	Cheirogaleidae	TM5	0.052979029	2.985011333	NS
I	Cheirogaleidae	TM6	0.770446263	0.733389151	NS
I	Cheirogaleidae	TM7	0.224019595	1.990512011	NS
I	Lemuriformes	TM1	0.37819732	0.403052967	NS
I	Lemuriformes	TM2	0.566455676	1.334528628	NS
I	Lemuriformes	TM3	0.015394726	0	*
I	Lemuriformes	TM4	1	0.870255842	NS
I	Lemuriformes	TM5	0.012312593	3.648209397	*
I	Lemuriformes	TM6	0.769383514	0.698505446	NS
I	Lemuriformes	TM7	0.236434174	1.885818042	NS
I	Strepsirrhini	TM1	0.538616846	0.466706747	NS
I	Strepsirrhini	TM2	0.373753578	1.57033329	NS
I	Strepsirrhini	TM3	0.026937586	0	*
I	Strepsirrhini	TM4	1	1.018523926	NS
I	Strepsirrhini	TM5	0.100137263	2.547872991	NS
I	Strepsirrhini	TM6	0.534978296	0.491779836	NS
I	Strepsirrhini	TM7	0.127287641	2.232754188	NS
I	Primates	TM1	0.375548307	0.443717441	NS
I	Primates	TM2	0.545287361	1.484294378	NS
I	Primates	TM3	0.027425054	0	*
I	Primates	TM4	1	0.964610109	NS
I	Primates	TM5	0.11070173	2.403325351	NS
I	Primates	TM6	1	0.771294249	NS
I	Primates	TM7	0.214487747	2.105615452	NS
I	Euarchontoglires	TM1	0.534978296	0.491779836	NS
I	Euarchontoglires	TM2	0.35517097	1.665369573	NS
I	Euarchontoglires	TM3	0.027573458	0	*
I	Euarchontoglires	TM4	0.770446263	0.733389151	NS
I	Euarchontoglires	TM5	0.201724482	2.002593945	NS
I	Euarchontoglires	TM6	1	0.857886831	NS
I	Euarchontoglires	TM7	0.113050798	2.37389745	NS
II	Microcebus	TM1	0.026937586	0	*
II	Microcebus	TM2	0.127287641	2.232754188	NS
II	Microcebus	TM3	0.204987066	0.235719989	NS
II	Microcebus	TM4	0.068761972	2.596272684	NS
II	Microcebus	TM5	1	0.962604963	NS

II	Microcebus	TM6	0.534672633	0.518225846	NS
II	Microcebus	TM7	0.340135491	1.765947801	NS
II	Cheirogaleidae	TM1	0.082470726	0.184794963	NS
II	Cheirogaleidae	TM2	0.566455676	1.334528628	NS
II	Cheirogaleidae	TM3	0.132403821	0.194423813	NS
II	Cheirogaleidae	TM4	0.051369144	2.592435357	NS
II	Cheirogaleidae	TM5	0.762246155	1.156418332	NS
II	Cheirogaleidae	TM6	0.374721126	0.424771163	NS
II	Cheirogaleidae	TM7	0.078514219	2.454600228	NS
II	Lemuriformes	TM1	0.131505024	0.213053137	NS
II	Lemuriformes	TM2	0.373753578	1.57033329	NS
II	Lemuriformes	TM3	0.208070643	0.224107739	NS
II	Lemuriformes	TM4	0.032325234	3.118420015	*
II	Lemuriformes	TM5	1	0.911965769	NS
II	Lemuriformes	TM6	1	0.812630849	NS
II	Lemuriformes	TM7	0.757379981	1.198660987	NS
II	Strepsirrhini	TM1	0.027496606	0	*
II	Strepsirrhini	TM2	0.373753578	1.57033329	NS
II	Strepsirrhini	TM3	0.208070643	0.224107739	NS
II	Strepsirrhini	TM4	0.032325234	3.118420015	*
II	Strepsirrhini	TM5	0.534897443	1.351899921	NS
II	Strepsirrhini	TM6	1	0.812630849	NS
II	Strepsirrhini	TM7	0.757379981	1.198660987	NS
II	Euarchontoglires	TM1	0.133011436	0.193490944	NS
II	Euarchontoglires	TM2	1	1.018523926	NS
II	Euarchontoglires	TM3	0.130604584	0.203558588	NS
II	Euarchontoglires	TM4	0.017241668	3.466662637	*
II	Euarchontoglires	TM5	0.755453188	1.215920634	NS
II	Euarchontoglires	TM6	0.770446263	0.733389151	NS
II	Euarchontoglires	TM7	0.544536236	1.491346538	NS
III	Microcebus	TM1	0.132623631	0	NS
III	Microcebus	TM2	0.062506624	3.041280203	NS
III	Microcebus	TM3	0.703131472	0.384202726	NS
III	Microcebus	TM4	0.28649934	1.904519216	NS
III	Microcebus	TM5	0.43750096	1.646211521	NS
III	Microcebus	TM6	0.131800652	0	NS
III	Microcebus	TM7	0.474241535	1.468808022	NS
III	Cheirogaleidae	TM1	0.3706493	0	NS
III	Cheirogaleidae	TM2	0.057803898	3.740405573	NS
III	Cheirogaleidae	TM3	0.366437303	0	NS
III	Cheirogaleidae	TM4	0.383166655	2.113482238	NS
III	Cheirogaleidae	TM5	0.362688509	0	NS
III	Cheirogaleidae	TM6	0.366437303	0	NS
III	Cheirogaleidae	TM7	0.050362257	3.952920818	NS
III	Lemuriformes	TM1	0.688908855	1.181355125	NS
III	Lemuriformes	TM2	0.386967449	2.064863153	NS
III	Lemuriformes	TM3	0.220744063	0	NS
III	Lemuriformes	TM4	1	1.071568415	NS
III	Lemuriformes	TM5	0.368068411	0	NS
III	Lemuriformes	TM6	1	0.539156958	NS
III	Lemuriformes	TM7	0.068309402	3.439421615	NS
III	Strepsirrhini	TM1	1	1.066792429	NS
III	Strepsirrhini	TM2	0.408633341	1.846472576	NS
III	Strepsirrhini	TM3	0.696484148	0.490770557	NS

III	Strepsirrhini	TM4	1	0.967451106	NS
III	Strepsirrhini	TM5	0.222857902	0	NS
III	Strepsirrhini	TM6	0.696484148	0.490770557	NS
III	Strepsirrhini	TM7	0.089228925	3.039311542	NS
III	Primates	TM1	0.688908855	1.181355125	NS
III	Primates	TM2	0.386967449	2.064863153	NS
III	Primates	TM3	0.220744063	0	NS
III	Primates	TM4	1	1.071568415	NS
III	Primates	TM5	0.368068411	0	NS
III	Primates	TM6	1	0.539156958	NS
III	Primates	TM7	0.068309402	3.439421615	NS
III	Euarchontoglires	TM1	0.688908855	1.181355125	NS
III	Euarchontoglires	TM2	0.688908855	1.181355125	NS
III	Euarchontoglires	TM3	0.220744063	0	NS
III	Euarchontoglires	TM4	1	1.071568415	NS
III	Euarchontoglires	TM5	1	0.598927814	NS
III	Euarchontoglires	TM6	1	0.539156958	NS
III	Euarchontoglires	TM7	0.068309402	3.439421615	NS
IV	Microcebus	TM1	1	0.8902204	NS
IV	Microcebus	TM2	0.463155063	1.518511301	NS
IV	Microcebus	TM3	0.133423622	0	NS
IV	Microcebus	TM4	0.261417097	2.091674871	NS
IV	Microcebus	TM5	0.414752837	1.795198147	NS
IV	Microcebus	TM6	0.445899998	1.602035114	NS
IV	Microcebus	TM7	0.133423622	0	NS
IV	Cheirogaleidae	TM1	0.595409788	0	NS
IV	Cheirogaleidae	TM2	0.271737619	2.435450173	NS
IV	Cheirogaleidae	TM3	0.595065456	0	NS
IV	Cheirogaleidae	TM4	0.079667159	4.319936432	NS
IV	Cheirogaleidae	TM5	0.596893438	0	NS
IV	Cheirogaleidae	TM6	0.255209678	2.562652437	NS
IV	Cheirogaleidae	TM7	0.595065456	0	NS
IV	Strepsirrhini	TM1	0.605277842	0	NS
IV	Strepsirrhini	TM2	0.330945942	2.018641851	NS
IV	Strepsirrhini	TM3	0.602120065	0	NS
IV	Strepsirrhini	TM4	0.114025886	3.439722901	NS
IV	Strepsirrhini	TM5	1	0.966175688	NS
IV	Strepsirrhini	TM6	0.311999279	2.124420529	NS
IV	Strepsirrhini	TM7	0.602120065	0	NS
IV	Euarchontoglires	TM1	0.594180031	0	NS
IV	Euarchontoglires	TM2	0.212709259	3.058710484	NS
IV	Euarchontoglires	TM3	0.596694971	0	NS
IV	Euarchontoglires	TM4	0.240662338	2.777649491	NS
IV	Euarchontoglires	TM5	1	0	NS
IV	Euarchontoglires	TM6	0.198991401	3.218257231	NS
IV	Euarchontoglires	TM7	0.596694971	0	NS
V	Microcebus	TM1	0.081779029	0.176719194	NS
V	Microcebus	TM2	0.772657504	1.268952262	NS
V	Microcebus	TM3	0.769899579	0.666295903	NS
V	Microcebus	TM4	0.576357431	0.568945774	NS
V	Microcebus	TM5	1	0.748158743	NS
V	Microcebus	TM6	0.136830992	2.325507614	NS
V	Microcebus	TM7	0.136830992	2.325507614	NS
V	Cheirogaleidae	TM1	0.745603833	0.549484408	NS

V	Cheirogaleidae	TM2	0.745603833	0.549484408	NS
V	Cheirogaleidae	TM3	0.319720061	0.262255596	NS
V	Cheirogaleidae	TM4	1	0.823266298	NS
V	Cheirogaleidae	TM5	1	1.079848882	NS
V	Cheirogaleidae	TM6	0.018212625	3.586773086	*
V	Cheirogaleidae	TM7	0.518523455	1.430020846	NS
V	Lemuriformes	TM1	0.534978296	0.491779836	NS
V	Lemuriformes	TM2	0.534978296	0.491779836	NS
V	Lemuriformes	TM3	0.204987066	0.235719989	NS
V	Lemuriformes	TM4	1	1.077788285	NS
V	Lemuriformes	TM5	0.518523455	1.430020846	NS
V	Lemuriformes	TM6	0.113050798	2.37389745	NS
V	Lemuriformes	TM7	0.340135491	1.765947801	NS
V	Strepsirrhini	TM1	0.37819732	0.403052967	NS
V	Strepsirrhini	TM2	0.770279982	0.661473655	NS
V	Strepsirrhini	TM3	0.132403821	0.194423813	NS
V	Strepsirrhini	TM4	0.397214238	1.579696842	NS
V	Strepsirrhini	TM5	0.366294559	1.606216512	NS
V	Strepsirrhini	TM6	0.236434174	1.885818042	NS
V	Strepsirrhini	TM7	0.553262922	1.415615117	NS
V	Primates	TM1	0.375093575	0.422562566	NS
V	Primates	TM2	0.769479564	0.694556309	NS
V	Primates	TM3	0.375584685	0.445325224	NS
V	Primates	TM4	0.386227939	1.667814299	NS
V	Primates	TM5	0.350786439	1.691888237	NS
V	Primates	TM6	1	1.077788285	NS
V	Primates	TM7	0.544536236	1.491346538	NS
VI	Microcebus	TM1	0.283220107	1.707936693	NS
VI	Microcebus	TM2	1	1.008570113	NS
VI	Microcebus	TM3	0.788624778	0.781086935	NS
VI	Microcebus	TM4	0.295855607	0.457404965	NS
VI	Microcebus	TM5	1	0.882115778	NS
VI	Microcebus	TM6	0.580772477	1.413564331	NS
VI	Microcebus	TM7	1	1.070353165	NS
VI	Cheirogaleidae	TM1	1	0.96841978	NS
VI	Cheirogaleidae	TM2	0.254471194	1.772990215	NS
VI	Cheirogaleidae	TM3	0.374721126	0.424771163	NS
VI	Cheirogaleidae	TM4	0.257051389	0.364763604	NS
VI	Cheirogaleidae	TM5	0.211414911	2.153083432	NS
VI	Cheirogaleidae	TM6	0.374721126	0.424771163	NS
VI	Cheirogaleidae	TM7	0.236434174	1.885818042	NS
VI	Lemuriformes	TM1	1	1.018523926	NS
VI	Lemuriformes	TM2	0.238366712	1.871747847	NS
VI	Lemuriformes	TM3	0.375584685	0.445325224	NS
VI	Lemuriformes	TM4	0.082072831	0.175675494	NS
VI	Lemuriformes	TM5	0.123226923	2.272306493	NS
VI	Lemuriformes	TM6	0.375584685	0.445325224	NS
VI	Lemuriformes	TM7	0.224019595	1.990512011	NS
VI	Primates	TM1	1	0.820776155	NS
VI	Primates	TM2	0.708048549	1.392122726	NS
VI	Primates	TM3	0.131800652	0	NS
VI	Primates	TM4	0.472506477	0.332303194	NS
VI	Primates	TM5	0.43750096	1.646211521	NS
VI	Primates	TM6	0.474241535	1.468808022	NS

VI	Primates	TM7	0.246790026	2.236695006	NS
VII	Microcebus	TM1	0.434396622	1.667722458	NS
VII	Microcebus	TM2	0.127739906	2.571683981	NS
VII	Microcebus	TM3	0.695203491	0.449806551	NS
VII	Microcebus	TM4	0.129942405	0	NS
VII	Microcebus	TM5	1	0.499799387	NS
VII	Microcebus	TM6	0.695203491	0.449806551	NS
VII	Microcebus	TM7	0.112981852	2.718694361	NS
VII	Cheirogaleidae	TM1	0.330945942	2.018641851	NS
VII	Cheirogaleidae	TM2	0.330945942	2.018641851	NS
VII	Cheirogaleidae	TM3	1	0.870244336	NS
VII	Cheirogaleidae	TM4	0.359019693	0	NS
VII	Cheirogaleidae	TM5	0.59829799	0	NS
VII	Cheirogaleidae	TM6	0.602120065	0	NS
VII	Cheirogaleidae	TM7	0.084840876	4.008202584	NS
VII	Lemuriformes	TM1	1	0.972377558	NS
VII	Lemuriformes	TM2	0.271737619	2.435450173	NS
VII	Lemuriformes	TM3	1	1.021611706	NS
VII	Lemuriformes	TM4	0.598337668	0	NS
VII	Lemuriformes	TM5	0.596893438	0	NS
VII	Lemuriformes	TM6	0.595065456	0	NS
VII	Lemuriformes	TM7	0.05844571	5.03106327	NS
VII	Strepsirrhini	TM1	1	0.707828145	NS
VII	Strepsirrhini	TM2	0.029149157	3.490816447	*
VII	Strepsirrhini	TM3	0.47415965	0.334012056	NS
VII	Strepsirrhini	TM4	0.7416784	0.641487918	NS
VII	Strepsirrhini	TM5	0.133344799	0	NS
VII	Strepsirrhini	TM6	0.47415965	0.334012056	NS
VII	Strepsirrhini	TM7	0.023734098	3.709789809	*
VIII	Microcebus	TM1	0.616684102	1.279123458	NS
VIII	Microcebus	TM2	0.616684102	1.279123458	NS
VIII	Microcebus	TM3	0.069566163	0.253252595	NS
VIII	Microcebus	TM4	0.624807196	0.683241207	NS
VIII	Microcebus	TM5	0.180113971	1.999439189	NS
VIII	Microcebus	TM6	0.448031274	0.596225729	NS
VIII	Microcebus	TM7	0.301674295	1.721145364	NS
VIII	Cheirogaleidae	TM1	0.208070643	0.224107739	NS
VIII	Cheirogaleidae	TM2	0.054503626	2.926994208	NS
VIII	Cheirogaleidae	TM3	0.204987066	0.235719989	NS
VIII	Cheirogaleidae	TM4	0.224019595	1.990512011	NS
VIII	Cheirogaleidae	TM5	1	0.962604963	NS
VIII	Cheirogaleidae	TM6	1	0.857886831	NS
VIII	Cheirogaleidae	TM7	1	0.857886831	NS
VIII	Strepsirrhini	TM1	0.730341801	1.18963246	NS
VIII	Strepsirrhini	TM2	0.730341801	1.18963246	NS
VIII	Strepsirrhini	TM3	0.079868828	0	NS
VIII	Strepsirrhini	TM4	1	1.074548729	NS
VIII	Strepsirrhini	TM5	1	0.832101809	NS
VIII	Strepsirrhini	TM6	1	0.745502601	NS
VIII	Strepsirrhini	TM7	0.141100642	2.692030388	NS
VIII	Euarchontoglires	TM1	0.145849317	2.179996348	NS
VIII	Euarchontoglires	TM2	0.772657504	1.268952262	NS
VIII	Euarchontoglires	TM3	0.01561596	0	*
VIII	Euarchontoglires	TM4	1	0.828708138	NS

VIII	Euarchontoglires	TM5	1	0.748158743	NS
VIII	Euarchontoglires	TM6	0.56424206	1.346156689	NS
VIII	Euarchontoglires	TM7	0.56424206	1.346156689	NS
IX	Microcebus	TM1	0.757379981	1.198660987	NS
IX	Microcebus	TM2	0.757379981	1.198660987	NS
IX	Microcebus	TM3	0.027573458	0	*
IX	Microcebus	TM4	0.544536236	1.491346538	NS
IX	Microcebus	TM5	0.518523455	1.430020846	NS
IX	Microcebus	TM6	1	0.857886831	NS
IX	Microcebus	TM7	0.750910114	1.268114233	NS
IX	Cheirogaleidae	TM1	1	1.018523926	NS
IX	Cheirogaleidae	TM2	0.554676431	1.406028791	NS
IX	Cheirogaleidae	TM3	0.015853999	0	*
IX	Cheirogaleidae	TM4	0.386227939	1.667814299	NS
IX	Cheirogaleidae	TM5	0.755453188	1.215920634	NS
IX	Cheirogaleidae	TM6	0.375584685	0.445325224	NS
IX	Cheirogaleidae	TM7	0.224019595	1.990512011	NS
IX	Strepsirrhini	TM1	1	0.96841978	NS
IX	Strepsirrhini	TM2	0.566455676	1.334528628	NS
IX	Strepsirrhini	TM3	0.015394726	0	*
IX	Strepsirrhini	TM4	0.397214238	1.579696842	NS
IX	Strepsirrhini	TM5	0.762246155	1.156418332	NS
IX	Strepsirrhini	TM6	0.374721126	0.424771163	NS
IX	Strepsirrhini	TM7	0.078514219	2.454600228	NS

Table S10 – P-values from Fisher exact tests for biases of pervasive selection occurring within individual loop domains with respect to the other seven. Asterisks (*) indicate a p-value less than 0.05 given a null distribution of X^2_1.

Subfamily	Filter	Loop Domain	p-value	Odds Ratio	Significant
I	Microcebus	L1	0.082484061	0.505010614	NS
I	Microcebus	L2	0.65347923	1.404098116	NS
I	Microcebus	L3	1	1.08090091	NS
I	Microcebus	L4	0.418383639	1.766631716	NS
I	Microcebus	L5	0.066938401	2.529891805	NS
I	Microcebus	L6	0.349431592	0.275664583	NS
I	Microcebus	L7	0.100528381	5.019019417	NS
I	Microcebus	L8	0.858584504	1.061828028	NS
I	Cheirogaleidae	L1	0.100309834	0.501536589	NS
I	Cheirogaleidae	L2	0.142262217	2.652063918	NS
I	Cheirogaleidae	L3	0.680115251	1.224943211	NS
I	Cheirogaleidae	L4	0.230378385	2.008510523	NS
I	Cheirogaleidae	L5	0.220770676	1.819613375	NS
I	Cheirogaleidae	L6	0.340393596	0.311628939	NS
I	Cheirogaleidae	L7	0.082901559	5.681672485	NS
I	Cheirogaleidae	L8	1	0.965188606	NS
I	Lemuriformes	L1	0.006175581	0.32522281	*
I	Lemuriformes	L2	0.669618776	1.288421608	NS
I	Lemuriformes	L3	0.440017021	1.617679908	NS
I	Lemuriformes	L4	0.440017021	1.617679908	NS
I	Lemuriformes	L5	0.001689232	4.007518158	*
I	Lemuriformes	L6	0.23189318	0.253293195	NS
I	Lemuriformes	L7	0.01537091	9.434022575	*
I	Lemuriformes	L8	1	0.941140228	NS
I	Strepsirrhini	L1	0.0040765	0.314843236	*
I	Strepsirrhini	L2	0.675282455	1.253614376	NS
I	Strepsirrhini	L3	0.447988558	1.572978068	NS
I	Strepsirrhini	L4	0.139524078	2.288784672	NS
I	Strepsirrhini	L5	0.007894057	3.257729612	*
I	Strepsirrhini	L6	0.233936619	0.246545767	NS
I	Strepsirrhini	L7	0.016428172	9.176206534	*
I	Strepsirrhini	L8	1	1.021801219	NS
I	Primates	L1	0.009464965	0.347866743	*
I	Primates	L2	0.658697491	1.363516019	NS
I	Primates	L3	0.42517886	1.71430691	NS
I	Primates	L4	0.42517886	1.71430691	NS
I	Primates	L5	0.070709689	2.446528569	NS

I	Primates	L6	0.231070034	0.267825327	NS
I	Primates	L7	0.013382585	9.990971184	*
I	Primates	L8	0.722743734	1.152792367	NS
I	Euarchontoglires	L1	0.036145742	0.429669761	*
I	Euarchontoglires	L2	0.180583096	2.33319195	NS
I	Euarchontoglires	L3	1	1.08090091	NS
I	Euarchontoglires	L4	0.418383639	1.766631716	NS
I	Euarchontoglires	L5	0.066938401	2.529891805	NS
I	Euarchontoglires	L6	0.349431592	0.275664583	NS
I	Euarchontoglires	L7	0.012450545	10.29238498	*
I	Euarchontoglires	L8	1	0.932753556	NS
II	Microcebus	L1	0.000181375	0.150359727	*
II	Microcebus	L2	1	0.720111652	NS
II	Microcebus	L3	0.019180467	4.055442254	*
II	Microcebus	L4	0.680115251	1.224943211	NS
II	Microcebus	L5	7.91E-06	7.384573173	*
II	Microcebus	L6	1	1.061353078	NS
II	Microcebus	L7	0.082901559	5.681672485	NS
II	Microcebus	L8	0.131093132	0.502705274	NS
II	Cheirogaleidae	L1	6.96E-05	0.165629049	*
II	Cheirogaleidae	L2	0.669618776	1.288421608	NS
II	Cheirogaleidae	L3	0.001834361	5.529342217	*
II	Cheirogaleidae	L4	0.130644377	2.355228794	NS
II	Cheirogaleidae	L5	1.09E-05	6.505272671	*
II	Cheirogaleidae	L6	1	0.853905509	NS
II	Cheirogaleidae	L7	0.473249224	1.801677176	NS
II	Cheirogaleidae	L8	0.057213699	0.465738282	NS
II	Lemuriformes	L1	0.000118096	0.211798163	*
II	Lemuriformes	L2	1	1.050479644	NS
II	Lemuriformes	L3	0.005340828	4.408163821	*
II	Lemuriformes	L4	0.281223854	1.90403355	NS
II	Lemuriformes	L5	2.62E-06	6.668636879	*
II	Lemuriformes	L6	1	0.976863521	NS
II	Lemuriformes	L7	0.15436895	3.762584595	NS
II	Lemuriformes	L8	0.053579218	0.490670961	NS
II	Strepsirrhini	L1	0.000112927	0.235844523	*
II	Strepsirrhini	L2	1	0.980437182	NS
II	Strepsirrhini	L3	0.007525726	4.087777714	*
II	Strepsirrhini	L4	0.156884606	2.41678507	NS
II	Strepsirrhini	L5	6.12E-06	6.093738222	*
II	Strepsirrhini	L6	1	0.909065701	NS
II	Strepsirrhini	L7	0.170168609	3.513114885	NS
II	Strepsirrhini	L8	0.060302556	0.513906941	NS

II	Euarchontoglires	L1	0.002315255	0.311293343	*
II	Euarchontoglires	L2	1	1.075815916	NS
II	Euarchontoglires	L3	0.02068534	3.512397464	*
II	Euarchontoglires	L4	0.072019705	2.665570157	NS
II	Euarchontoglires	L5	7.34E-05	5.143626624	*
II	Euarchontoglires	L6	0.783075702	0.709501172	NS
II	Euarchontoglires	L7	0.149196055	3.852265931	NS
II	Euarchontoglires	L8	0.072997084	0.505294397	NS
III	Microcebus	L1	0.599557949	0.773409702	NS
III	Microcebus	L2	0.65347923	1.404098116	NS
III	Microcebus	L3	0.239300654	0	NS
III	Microcebus	L4	1	1.08090091	NS
III	Microcebus	L5	0.139391688	2.03083807	NS
III	Microcebus	L6	0.05966636	0	NS
III	Microcebus	L7	0.000863416	21.12196876	*
III	Microcebus	L8	0.858584504	1.061828028	NS
III	Cheirogaleidae	L1	0.738438854	1.106498797	NS
III	Cheirogaleidae	L2	1	0.58598294	NS
III	Cheirogaleidae	L3	0.244141262	0	NS
III	Cheirogaleidae	L4	1	0.991686356	NS
III	Cheirogaleidae	L5	0.022459394	2.797769052	*
III	Cheirogaleidae	L6	0.036446006	0	*
III	Cheirogaleidae	L7	0.473249224	1.801677176	NS
III	Cheirogaleidae	L8	0.862845602	1.06234323	NS
III	Lemuriformes	L1	0.126126715	1.711041637	NS
III	Lemuriformes	L2	1	0.58598294	NS
III	Lemuriformes	L3	0.244141262	0	NS
III	Lemuriformes	L4	0.70781866	0.45764076	NS
III	Lemuriformes	L5	0.244961876	1.846231928	NS
III	Lemuriformes	L6	0.557916229	0.536588812	NS
III	Lemuriformes	L7	0.473249224	1.801677176	NS
III	Lemuriformes	L8	0.486336483	0.727516184	NS
III	Strepsirrhini	L1	0.341736294	1.388352318	NS
III	Strepsirrhini	L2	0.235629522	0	NS
III	Strepsirrhini	L3	0.149105947	0	NS
III	Strepsirrhini	L4	1	0.827775343	NS
III	Strepsirrhini	L5	0.027039494	2.723303958	*
III	Strepsirrhini	L6	0.158318732	0.211961531	NS
III	Strepsirrhini	L7	0.023682301	7.862134352	*
III	Strepsirrhini	L8	0.418724128	0.737667599	NS
III	Primates	L1	0.378036921	1.304434046	NS
III	Primates	L2	1	0.880372724	NS
III	Primates	L3	0.33400158	0.314531596	NS

III	Primates	L4	1	0.677146167	NS
III	Primates	L5	0.208412308	1.817510061	NS
III	Primates	L6	0.603064578	0.577774581	NS
III	Primates	L7	0.037609801	6.424672696	*
III	Primates	L8	0.292864474	0.70410309	NS
III	Euarchontoglires	L1	0.43778144	1.285222393	NS
III	Euarchontoglires	L2	1	1.026178014	NS
III	Euarchontoglires	L3	0.490502195	0.365883155	NS
III	Euarchontoglires	L4	1	0.789529233	NS
III	Euarchontoglires	L5	0.031199926	2.578969404	*
III	Euarchontoglires	L6	0.784212934	0.675966425	NS
III	Euarchontoglires	L7	0.02645609	7.496712005	*
III	Euarchontoglires	L8	0.05373124	0.476759901	NS
IV	Microcebus	L1	0.018666674	0.320356871	*
IV	Microcebus	L2	0.620663774	0	NS
IV	Microcebus	L3	0.178872667	2.319271744	NS
IV	Microcebus	L4	0.011397323	4.725183056	*
IV	Microcebus	L5	0.003146602	4.258066949	*
IV	Microcebus	L6	0.160297667	2.360822469	NS
IV	Microcebus	L7	0.066532153	6.525217598	NS
IV	Microcebus	L8	0.004502107	0.209129139	*
IV	Cheirogaleidae	L1	0.423509347	0.660581046	NS
IV	Cheirogaleidae	L2	0.615982034	0	NS
IV	Cheirogaleidae	L3	0.641054404	1.520817335	NS
IV	Cheirogaleidae	L4	0.15463796	2.510173763	NS
IV	Cheirogaleidae	L5	0.008929601	3.778456346	*
IV	Cheirogaleidae	L6	0.279891927	1.905659608	NS
IV	Cheirogaleidae	L7	0.005271123	14.55792248	*
IV	Cheirogaleidae	L8	0.00159493	0.144078471	*
IV	Strepsirrhini	L1	0.423509347	0.660581046	NS
IV	Strepsirrhini	L2	0.615982034	0	NS
IV	Strepsirrhini	L3	0.15463796	2.510173763	NS
IV	Strepsirrhini	L4	0.641054404	1.520817335	NS
IV	Strepsirrhini	L5	0.008929601	3.778456346	*
IV	Strepsirrhini	L6	0.279891927	1.905659608	NS
IV	Strepsirrhini	L7	0.005271123	14.55792248	*
IV	Strepsirrhini	L8	0.00159493	0.144078471	*
IV	Euarchontoglires	L1	0.32639514	0.628058498	NS
IV	Euarchontoglires	L2	0.618098024	0	NS
IV	Euarchontoglires	L3	0.166609481	2.411150949	NS
IV	Euarchontoglires	L4	0.646860314	1.462726106	NS
IV	Euarchontoglires	L5	0.010887625	3.604343068	*
IV	Euarchontoglires	L6	0.291108229	1.827590779	NS

IV	Euarchontoglires	L7	0.005823634	13.99471981	*
IV	Euarchontoglires	L8	0.007244832	0.217713337	*
V	Microcebus	L1	0.030378763	0.402505233	*
V	Microcebus	L2	0.639056177	1.540117577	NS
V	Microcebus	L3	0.68734077	1.185755987	NS
V	Microcebus	L4	0.400951806	1.942592244	NS
V	Microcebus	L5	7.52E-05	5.963954903	*
V	Microcebus	L6	0.755274443	0.642130101	NS
V	Microcebus	L7	0.087195972	5.50148473	NS
V	Microcebus	L8	0.095727037	0.483502296	NS
V	Cheirogaleidae	L1	0.071895308	0.463128373	NS
V	Cheirogaleidae	L2	0.643635079	1.492197245	NS
V	Cheirogaleidae	L3	1	0.528415862	NS
V	Cheirogaleidae	L4	0.090411571	2.747924154	NS
V	Cheirogaleidae	L5	0.000100487	5.718697511	*
V	Cheirogaleidae	L6	0.755350011	0.622030845	NS
V	Cheirogaleidae	L7	0.091566708	5.331956428	NS
V	Cheirogaleidae	L8	0.095702154	0.465577812	NS
V	Lemuriformes	L1	0.020443303	0.373423421	*
V	Lemuriformes	L2	0.648450822	1.446927775	NS
V	Lemuriformes	L3	0.412054303	1.8218735	NS
V	Lemuriformes	L4	0.412054303	1.8218735	NS
V	Lemuriformes	L5	0.000132729	5.493199451	*
V	Lemuriformes	L6	0.534968427	1.367479445	NS
V	Lemuriformes	L7	0.096011568	5.170981275	NS
V	Lemuriformes	L8	0.02774386	0.368415675	*
V	Strepsirrhini	L1	2.40E-05	0.151516509	*
V	Strepsirrhini	L2	0.686926106	1.188834544	NS
V	Strepsirrhini	L3	0.464868639	1.489947223	NS
V	Strepsirrhini	L4	0.052462442	2.963783274	NS
V	Strepsirrhini	L5	0.00071577	4.282442251	*
V	Strepsirrhini	L6	1	0.786134599	NS
V	Strepsirrhini	L7	0.129022172	4.254865199	NS
V	Strepsirrhini	L8	0.866690743	1.062867091	NS
V	Primates	L1	8.50E-06	0.143201367	*
V	Primates	L2	0.698884187	1.129784443	NS
V	Primates	L3	0.48279041	1.414440894	NS
V	Primates	L4	0.06177636	2.80763919	NS
V	Primates	L5	7.27E-06	6.352177702	*
V	Primates	L6	0.783685542	0.746079242	NS
V	Primates	L7	0.139001791	4.045163694	NS
V	Primates	L8	0.868435204	0.884079144	NS
VI	Microcebus	L1	5.15E-06	0.084303374	*

VI	Microcebus	L2	1	0.637424015	NS
VI	Microcebus	L3	0.001143493	6.092897665	*
VI	Microcebus	L4	0.029950195	3.541918044	*
VI	Microcebus	L5	2.90E-05	6.228133083	*
VI	Microcebus	L6	0.114630719	2.266870568	NS
VI	Microcebus	L7	0.447276913	1.959080183	NS
VI	Microcebus	L8	0.006330668	0.28453686	*
VI	Cheirogaleidae	L1	0.001414688	0.174726948	*
VI	Cheirogaleidae	L2	0.620663774	0	NS
VI	Cheirogaleidae	L3	0.011397323	4.725183056	*
VI	Cheirogaleidae	L4	0.052153082	3.409992366	NS
VI	Cheirogaleidae	L5	0.003146602	4.258066949	*
VI	Cheirogaleidae	L6	0.303353589	1.755126534	NS
VI	Cheirogaleidae	L7	0.066532153	6.525217598	NS
VI	Cheirogaleidae	L8	0.047817828	0.383861252	*
VI	Lemuriformes	L1	0.000850102	0.201785063	*
VI	Lemuriformes	L2	1	0.697668509	NS
VI	Lemuriformes	L3	0.021576989	3.914917839	*
VI	Lemuriformes	L4	0.400951806	1.942592244	NS
VI	Lemuriformes	L5	0.002100454	4.179814781	*
VI	Lemuriformes	L6	0.100789267	2.513842659	NS
VI	Lemuriformes	L7	0.087195972	5.50148473	NS
VI	Lemuriformes	L8	0.040269255	0.396057625	*
VI	Primates	L1	0.001365148	0.181947576	*
VI	Primates	L2	0.618098024	0	NS
VI	Primates	L3	0.046894274	3.549730176	*
VI	Primates	L4	0.046894274	3.549730176	*
VI	Primates	L5	7.52E-05	6.611554045	*
VI	Primates	L6	1	0.792817611	NS
VI	Primates	L7	0.362871152	2.625352524	NS
VI	Primates	L8	0.159603153	0.506591385	NS
VII	Microcebus	L1	2.55E-08	0.034156612	*
VII	Microcebus	L2	1	0.541547011	NS
VII	Microcebus	L3	0.464868639	1.489947223	NS
VII	Microcebus	L4	0.254291734	2.165481451	NS
VII	Microcebus	L5	0.266680742	1.689788833	NS
VII	Microcebus	L6	0.775322759	1.111936426	NS
VII	Microcebus	L7	0.129022172	4.254865199	NS
VII	Microcebus	L8	0.002085463	2.714793637	*
VII	Cheirogaleidae	L1	1.74E-06	0.044662352	*
VII	Cheirogaleidae	L2	1	0.697668509	NS
VII	Cheirogaleidae	L3	0.400951806	1.942592244	NS
VII	Cheirogaleidae	L4	0.400951806	1.942592244	NS

VII	Cheirogaleidae	L5	0.350375001	1.756181635	NS
VII	Cheirogaleidae	L6	1	1.026331801	NS
VII	Cheirogaleidae	L7	0.087195972	5.50148473	NS
VII	Cheirogaleidae	L8	0.023859018	2.279526122	*
VII	Lemuriformes	L1	4.33E-06	0	*
VII	Lemuriformes	L2	1	0.961626474	NS
VII	Lemuriformes	L3	1	0.751497909	NS
VII	Lemuriformes	L4	1	0.751497909	NS
VII	Lemuriformes	L5	0.283757836	1.877936792	NS
VII	Lemuriformes	L6	1	0.89521013	NS
VII	Lemuriformes	L7	0.051567475	7.634764362	NS
VII	Lemuriformes	L8	0.004513415	3.341919594	*
VII	Strepsirrhini	L1	3.75E-07	0	*
VII	Strepsirrhini	L2	1	0.796068086	NS
VII	Strepsirrhini	L3	0.191404253	2.233483489	NS
VII	Strepsirrhini	L4	0.659442175	1.358129768	NS
VII	Strepsirrhini	L5	0.052120082	2.626801306	NS
VII	Strepsirrhini	L6	1	0.735902944	NS
VII	Strepsirrhini	L7	0.382499133	2.444033741	NS
VII	Strepsirrhini	L8	0.010547438	2.589423132	*
VIII	Microcebus	L1	6.98E-06	0.116249456	*
VIII	Microcebus	L2	0.221716232	2.077946597	NS
VIII	Microcebus	L3	0.010883429	4.14732344	*
VIII	Microcebus	L4	0.447988558	1.572978068	NS
VIII	Microcebus	L5	0.002061373	3.875696121	*
VIII	Microcebus	L6	0.015464893	3.047590269	*
VIII	Microcebus	L7	0.119272702	4.484877146	NS
VIII	Microcebus	L8	0.056814027	0.450641934	NS
VIII	Cheirogaleidae	L1	9.65E-06	0.089889187	*
VIII	Cheirogaleidae	L2	0.643635079	1.492197245	NS
VIII	Cheirogaleidae	L3	0.000104452	8.372947586	*
VIII	Cheirogaleidae	L4	0.090411571	2.747924154	NS
VIII	Cheirogaleidae	L5	0.122752815	2.173741063	NS
VIII	Cheirogaleidae	L6	0.021959502	3.039102979	*
VIII	Cheirogaleidae	L7	0.091566708	5.331956428	NS
VIII	Cheirogaleidae	L8	0.040902781	0.381790293	*
VIII	Strepsirrhini	L1	0.394730787	0.714197389	NS
VIII	Strepsirrhini	L2	1	0.602273896	NS
VIII	Strepsirrhini	L3	0.432402125	1.664726416	NS
VIII	Strepsirrhini	L4	0.001574896	5.707183279	*
VIII	Strepsirrhini	L5	0.773874441	1.123306673	NS
VIII	Strepsirrhini	L6	0.558552858	0.551926979	NS
VIII	Strepsirrhini	L7	0.014355874	9.705251077	*

VIII	Strepsirrhini	L8	0.16139343	0.56545591	NS
VIII	Euarchontoglires	L1	0.014350159	0.39755861	*
VIII	Euarchontoglires	L2	0.692873388	1.158641072	NS
VIII	Euarchontoglires	L3	0.015224141	3.805621363	*
VIII	Euarchontoglires	L4	0.00322861	4.911569644	*
VIII	Euarchontoglires	L5	0.583854756	1.291059248	NS
VIII	Euarchontoglires	L6	0.56436128	0.482199481	NS
VIII	Euarchontoglires	L7	0.001663663	17.31974159	*
VIII	Euarchontoglires	L8	0.24301651	0.634328767	NS
IX	Microcebus	L1	0.514670006	0.784126754	NS
IX	Microcebus	L2	0.686926106	1.188834544	NS
IX	Microcebus	L3	0.254291734	2.165481451	NS
IX	Microcebus	L4	0.464868639	1.489947223	NS
IX	Microcebus	L5	0.266680742	1.689788833	NS
IX	Microcebus	L6	0.56148521	0.494849356	NS
IX	Microcebus	L7	0.018671166	8.698797503	*
IX	Microcebus	L8	0.310699831	0.655573144	NS
IX	Cheirogaleidae	L1	0.875414447	0.906550113	NS
IX	Cheirogaleidae	L2	1	1.050479644	NS
IX	Cheirogaleidae	L3	0.720601987	1.313196545	NS
IX	Cheirogaleidae	L4	0.720601987	1.313196545	NS
IX	Cheirogaleidae	L5	0.424454159	1.476443043	NS
IX	Cheirogaleidae	L6	0.406230094	0.436854737	NS
IX	Cheirogaleidae	L7	0.025046581	7.675606944	*
IX	Cheirogaleidae	L8	0.6284663	0.800898826	NS
IX	Strepsirrhini	L1	0.873283075	1.077077758	NS
IX	Strepsirrhini	L2	0.704944597	1.102252841	NS
IX	Strepsirrhini	L3	0.492069168	1.379197321	NS
IX	Strepsirrhini	L4	0.492069168	1.379197321	NS
IX	Strepsirrhini	L5	0.598160635	1.223929713	NS
IX	Strepsirrhini	L6	0.403995976	0.458547776	NS
IX	Strepsirrhini	L7	0.022362951	8.056757757	*
IX	Strepsirrhini	L8	0.324700198	0.675463956	NS

Table S11 – Subfamily branches with evidence of episodic positive selection. Branch site model parameters for the null hypothesis (0) and alternative hypothesis (A).

				Null Hypothesis				Alternative Hypothesis								
Subfamily	**Node**	**lnL$_0$**	**lnL$_A$**	**p$_1$**	**p$_2$**	**ω$_1$**	**ω$_2$**	**p$_1$**	**p$_2$**	**p$_3$**	**ω$_1$**	**ω$_2$**	**ω$_3$**	**LRT**	**p-value**	**q-value**
I	92	-18074.62	-18047.69	0.58	0.42	0.17	1.00	0.57	0.41	0.02	0.17	1.00	999.00	53.85	2.1595E-13	0.000235849
	87	-18073.86	-18061.65	0.38	0.27	0.17	1.00	0.57	0.41	0.02	0.17	1.00	999.00	24.42	7.7274E-07	0.000471698
	88	-18074.62	-18066.56	0.58	0.42	0.17	1.00	0.58	0.41	0.02	0.17	1.00	999.00	16.11	0.000059892	0.000707547
	107	-18065.84	-18059.24	0.00	0.00	0.17	1.00	0.55	0.39	0.07	0.17	1.00	47.93	13.19	0.00028168	0.000943396
	97	-18074.62	-18068.61	0.58	0.42	0.17	1.00	0.57	0.41	0.02	0.17	1.00	454.04	12.02	0.00052634	0.001179245
	4	-18074.62	-18069.45	0.58	0.42	0.17	1.00	0.58	0.41	0.01	0.17	1.00	999.00	10.33	0.0013121	0.001415094
II	117	-23372.89	-23360.85	0.47	0.47	0.17	1.00	0.49	0.49	0.02	0.17	1.00	999.00	24.09	9.1947E-07	0.000175439
	51	-23372.91	-23362.29	0.50	0.50	0.17	1.00	0.48	0.48	0.03	0.17	1.00	999.00	21.23	4.0734E-06	0.000350877
	134	-23372.88	-23363.74	0.47	0.46	0.17	1.00	0.50	0.49	0.01	0.17	1.00	999.00	18.28	0.000019096	0.000526316
	138	-23372.91	-23365.56	0.50	0.50	0.17	1.00	0.49	0.49	0.02	0.17	1.00	842.87	14.70	0.00012603	0.000701754
	54	-23372.91	-23365.65	0.50	0.50	0.17	1.00	0.50	0.49	0.01	0.17	1.00	999.00	14.51	0.00013919	0.000877193
III	**NA**															
IV	16	-7462.33	-7441.97	0.60	0.40	0.15	1.00	0.59	0.39	0.01	0.15	1.00	999.00	40.73	1.7511E-10	0.000543478
V	118	-30877.80	-30850.07	0.37	0.32	0.25	1.00	0.52	0.45	0.04	0.25	1.00	999.00	55.46	9.5179E-14	0.000132979
	117	-30878.67	-30858.63	0.48	0.42	0.25	1.00	0.51	0.45	0.04	0.25	1.00	999.00	40.09	2.4267E-10	0.000265957
	116	-30878.92	-30866.04	0.53	0.47	0.25	1.00	0.52	0.46	0.02	0.25	1.00	999.00	25.75	3.8893E-07	0.000398936
	135	-30878.36	-30867.02	0.45	0.40	0.25	1.00	0.52	0.46	0.02	0.25	1.00	205.39	22.69	1.9072E-06	0.000531915
	47	-30878.92	-30872.57	0.53	0.47	0.25	1.00	0.53	0.47	0.00	0.25	1.00	999.00	12.71	0.00036468	0.000664894
	166	-30875.48	-30869.39	0.29	0.26	0.25	1.00	0.52	0.46	0.01	0.25	1.00	64.71	12.18	0.00048219	0.000797872
	107	-30874.20	-30868.45	0.22	0.20	0.25	1.00	0.49	0.44	0.07	0.25	1.00	20.96	11.50	0.00069764	0.000930851
	183	-30877.89	-30872.52	0.41	0.37	0.25	1.00	0.50	0.45	0.05	0.25	1.00	21.46	10.73	0.0010522	0.00106383
VI	34	-5447.78	-5424.80	0.47	0.52	0.16	1.00	0.45	0.51	0.05	0.16	1.00	332.48	45.95	1.2159E-11	0.000714286
	33	-5447.78	-5441.02	0.47	0.52	0.16	1.00	0.47	0.51	0.03	0.16	1.00	194.44	13.51	0.00023716	0.001428571
	22	-5447.42	-5441.43	0.39	0.42	0.16	1.00	0.48	0.51	0.01	0.16	1.00	152.05	11.98	0.0005379	0.002142857
	1	-5447.78	-5442.40	0.48	0.52	0.16	1.00	0.46	0.52	0.02	0.16	1.00	66.15	10.75	0.0010451	0.002857143
VII	97	-8685.16	-8657.49	0.34	0.33	0.16	1.00	0.50	0.48	0.01	0.16	1.00	999.00	55.34	1.0142E-13	0.000403226
	81	-8685.66	-8672.55	0.49	0.50	0.16	1.00	0.49	0.50	0.01	0.16	1.00	999.00	26.21	3.0595E-07	0.000806452
	123	-8685.58	-8676.83	0.44	0.45	0.16	1.00	0.49	0.50	0.01	0.16	1.00	573.41	17.51	0.000028589	0.001209677
	66	-8685.05	-8678.93	0.45	0.46	0.15	1.00	0.47	0.46	0.06	0.15	1.00	14.65	12.22	0.00047213	0.001612903
	124	-8685.51	-8679.65	0.43	0.44	0.15	1.00	0.49	0.50	0.01	0.16	1.00	703.40	11.73	0.00061624	0.002016129
IX	115	-17195.12	-17138.91	0.34	0.23	0.13	1.00	0.53	0.37	0.10	0.13	1.00	363.24	112.43	2.8734E-26	0.000223214
	171	-17214.08	-17185.27	0.60	0.40	0.14	1.00	0.59	0.40	0.02	0.14	1.00	575.62	57.64	3.1553E-14	0.000446429
	212	-17211.79	-17185.54	0.55	0.37	0.14	1.00	0.57	0.37	0.06	0.14	1.00	999.00	52.49	4.3149E-13	0.000669643
	225	-17214.08	-17195.79	0.60	0.40	0.14	1.00	0.58	0.39	0.02	0.14	1.00	999.00	36.59	1.4557E-09	0.000892857
	121	-17212.86	-17201.05	0.54	0.36	0.14	1.00	0.58	0.39	0.04	0.14	1.00	58.91	23.63	1.1699E-06	0.001116071
	186	-17214.08	-17202.97	0.60	0.40	0.14	1.00	0.60	0.40	0.01	0.14	1.00	999.00	22.23	2.4235E-06	0.001339286
	118	-17207.46	-17201.14	0.46	0.31	0.13	1.00	0.55	0.37	0.08	0.13	1.00	11.40	12.66	0.00037449	0.0015625
	154	-17214.05	-17208.70	0.57	0.38	0.14	1.00	0.59	0.40	0.00	0.14	1.00	697.21	10.71	0.001064	0.001785714
	211	-17214.08	-17208.81	0.60	0.40	0.14	1.00	0.59	0.38	0.03	0.14	1.00	428.70	10.55	0.0011615	0.002008929
	22	-17214.08	-17209.16	0.60	0.40	0.14	1.00	0.59	0.40	0.01	0.14	1.00	999.00	9.84	0.0017039	0.002232143
	198	-17214.08	-17209.38	0.60	0.40	0.14	1.00	0.59	0.40	0.02	0.14	1.00	999.00	9.42	0.0021487	0.002455357

Table S12 – Individual sites under selection along specified branches. Branch site model parameters were used to test sites for positive selection by way of Bayes empirical Bayes. The alignment column (sites) and domains where those sites are located – loop (L) or transmembrane (TM) are provided for sites with posterior probabilities greater than 0.95. NS implies no individual site was significant by Bayes empirical Bayes.

Subfamily	Node	Sites	Domains
I	92	317, 348	L5,TM5
	87	NS	-
	88	NS	-
	107	464, 465	L8, L8
	97	338	L5
	4	NS	-
II	117	NS	-
	51	316, 326, 340	L5, L5, L5
	134	NS	-
	138	NS	-
	54	NS	-
III	**NA**	**-**	-
IV	16	490	L8
V	118	445, 457, 499, 518	TM7, L8, L8, L8
	117	462	L8
	116	NS	-
	135	273	L4
	47	NS	-
	166	256	T3
	107	242, 390, 400	TM3, L6, L7
	183	363	TM5
VI	34	438, 440, 443, 444	TM7 TM7, TM7, TM7
	33	NS	-
	22	NS	-
	1	NS	-
VII	97	466, 467, 492	L8,L8,L8
	81	NS	-
	123	NS	-
	66	216	TM2
	124	NS	-
IX	115	172, 215 , 227 ,238, 322, 369, 373, 433, 434, 437, 438 , 439, 440, 441 ,447, 448, 449, 452, 453, 455, 456. 457, 462, 463, 464, 465, 467	TM1, TM2, L3, TM3, L5, L6, L6, TM7, TM7, TM7, TM7, TM7, TM7, TM7 TM7, TM7, TM7, TM7, L8, L8, L8, L8, L8, L8, L8, L8
	171	528	L8
	212	147	L1
	225	527, 528	L8, L8
	121	415, 518	TM6, L8
	186	NS	-
	118	363, 386	TM3, L6

154	NS	-
211	NS	-
22	NS	-
198	NS	-

Table S13 – Sample information for individuals sequenced for this study.

Genus	Species	Sample ID	Sex	Tissue Type	Latitude	Longitude	Locality
Cheirogaleus	*medius*	DLC3619	Female	Liver	-	-	Duke Lemur Center
Cheirogaleus	*sibreei*	106186	Female	Ear	-19.62	47.68	Tsinjoarivo
Microcebus	*murinus*	DLC7028	Female	Blood	-	-	Duke Lemur Center
Microcebus	*murinus*	DLC7049	Female	Thigh Skin	-	-	Duke Lemur Center
Microcebus	*murinus*	DLC7163	Female	Thigh Skin	-	-	Duke Lemur Center
Microcebus	*murinus*	DLC7188	Female	Thigh Skin	-	-	Duke Lemur Center
Microcebus	*murinus*	DLC7128	Male	Blood	-	-	Duke Lemur Center
Microcebus	*murinus*	DLC7033	Male	Blood	-	-	Duke Lemur Center
Microcebus	*murinus*	DLC7032	Male	Blood	-	-	Duke Lemur Center
Microcebus	*murinus*	DLC7039	Male	Thigh Skin	-	-	Duke Lemur Center
Microcebus	*griseorufus*	RMR66	Female	Kidney	-23.68	44.59	Beza Mahafaly
Microcebus	*mittermeieri*	MBB011	Female	Ear	-14.74	49.49	Anjanaharibe Sud
Microcebus	*ravelobensis*	RMR55	Male	Unknown	-16.333333	46.783333	Ankarafantsika
Microcebus	*tavaratra*	RMR71	Female	Unknown	-13.05	49.05	Ankarana
Mirza	*zaza*	DLC2301	Female	Heart	-	-	Duke Lemur Center

Table S14– Transcriptome sequences used for TRINITY assembly and SNAP training.

SRA ID	Tissue	Replicate	Read Pairs	Trimmed Read Pairs
SRR1758989	cerebellum	1	40282218	36203305
SRR1758990	cerebellum	2	33701327	29725813
SRR1758991	frontal cortex	1	22282358	19420162
SRR1758992	frontal cortex	2	42671438	38211712
SRR1758993	temporal lobe	1	97678744	85967715
SRR1758994	colon	1	94987670	75049387
SRR1758995	kidney	1	20357117	17355807
SRR1758996	kidney	2	39391366	34870736
SRR1758997	liver	1	68821579	61258808
SRR1758998	lung	1	76923918	70589216
SRR1758999	skeletal muscle	1	18183486	16943154
SRR1759000	skeletal muscle	2	52445854	46545480
SRR1759001	skeletal muscle	3	17366481	15493101
SRR1759002	spleen	1	19307314	14823668
SRR1759003	spleen	2	38808580	31952914

Table S15 – NCBI records for new sequence data.

Genus	species	BioProject	Biosample	SRA	Genome
Microcebus	*griseorufus*	PRJNA512515	SAMN10707780	SRR8456524	Pending
Microcebus	*mittermeieri*	PRJNA512515	SAMN10707781	SRR8456525	Pending
Microcebus	*ravelobensis*	PRJNA512515	SAMN10707782	SRR8456522,SRR8456518, SRR8456519,SRR8456526, SRR8456527,SRR8456528, SRR8456529,SRR8456530	Pending
Microcebus	*tavaratra*	PRJNA512515	SAMN10707784	SRR8456520	Pending
Mirza	*zaza*	PRJNA512515	SAMN10707785	SRR8456521	Pending

Table S16 – BUSCO statistics for all genomes analyzed. New mouse and dwarf lemur genomes are highlighted in gray.

Species	Assembly	Complete	Single	Duplicate	Fragment	Missing
Cheirogaleus medius	Cmed_1.0	93.40%	92.70%	0.70%	3.4%%	3.20%
Cheirogaleus sibreei	Csib_1.0	72.80%	71.40%	1.40%	19.20%	8.00%
Daubentonia madagascarensis	DauMad_1.0	9.60%	9.50%	0.10%	35.40%	55.00%
Eulemur flavifrons	Eflavifronsk33QCA	92.10%	91.50%	0.60%	4.50%	3.40%
Eulemur macaco	Emacaco_refEf_BWA_oneround	93.00%	92.50%	0.50%	4.40%	2.60%
Galeopterus variegatus	G_variegatus-3.0.2	89.00%	87.50%	1.50%	5.90%	5.10%
Microcebus griseorufus	Mgri_1.0	48.70%	47.30%	1.40%	31.90%	19.40%
Microcebus mittermeieri	Mmit_1.0	49.10%	47.00%	2.10%	32.30%	18.60%
Microcebus murinus	Mmur_2.0	94.90%	93.20%	1.70%	2.50%	2.60%
Microcebus murinus	Mmur_3.0	95.00%	93.30%	1.70%	2.30%	2.70%
Microcebus murinus	Mmur_DLC7028	82.40%	81.20%	1.20%	10.90%	6.70%
Microcebus murinus	Mmur_DLC7032	83.40%	80.60%	2.80%	10.30%	6.30%
Microcebus murinus	Mmur_DLC7033v1	85.70%	83.00%	2.70%	8.40%	5.90%
Microcebus murinus	Mmur_DLC7033v2	88.90%	86.60%	2.30%	6.60%	4.50%
Microcebus murinus	Mmur_DLC7039	83.80%	82.10%	1.70%	9.90%	6.30%
Microcebus murinus	Mmur_DLC7049	75.90%	74.80%	1.10%	14.00%	10.10%
Microcebus murinus	Mmur_DLC7128	86.20%	84.40%	1.80%	8.00%	5.80%
Microcebus murinus	Mmur_DLC7163	84.10%	82.20%	1.90%	9.50%	6.40%
Microcebus murinus	Mmur_DLC7188	81.20%	79.60%	1.60%	11.40%	7.40%
Microcebus ravelobensis	Mrav_1.0	44.00%	42.90%	1.10%	33.20%	22.80%
Microcebus tavaratra	Mtav_1.0	57.80%	56.00%	1.80%	27.70%	14.50%
Mirza zaza	Mzaz_1.0	73.90%	72.80%	1.10%	18.40%	7.70%
Otolemur garnetti	OtoGar3	93.80%	92.60%	1.20%	2.50%	3.70%
Prolemur simus	Prosim_1.0	95.20%	94.40%	0.80%	2.60%	2.20%
Propithecus coquereli	Pcoq_1.0	91.30%	90.30%	1.00%	4.40%	4.30%
Tupaia chinensis	TupChi_1.0	91.40%	90.10%	1.30%	4.20%	4.40%

Supplementary References

Cantarel BL, Korf I, Robb SMC, Parra G, Ross E, Moore B, Holt C, Alvarado AS, Yandell M. 2008. MAKER: An easy-to-use annotation pipeline designed for emerging model organism genomes. Genome Res. 18:188-196.

Chen N. 2004. Using RepeatMasker to Identify Repetitive Elements in Genomic Sequences. Current Protocols in Bioinformatics 5:4.10.1-4.10.14.

Jurka J, Kapitonov VV, Pavlicek A, Klonowski P, Kohany O, Walichiewicz J. 2005. Repbase Update, a database of eukaryotic repetitive elements. CGR 110:462–467.

Korf I. 2004. Gene finding in novel genomes. BMC Bioinformatics. 5:59.

Larsen PA, Harris RA, Liu Y, Murali SC, Campbell CR, Brown AD, Sullivan BA, Shelton J, Brown SJ, Raveendran M, et al. 2017. Hybrid de novo genome assembly and centromere characterization of the gray mouse lemur (Microcebus murinus). BMC Biology 15:110.

Li B, Dewey C. 2011. RSEM: accurate transcript quantification from RNA-Seq data with or without a reference genome. BMC Bioinformatics 12:323.

Peng X, Thierry-Mieg J, Thierry-Mieg D, Nishida A, Pipes L, Bozinoski M, Thomas MJ, Kelly S, Weiss JM, Muzny MRD, Gibbs RA, Rogers J, Schroth GP, Katze MG, Mason CE. 2014. Tissue-specific transcriptome sequencing analysis expands the non-human primate reference transcriptome resource (NHPRTR). Nuc Acid Res. 43:D737-D742.

Simão FA, Waterhouse RM, Ioannidis P, Kriventseva EV, Zdobnov EM. 2015. BUSCO: assessing genome assembly and annotation completeness with single-copy orthologs. Bioinformatics. 31:3210-3212.

Stanke M, Schöffman O, Morgenstern B, Waack S. 2006. Gene prediction in eukaryotes with a generalized hidden Markov model that uses hints from external sources. BMC Bioinformatics. 7:62.