Supporting Information

Goodman et al. 10.1073/pnas.0911239106

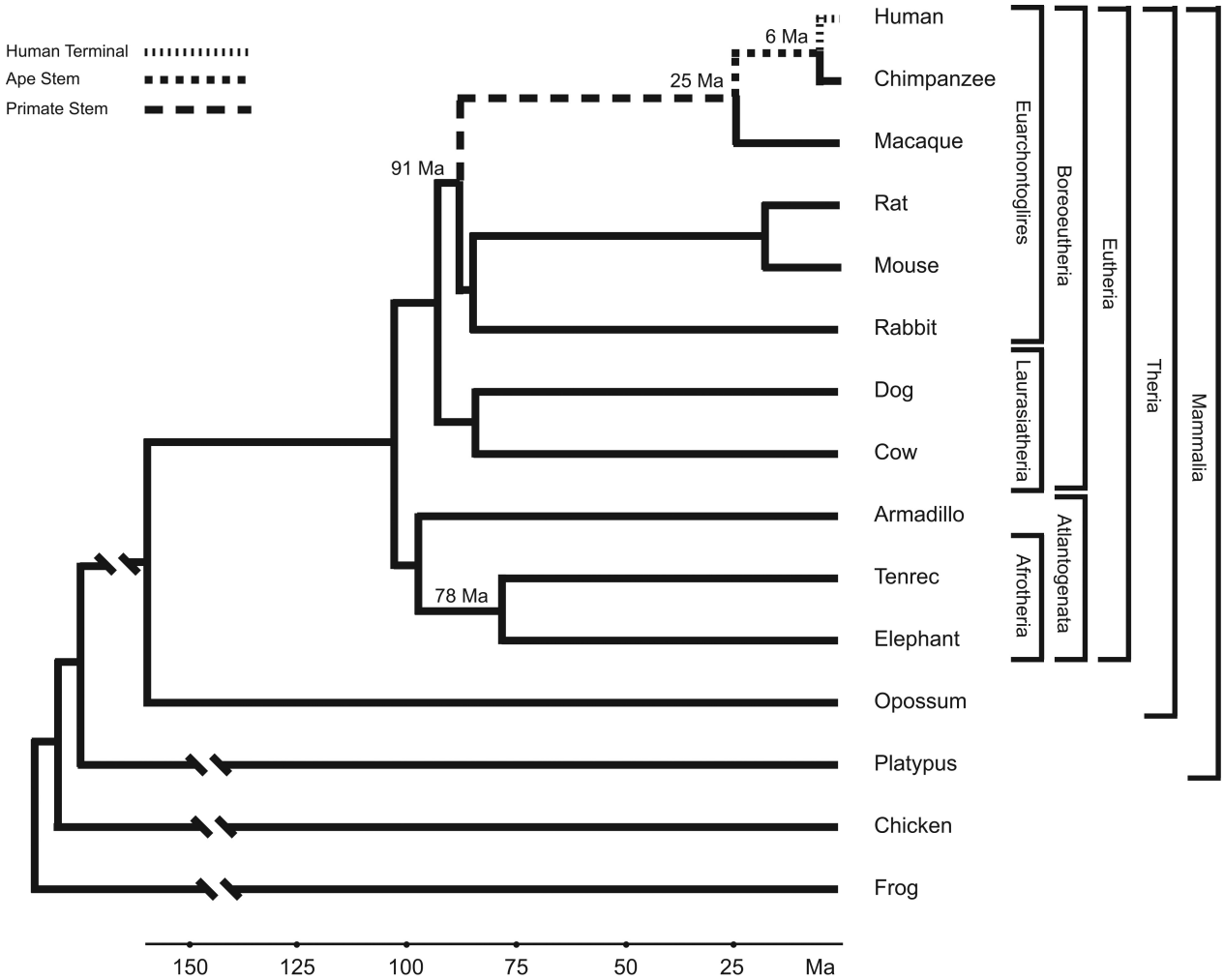


Fig. S1. Phylogenetic relationships of 15 species examined based on DNA and fossil evidence (1–4). Divergence date estimates for the human and chimpanzee last common ancestor (LCA), Old World monkey and ape LCA, and the primate and rodent LCA are given in million years (4, 5). The primate stem includes both the primate and preprimate periods. Non-therian vertebrates not drawn to scale.

1. Wildman DE, et al. (2007) Genomics, biogeography, and the diversification of placental mammals. *Proc Natl Acad Sci USA* 104:14395–14400.
2. Hallstrom BM, Kullberg M, Nilsson MA, Janke A (2007) Phylogenomic data analyses provide evidence that Xenarthra and Afrotheria are sister groups. *Mol Biol Evol* 24:2059–2068.
3. Prasad AB, et al. (2008) Confirming the phylogeny of mammals by use of large comparative sequence data sets. *Mol Biol Evol* 25:1795–1808.
4. Murphy WJ, Pringle TH, Crider TA, Springer MS, Miller W (2007) Using genomic data to unravel the root of the placental mammalian phylogeny. *Genome Res* 17:413–421.
5. Goodman M, et al. (1998) Toward a phylogenetic classification of primates based on DNA evidence complemented by fossil evidence. *Mol Phylogenet Evol* 9:585–598.

Table S1. Life history and phenotype variables among study taxa

Species name	Order	Gestation, days	Age of sexual maturity, mo	Life span, yrs	Litter size	Brain weight, g	Body weight, g	EQ[†]
Homo sapiens	Primates	270 (5)	198 (11)	75 (20)	1 (21)	1,300 (20)	44,000 (20)	8.7
Mus musculus	Rodentia	19–21 (1–3)	1.5 (1–3)	2 (1–3)	3–12 (1–3)	0.43 (24)	21 (24)	0.5
Loxodonta africana	Proboscidea	660 (28)	330–660 (4)	50–70 (15–18)	1 (16)	4,420 (23)	3,505,000 (23)	1.6
Echinops telfairi	Afrosoricida	42–49 (22)	~8 (6–10)	13 (19)	1–10 (22)	0.62 (26)	88 (26)	0.3
Bos taurus	Cetartiodactyla	277–290 (4)	18 (4)	20 (4)	1 (4)	473.5 (25)	489,900 (25)	0.6
Canis familiaris	Carnivora	63 (4)	10–24 (12–14)	12 (12–14)	3–10 (4)	81.14 (25)	12,470 (25)	1.3

[†]Jerison (ref. 27) EQ = brain weight/[(body weight)$^{2/3}$ · 0.12].

1. Berry R (1970) The natural history of the house mouse. *Field Studies* 3:219–262.
2. Bronson F (1979) The reproductive ecology of the house mouse. *Q Rev Biol* 54:265–299.
3. Lowery G (1974) *The Mammals of Louisiana and Its Adjacent Waters* (Louisiana State Univ Press, Baton Rouge, LA).
4. Nowak R (1991) in *Walker's Mammals of the World* (Johns Hopkins Press, Baltimore), 5th Ed, Vol II, pp 860–862, 1076–1078, 1282–1286, 1425–1428.
5. Harrison R (1964) Human biology. *Br Med J* 2:1388.
6. Eisenberg J (1975) Tenrecs and solenodons in captivity. *Int Zoo Yb* 15:6–12.
7. Eisenberg J, Gould E (1970) The tenrecs: A study in mammalian behavior and evolution. *Smithsonian Contrib Zool* 27:78–89.
8. Eisenberg J, Gould E (1966) The behavior of Solenodon paradoxus in captivity with comments on the behavior of other Insectivora. *Zoologica* 51:49–58.
9. Godfrey GK, Oliver WLR (1978) The reproduction and development of the pigmy hedgehog. *Dodo* 15:38–52.
10. Mallinson JJC (1974) Establishing mammal gestation at the Jersey Zoological Park. *Int Zoo Yb* 14:184–187.
11. Harvey P, Martin R, Clutton-Brock T (1987) in *Primate Societies*, eds Smuts BB, Cheney DL, Seyfarth RM, Wrangham RW, Struhsaker T (Univ of Chicago Press, Chicago), pp 181–196.
12. Asdell SA (1964) *Patterns of Mammalian Reproduction* (Cornell Univ Press, Ithaca, NY).
13. Bueler L (1973) *Wild Dogs of the World* (Stein and Day, New York).
14. Grzimek B (1972) *Grzimek's Animal Life Encyclopedia, Mammals IV* (Van Nostrand Reinhold, New York), Vol 13, pp 325–327.
15. Kingdon J (1979) *East African Mammals. An Atlas of Evolution in Africa. Vol. III. Part B. Large Mammals* (Academic Press, London).
16. Laursen L, Bekoff M (1978) Loxodonta africana. *Mammalian Species* 92:1–8.
17. Moss C (1983) Oestrous behaviour and female choice in the African elephant. *Behaviour* 86:167–196.
18. Smithers RHN (1983) *The Mammals of the Southern African Subregion* (Univ of Pretoria, Pretoria, South Africa).
19. Jones M (1982) Longevity of captive mammals. *Zoologische Garten* 52:113–128.
20. Harrison GA, Tanner JM, Pilbean DR, Baker PT, eds (1988) Human Biology: An Introduction to Human Evolution, Variation, Growth and Adaptability (Oxford Univ Press, Oxford), 3rd Ed.
21. Hayssen V, Van Tienhoven A (1993) *Asdell's Patterns of Mammalian Reproduction*: *A Compendium of Species-Specific Data* (Cornell Univ Press, Ithaca, NY).
22. Norwak R (1991) *Walker's Mammals of the World* (John Hopkins Univ Press, Baltimore), 5th Ed, Vol I, p 137.
23. Shoshani J, Kupsky WJ, Marchant GH (2006) Elephant brain Part 1: Gross morphology, functions, comparative anatomy, and evolution. *Brain Res Bull* 70:124–157.
24. Count EW (1947) Brain and body weight in man. *Ann New York Acad Sci* 46:993–1122.
25. Crile G, Quiring DP (1940) A record of the body weight of certain organ and gland weights of 3,690 animals. *Ohio J Sci* XL:219–259.
26. Stephan H, Frahm H, Baron G (1981) New and revised data on volumes of brain structures in insectivores and primates. *Folia Primatol* (*Basel*) 35:1–29.
27. Jerison HJ (1973) *Evolution of the Brain and Intelligence* (Academic Press, New York).
28. Allen WR (2006) Ovulation, pregnancy, placentation and husbandry in the African elephant (*Loxodonta africana*). *Phil Trans R Soc B* 361:821–834.

Table S2. Lineage coding sequence evolution (7,768 RefSeqs, compiled June 18, 2009)

	Median dN	Median rN	Median dS	Median rS	Median dN/dS
Human	0.015	0.167	0.128	1.408	0.118
Mouse	0.036	0.396	0.411	4.519	0.088
Elephant	0.018	0.226	0.118	1.513	0.150
Tenrec	0.033	0.419	0.283	3.629	0.115

	Mean dN	Mean rN	Mean dS	Mean rS	Mean dN/dS
Human	0.018	0.201	0.135	1.487	0.135
Mouse	0.044	0.483	0.422	4.632	0.104
Elephant	0.022	0.278	0.129	1.652	0.169
Tenrec	0.038	0.487	0.301	3.853	0.126

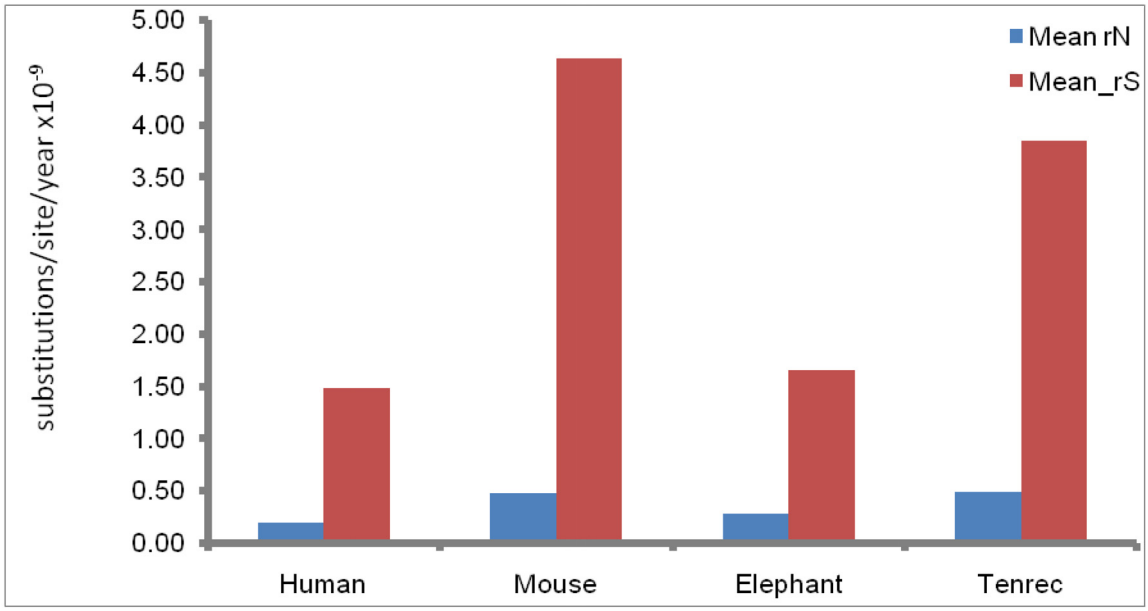


Table S3. Wilcoxon signed-rank tests

Hypothesis tested	Wilcoxon signed-rank test, W	*P*
Human genomic > dN/dS mouse genomic	35375878	<2.2e-16
Human genomic > dN/dS tenrec genomic	30611291	0.1151
Elephant genomic > dN/dS human genomic	26211674	<2.2e-16
Elephant genomic > dN/dS mouse genomic	39648013	<2.2e-16
Elephant genomic > dN/dS tenrec genomic	34990629	<2.2e-16
Tenrec genomic > dN/dS mouse genomic	24821650	<2.2e-16
Human genomic ≠ rN mouse genomic	43852137	<2.2e-16
Human genomic ≠ rN tenrec genomic	45591287	<2.2e-16
Elephant genomic ≠ rN human genomic	35262695	<2.2e-16
Elephant genomic ≠ rN mouse genomic	20611909	<2.2e-16
Elephant genomic ≠ rN tenrec genomic	41486194	<2.2e-16
Tenrec genomic ≠ rN mouse genomic	31272130	8.156e-05
Human genomic ≠ rS mouse genomic	1455856	<2.2e-16
Human genomic ≠ rS tenrec genomic	3713869	<2.2e-16
Elephant genomic ≠ rS human genomic	27378955	<2.2e-16
Elephant genomic ≠ rS mouse genomic	2773387	<2.2e-16
Elephant genomic ≠ rS tenrec genomic	54643701	<2.2e-16
Tenrec genomic ≠ rS mouse genomic	20130433	<2.2e-16

Table S4. Coding sequence evolution by bin for human (A), mouse (B), elephant (C), and tenrec (D) lineages, and the effect of length on dN/dS (E) for all four lineages. S4A. Coding sequence evolution by bin for human (*Homo sapiens*)

dN/dS bins	No. RefSeqs	Median length	Median dN	rN	Median dS	rS	Median dN/dS
0–0.025	784	1254	0.002	0.022	0.141	1.549	0.016
0.025–0.05	1036	1178	0.005	0.055	0.139	1.527	0.037
0.05–0.075	882	1103	0.008	0.088	0.134	1.473	0.061
0.075–0.1	731	1104	0.012	0.132	0.135	1.484	0.087
0.1–0.15	1131	1050	0.016	0.176	0.129	1.418	0.122
0.15–0.2	882	978	0.024	0.264	0.138	1.516	0.172
0.2–0.3	1079	930	0.031	0.341	0.125	1.374	0.241
0.3–0.4	542	876	0.041	0.451	0.122	1.341	0.339
0.4–0.5	301	753	0.045	0.495	0.102	1.121	0.444
0.5–1	332	548	0.056	0.615	0.086	0.945	0.628
>1	68	365	0.067	0.736	0.049	0.538	1.27
dN/dS bins	No. RefSeqs	Mean length	Mean dN	rN	Mean dS	rS	Mean dN/dS
0–0.025	784	1467	0.002	0.022	0.146	1.604	0.015
0.025–0.05	1036	1403	0.006	0.066	0.145	1.593	0.039
0.05–0.075	882	1343	0.009	0.099	0.136	1.495	0.064
0.075–0.1	731	1325	0.013	0.143	0.14	1.538	0.09
0.1–0.15	1131	1276	0.017	0.187	0.137	1.505	0.126
0.15–0.2	882	1230	0.025	0.275	0.138	1.516	0.178
0.2–0.3	1079	1155	0.032	0.352	0.129	1.418	0.246
0.3–0.4	542	991	0.042	0.462	0.122	1.341	0.343
0.4–0.5	301	904	0.051	0.560	0.114	1.253	0.445
0.5–1	332	742	0.058	0.637	0.093	1.022	0.626
>1	68	418	0.075	0.824	0.053	0.582	1.423

Table S4B. Coding sequence evolution for mouse (*Mus musculus*)

dN/dS Bins	No. RefSeqs	Median length	Median dN	rN	Median dS	rS	Median dN/dS
0–0.025	1000	1128	0.006	0.066	0.412	4.527	0.016
0.025–0.05	1286	1142	0.016	0.176	0.428	4.703	0.038
0.05–0.075	1124	1056	0.026	0.286	0.419	4.604	0.062
0.075–0.1	890	975	0.036	0.396	0.419	4.604	0.087
0.1–0.15	1406	969	0.052	0.571	0.421	4.626	0.122
0.15–0.2	817	963	0.07	0.769	0.408	4.484	0.172
0.2–0.3	800	927	0.095	1.044	0.396	4.352	0.237
0.3–0.4	269	816	0.125	1.374	0.362	3.978	0.338
0.4–0.5	103	789	0.144	1.582	0.331	3.637	0.431
0.5–1	64	521	0.173	1.901	0.286	3.143	0.587
>1	9	267	0.075	0.824	0.013	0.143	5.641
dN/dS Bins	No. RefSeqs	Mean length	Mean dN	rN	Mean dS	rS	Mean dN/dS
0–0.025	1000	1337	0.007	0.077	0.421	4.626	0.016
0.025–0.05	1286	1381	0.017	0.187	0.433	4.758	0.039
0.05–0.075	1124	1293	0.027	0.297	0.426	4.681	0.063
0.075–0.1	890	1229	0.037	0.407	0.422	4.637	0.089
0.1–0.15	1406	1211	0.053	0.582	0.427	4.692	0.125
0.15–0.2	817	1154	0.074	0.813	0.424	4.659	0.175
0.2–0.3	800	1132	0.1	1.099	0.411	4.516	0.243
0.3–0.4	269	978	0.128	1.407	0.376	4.132	0.342
0.4–0.5	103	913	0.151	1.659	0.345	3.791	0.438
0.5–1	64	649	0.188	2.066	0.318	3.495	0.592
>1	9	562	0.079	0.868	0.055	0.604	1.438

Table S4C. Coding sequence evolution for elephant (*Loxodonta africana*)

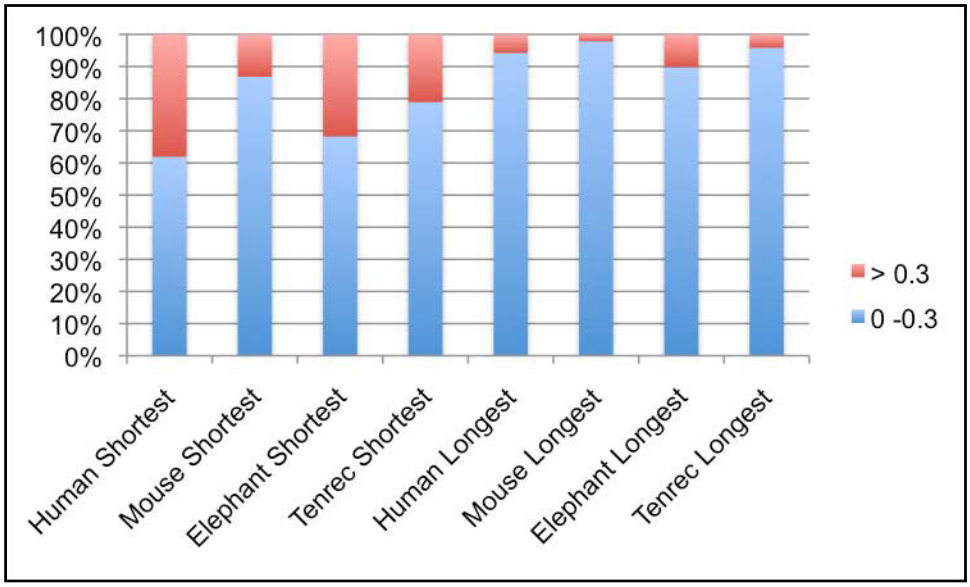
dN/dS Bins	No. RefSeqs	Median length	Median dN	rN	Median dS	rS	Median dN/dS
0–0.025	397	1215	0.002	0.026	0.147	1.885	0.017
0.025–0.05	815	1065	0.005	0.064	0.13	1.667	0.038
0.05–0.075	787	1179	0.008	0.103	0.132	1.692	0.062
0.075–0.1	705	1110	0.011	0.141	0.126	1.615	0.087
0.1–0.15	1190	1077	0.015	0.192	0.127	1.628	0.121
0.15–0.2	951	1050	0.021	0.269	0.12	1.538	0.173
0.2–0.3	1316	993	0.028	0.359	0.113	1.449	0.242
0.3–0.4	686	929	0.035	0.449	0.102	1.308	0.341
0.4–0.5	352	896	0.045	0.577	0.1	1.282	0.444
0.5–1	464	713	0.054	0.692	0.084	1.077	0.637
>1	105	474	0.073	0.936	0.061	0.782	1.254
dN/dS Bins	No. RefSeqs	Mean length	Mean dN	rN	Mean dS	rS	Mean dN/dS
0–0.025	397	1389	0.003	0.038	0.154	1.974	0.017
0.025–0.05	815	1274	0.006	0.077	0.139	1.782	0.04
0.05–0.075	787	1404	0.009	0.115	0.141	1.808	0.065
0.075–0.1	705	1375	0.012	0.154	0.131	1.679	0.091
0.1–0.15	1190	1272	0.017	0.218	0.134	1.718	0.127
0.15–0.2	951	1283	0.023	0.295	0.133	1.705	0.176
0.2–0.3	1316	1220	0.03	0.385	0.122	1.564	0.249
0.3–0.4	686	1125	0.04	0.513	0.114	1.462	0.349
0.4–0.5	352	1075	0.047	0.603	0.104	1.333	0.455
0.5–1	464	853	0.064	0.821	0.097	1.244	0.659
>1	105	616	0.068	0.872	0.055	0.705	1.247

Table S4D. Coding sequence evolution for tenrec (*Echinops telfairi*)

dN/dS Bins	No. RefSeqs	Median length	Median dN	rN	Median dS	rS	Median dN/dS
0–0.025	470	1085	0.005	0.064	0.307	3.936	0.016
0.025–0.05	928	1172	0.012	0.154	0.314	4.026	0.038
0.05–0.075	1032	1167	0.019	0.244	0.308	3.949	0.062
0.075–0.1	914	1073	0.026	0.333	0.294	3.769	0.087
0.1–0.15	1588	1002	0.035	0.449	0.29	3.718	0.122
0.15–0.2	1022	972	0.048	0.615	0.276	3.538	0.172
0.2–0.3	1025	963	0.063	0.808	0.255	3.269	0.241
0.3–0.4	443	867	0.082	1.051	0.25	3.205	0.339
0.4–0.5	175	732	0.107	1.372	0.243	3.115	0.446
0.5–1	161	519	0.119	1.526	0.192	2.462	0.588
>1	10	267	0.065	0.833	0.039	0.500	2.893
dN/dS Bins	No. RefSeqs	Mean length	Mean dN	rN	Mean dS	rS	Mean dN/dS
0–0.025	470	1271	0.005	0.064	0.317	4.064	0.016
0.025–0.05	928	1407	0.013	0.167	0.334	4.282	0.038
0.05–0.075	1032	1395	0.02	0.256	0.321	4.115	0.063
0.075–0.1	914	1306	0.027	0.346	0.307	3.936	0.089
0.1–0.15	1588	1222	0.038	0.487	0.302	3.872	0.126
0.15–0.2	1022	1196	0.051	0.654	0.291	3.731	0.175
0.2–0.3	1025	1164	0.066	0.846	0.272	3.487	0.245
0.3–0.4	443	1006	0.088	1.128	0.255	3.269	0.345
0.4–0.5	175	944	0.111	1.423	0.25	3.205	0.444
0.5–1	161	683	0.117	1.500	0.194	2.487	0.605
>1	10	363	0.116	1.487	0.086	1.103	1.345

Table S4E. Effects of multiple sequence alignment length on dN/dS

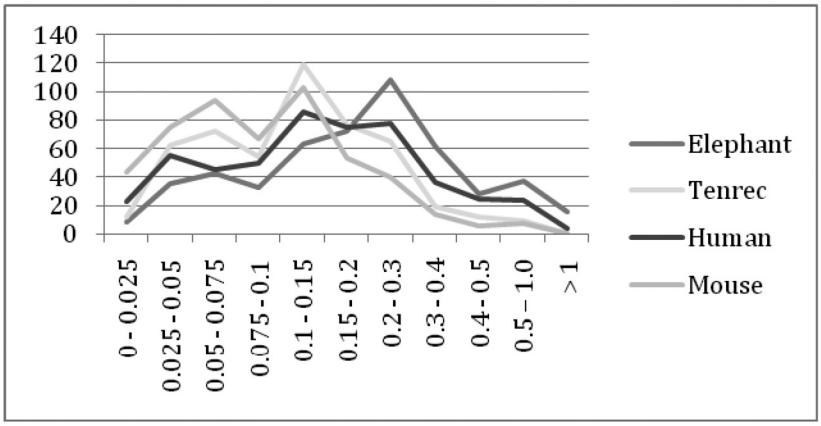
		Human	Mouse	Elephant	Tenrec
Shortest 1000	dN/dS <0.3	619	868	682	789
	dN/dS >0.3	381	132	318	211
Longest 1000	dN/dS <0.3	942	978	898	958
	dN/dS >0.3	58	22	102	42



The 1,000 shortest RefSeqs (average length 348 bp) are compared with the 1,000 longest RefSeqs (average length 2935 bp) for the 4 lineages. RefSeqs were binned by dN/dS. dN/dS bins utilized: 0–0.1, 0.1–0.2, 0.2–0.3, 0.3–0.4, 0.4–0.5, and 0.5–1.0, and >1. Bins <0.3 are grouped and shown in blue. Bins >0.3 are grouped and shown in red. Percent of the total 1000 RefSeqs with dN/dS <0.3 or >0.3 are shown.

Table S5. Lineage coding sequence evolution for GOTerm mitochondrion (GO:0005739) related RefSeqs (total 501 RefSeqs)

dN/dS Bin	Elephant	Tenrec	Human	Mouse
0 - 0.025	8	12	23	43
0.025 - 0.05	35	62	55	75
0.05 - 0.075	42	72	45	94
0.075 - 0.1	32	54	50	67
0.1 - 0.15	63	119	86	103
0.15 - 0.2	72	77	75	53
0.2 - 0.3	108	65	78	40
0.3 - 0.4	61	19	36	14
0.4 - 0.5	28	12	25	5
0.5 – 1.0	37	9	24	7
> 1	15	0	4	0



	Total N	Total S	Total N*dN	Total S*dS	Mean dN	Mean_dS	Mean dN/dS
Human	370367	132190	7437.70	17560.40	0.020082	0.132842	0.151172
Mouse	370367	132190	15634.40	55600.40	0.042213	0.420610	0.100362
Elephant	370367	132190	9199.40	16296.70	0.024839	0.123282	0.201477
Tenrec	370367	132190	13725.00	39148.70	0.037058	0.296155	0.125130

Hypothesis Tested *Is the mean dN/dS of the mitochondrion related RefSeqs (501) significantly greater than the mean dN/dS of the total RefSeqs (7267) shown in Table S2?*	**Wilcoxon Signed-Rank Test (W)**	**p-value**
Human	W= 2032868	**p = 1.205e-05**
Mouse	W= 1869401	p = 0.3127
Elephant	W= 2155303	**p = 5.257e-12**
Tenrec	W= 1856136	p = 0.4615

Table S6. Number of genes per bin for gene ontology (GO) terms related to aerobic energy metabolism and mitochondria with DAVID enrichment scores > 2 for each lineage

GOTERMs	Species	0 - .025	.025 - .05	.05 - .075	.075 - .1	.1- .15	.15 -.2	.2 - .3	.3 - .4	.4 - .5	.5 - 1	> 1
GO:0005739 mitochondrion	Elephant							89	45			14
	Tenrec			60								
	Human						66	67			19	
	Mouse			79	60	86						
GO:0005740 mitochondrial envelope	Elephant							37				
	Tenrec			29								
	Human						25					
	Mouse	22		35								
GO:0005743 mitochondrial inner membrane	Elephant							25				
	Tenrec			21								
	Human						22					
	Mouse			25								
GO:0005741 mitochondrial outer membrane	Elephant											
	Tenrec		10									
	Human											
	Mouse		10									
GO:0031966 mitochondrial membrane	Elephant							33				
	Tenrec			28								
	Human						24					
	Mouse			32								
GO:0044429 mitochondrial part	Elephant						38	55				
	Tenrec			41								
	Human							50				
	Mouse			47	34	52						
GO:0043227 membrane-bounded organelle	Elephant	154	275	278								
	Tenrec	157	317	341	310							
	Human	304	379	289								
	Mouse	330	441	390								
GO:0043231 intracellular membrane-bounded organelle	Elephant	154	275	276								
	Tenrec	156	317	341	310							
	Human	304	378	289								
	Mouse	329	441	390								
GO:0043229 intracellular organelle	Elephant	168	309	310								
	Tenrec	173	373	375	344							
	Human	343	430	326								
	Mouse	383	493	429								
GO:0043226 organelle	Elephant	168	309	311								
	Tenrec	174	373	375	344							
	Human	343	431	326								
	Mouse	384	493	429								
GO:0031090 organelle membrane	Elephant											
	Tenrec											
	Human											
	Mouse											
GO:0019866 organelle inner membrane	Elephant							26				
	Tenrec			23								
	Human						22					

	Mouse			26								
GO:0031968 organelle outer membrane	Elephant											
	Tenrec		10									
	Human											
	Mouse		11									
GO:0019867 outer membrane	Elephant											
	Tenrec		11									
	Human											
	Mouse		15									
GO:0031967 organelle envelope	Elephant							48				
	Tenrec			36								
	Human						28					
	Mouse	40		47								
GO:0031975 envelope	Elephant							48				
	Tenrec			36								
	Human						28					
	Mouse	40		47								
GO:0006118 electron transport	Elephant										23	
	Tenrec											
	Human											
	Mouse											
GO:0006091 generation of precursor metabolites & energy	Elephant										27	
	Tenrec											
	Human											
	Mouse											
GO:0016491 oxidoreductase activity	Elephant										30	
	Tenrec											
	Human											
	Mouse											

Table S7. Number of genes per gene ontology (GO) term with DAVID enrichment scores >2 for the top 5% of Refseqs (389) with the more elevated dN/dS ratios

GOTerm	Elephant	Tenrec	Human	Mouse	Cow	Dog
GO:0006935~chemotaxis		8				
GO:0007610~behavior		9				
GO:0007626~locomotory behavior		8				
GO:0042330~taxis		8				
GO:0005506~iron ion binding						10
GO:0005529~sugar binding						9
GO:0019825~oxygen binding						5
GO:0019838~growth factor binding		7				
GO:0019955~cytokine binding		9				
GO:0019965~interleukin binding		8				
GO:0020037~heme binding						6
GO:0030246~carbohydrate binding						9
GO:0046906~tetrapyrrole binding						6
GO:0004907~interleukin receptor activity		8				
GO:0016491~oxidoreductase activity	20					
GO:0016705~oxidoreductase activity						7
GO:0016712~oxidoreductase activity						5
GO:0016712~unspecific monooxygenase activity						4
GO:0001775~cell activation		11	13	12	14	12
GO:0042110~T cell activation		6	9	9	9	10
GO:0045321~leukocyte activation		11	11	12	13	12
GO:0046649~lymphocyte activation		9	11	11	12	12
GO:0005887~integral to plasma membrane				29		
GO:0031226~intrinsic to plasma membrane				29		
GO:0042598~vesicular fraction						8
GO:0044459~plasma membrane part				39		
GO:0005792~microsome						7
GO:0005576~extracellular region	27	32	27	39		38
GO:0005615~extracellular space	17	18	19	28		22
GO:0044421~extracellular region part	21	23	21	33		28
GO:0016020~membrane	119	123	91	124	113	136
GO:0016021~integral to membrane	92	97	81	101	98	113
GO:0031224~intrinsic to membrane	92	97	81	101	98	113
GO:0044425~membrane part	108	112	89	113	103	123
GO:0005739~mitochondrion	37		21			
GO:0006091~generation of precursor metabolites	21					
GO:0030154~cell differentiation			36			
GO:0032502~developmental process			44			
GO:0048468~cell development			22			
GO:0048869~cellular developmental process			36			
GO:0030217~T cell differentiation			6			
GO:0030098~lymphocyte differentiation			6			
GO:0002252~immune effector process					7	9
GO:0002253~activation of immune response					6	7
GO:0002526~acute inflammatory response						7
GO:0002541~activation of plasma proteins during acute...					5	4
GO:0002682~regulation of immune system process					6	9
GO:0002684~positive regulation of immune system process					6	9
GO:0006956~complement activation					5	4
GO:0006959~humoral immune response					6	5
GO:0045087~innate immune response					11	7
GO:0051239~regulation of multicellular organismal process			11			12
GO:0051240~positive regulation of multicellular organismal...						9
GO:0050778~positive regulation of immune response					6	9
GO:0050778~positive regulation of multicellular organismal...					7	
GO:0050776~regulation of immune response					6	9
GO:0002521~leukocyte differentiation			6			
GO:0002520~immune system development			11			
GO:0030097~hemopoiesis			10			
GO:0048534~hemopoietic or lymphoid organ development			11			
GO:0006118~electron transport	16					
GO:0019866~organelle inner membrane	13					
GO:0031967~organelle envelope	15					

GOTerm	Elephant	Tenrec	Human	Mouse	Cow	Dog
GO:0031975~envelope	15					
GO:0005740~mitochondrial envelope	15					
GO:0005743~mitochondrial inner membrane	12					
GO:0031966~mitochondrial membrane	13					
GO:0044429~mitochondrial part	19					
GO:0004497~monooxygenase activity						6
GO:0004871~signal transducer activity		47	37	45	42	50
GO:0004872~receptor activity		45	34	43	40	47
GO:0004888~transmembrane receptor activity		29	24	28	28	37
GO:0060089~molecular transducer activity		47	37	45	32	50
GO:0005102~receptor binding			16			
GO:0005125~cytokine activity			12	18		12
GO:0006950~response to stress		21			19	23
GO:0006952~defense response		23			22	27
GO:0006954~inflammatory response		14		12	13	17
GO:0009605~response to external stimulus		21		19	17	24
GO:0009611~response to wounding		17		14	14	19
GO:0009607~response to biotic stimulus				13		
GO:0051704~multi-organism process				11		
GO:0051707~response to other organism				10		
GO:0009410~response to xenobiotic stimulus						4
GO:0042221~response to chemical stimulus		14				
GO:0006805~xenobiotic metabolic process						4
GO:0007166~cell surface receptor linked signal transduction			29			
GO:0008544~epidermis development			6			
GO:0009913~epidermal cell differentiation			5			
GO:0031424~keratinization			5			
GO:0048729~tissue morphogenesis			5			
GO:0048730~epidermis morphogenesis			5			
GO:0007398~ectoderm development			6			
GO:0009888~tissue development			9			
GO:0005164~tumor necrosis factor receptor binding				4		
GO:0032813~tumor necrosis factor receptor superfamily				4		

Ratios defined as dN/dS >0.61, >0.38, >0.51, >0.32, >0.38, and >0.41 in elephant, tenrec, human, mouse, cow, and dog lineages, respectively.

Table S8. Mitochondrial functioning genes showing evidence suggesting positive selection (dN/dS >1) during one or another of the successive evolutionary periods in descent to the human species and dN/dS >0.61 (top 5% of RefSeqs) in elephant

Mitochondrial functioning genes (GO:0005739~mitochondrion*)	Evidence of positive selection			
	Primate stem	Ape stem	Human terminal	Elephant terminal
Not observed in the human terminal branch				
Similar to mitofusin 1 isoform 1 (LOC441511)	√	√		
Mitochondrial ribosomal protein L33 (MRPL33)	√	√		√
Mitochondrial ribosome recycling factor (MRRF)	√	√		
NADH dehydrogenase (ubiquinone) Fe-S protein 4, 18KDA (NADH-coenzyme Q reductase) (NDUFS4)	√	√		
Aminoadipate aminotransferase (AADAT)		√		√
Cytochrome *c* oxidase subunit VIIC (COX7C)		√		
NADH dehydrogenase (ubiquinone)1 alpha subcomplex, 3, 9KDA (NDUFA3)		√		
Phorbol-12-myristate-13-acetate-induced protein 1 (PMAIP1)		√		
Succinate dehydrogenase complex, subunit C, integral membrane protein, 15KDA (SDHC)		√		
Superoxide dismutase 1, soluble [amyotrophic lateral sclerosis 1 (adult)] (SOD1)		√		
Observed in the human terminal branch				
Benzodiazapine receptor (peripheral) (TSPO)	√		√	
Cytochrome *c* oxidase subunit 8A (ubiquitous) (COX8A)		√	√	√
Mitochondrial ribosomal protein L52 (MRPL52)		√	√	
NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 1, 7.5KDA (NDUFA1)		√	√	
ATP synthase, H^+-transporting, mitochondrial F_O complex, subunit B1 (ATP5F1)			√	√
J-type cochaperone HSC20 (HSCB)			√	√
Methylmalonyl-CoA epimerase (MCEE)			√	√
Not observed in any period				
GM2 ganglioside activator (GM2A)				
Mitochondrial ribosomal protein S27 (MRPS27)				
Mitochondrial transcription termination factor (MTERF)				
Pyrophosphatase (inorganic) 2 (PPA2)				

*For the human terminal, mitochondrial functioning genes were determined using SP_PIR_KEYWORDS mitochondrion.