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the **TIMETREE** *of* **LIFE**

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Placental mammals (Eutheria)

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Abstract

Living eutherian mammals (~5000 sp.), or Placentalia, are classified into 18–20 orders. Molecular data support four major groups of orders, two of Gondwanan origin (Afrotheria and Xenarthra) and two of Laurasian origin (Euarchontoglires and Laurasiatheria). Most recent molecular analyses support a close relationship of the Gondwanan groups and of the Laurasian groups. The divergence time of ~103 million years ago (Ma) between Afrotheria and Xenarthra coincides with the separation of Africa and South America. The eutherian timetree demonstrates that nearly all divergences among orders took place before the Mesozoic–Cenozoic boundary (66 Ma) while nearly all divergences within orders were in the Cenozoic.

Eutherians form a monophyletic group of taxa that are distinguished from other mammals by a number of characters, the most prominent among these being their extended gestation period, faster overall growth, and higher reproductive rates than marsupials and monotremes (1). Fossil evidence indicates that eutherians originated in the early Cretaceous ~125 Ma (2). All extant eutherians are members of the crown-group Placentalia, which we refer to henceforth as placentals. There is still debate about the phylogenetic placement of many fossil eutherians; whether they are stem or crown placentals is controversial (3, 4). Living placental mammals have traditionally been divided into 18 orders based on morphological data (5). As discussed later, molecular data accumulated in the past 15 years have led to revisions in the composition of several orders, resulting in as many as 20 currently recognized orders of placental mammals (6, 7).

Beginning in the early 1990s, molecular phylogenetic studies revealed differences from the traditional ordinal

classification based on morphology. Analysis of mitochondrial DNA data indicated that cetaceans were the closest relatives of hippos, which led to the establishment of Cetartiodactyla, containing artiodactyls and cetaceans (8). Analyses of lens αA crystallin amino acid sequences provided evidence for a superordinal clade of mammals that contained paenungulates (elephants, hyracoids, sirenians; Fig. 1), aardvarks, and elephant shrews (9). Subsequent inclusion of golden moles and tenrecs in this African group, based on mitochondrial and nuclear gene sequences, provided compelling evidence for an ancient endemic assemblage, dubbed Afrotheria, which includes nearly a third of all placental mammal orders (10–12).

As larger molecular data sets were compiled and analyzed, other novel superorders of mammals began to emerge. One group contained the non-afrotherian insectivores (Eulipotyphla), bats, perissodactyls, cetartiodactyls, carnivores, and pangolins, and another group contained primates, tree shrews, flying lemurs, rodents, and lagomorphs (13–18). Today, placental mammals are divided into four major clades (Afrotheria, Xenarthra, Euarchontoglires, and Laurasiatheria) (Fig. 2) (13–22). These four groups are independently supported by one or more rare genomic changes (RGCs) (23–28). Though early analyses of complete mitochondrial genomes conflicted with these nuclear gene sequence-based trees (29),



Fig. 1 An African Savannah Elephant (*Loxodonta africana*) with its calf. Credit: E. Eizirik.

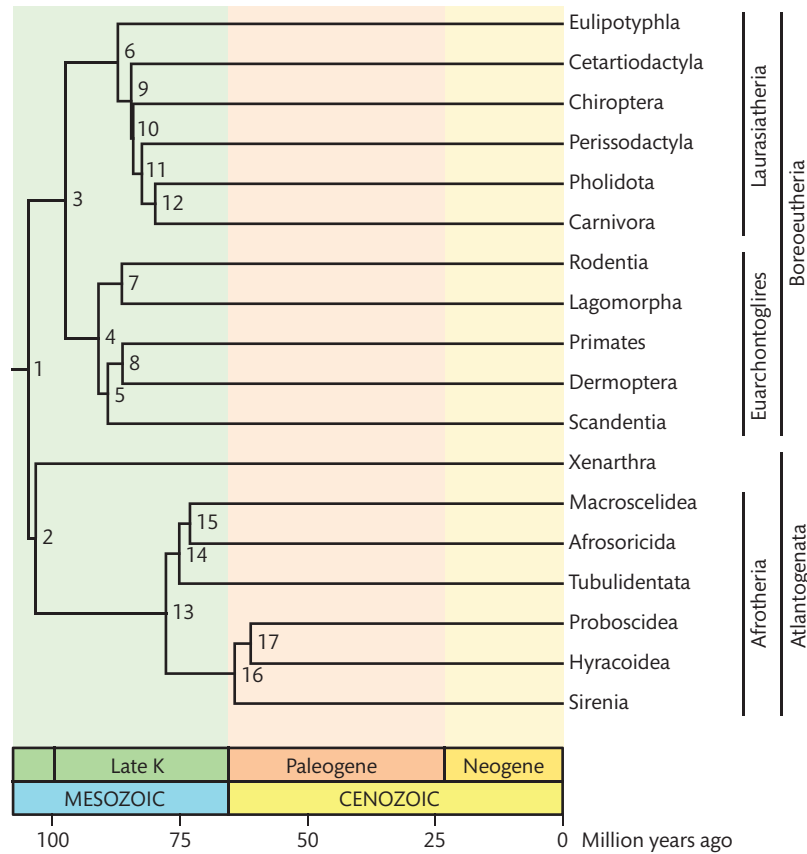


Fig. 2 A timetree of placental mammals (Eutheria). Divergence times are shown in Table 1. *Abbreviation:* K (Cretaceous).

more recent studies that improve taxonomic sampling and modeling of sequence evolution, including both mitochondrial RNA and protein-coding gene sequences, have produced phylogenies containing the four major clades (30–33).

With the increasing number of mammalian genomes being sequenced (34), an enormous amount of genomic data have come to bear on interordinal relationships in the form of RGCs (35), uncovering strong support for the four-clade hypothesis for placentals and for the interrelationships within Afrotheria and Laurasiatheria (27, 28). Regarding the root of the placental tree, three competing hypotheses exist. The first suggests that Afrotheria is the basal placental lineage (13–17, 36), whereas other studies favor the classical Epitheria hypothesis, with xenarthrans occupying the basal position within Placentalia (2, 27). However, most recent studies of RGCs (37), mitochondrial genomes (33), LINE-1 elements (38), and whole genome collections of protein-coding genes (39) are converging on the Atlantogenata hypothesis (19). In

Atlantogenata, afrotherians and xenarthrans are each other's closest relatives. This hypothesis has implications for understanding the earliest biogeographic history of Placentalia. Afrotheria and Xenarthra are of presumed Gondwanan origin, and they likely originated in Africa and South America, respectively. Euarchotheria and Laurasiatheria, in turn, are most likely of Laurasian origin, and together form a clade named Boreoeutheria to reflect its northern hemisphere ancestry (13–15, 17, 39).

The application of dating approaches using standard and relaxed molecular clocks to large data sets has produced divergence estimates within and between nearly all placental mammal orders. The overwhelming majority of these studies agree that divergences among orders of placental mammals occurred more than 66 Ma (13–15, 17, 40–50). In addition, most large divergence-dating studies support a common ancestor for Placentalia at ~105–100 million years ago (Fig. 2, Table 1). A divergence estimate of ~103 million years for Afrotheria and Xenarthra (37) is coincident with the plate tectonic separation of Africa

Table 1. Divergence times (Ma) and their confidence/credibility intervals (CI) among placental mammals (Eutheria).

Timetree		Estimates								
Node	Time	Ref. (37)		Ref. (44)	Ref. (42)		Ref. (46)		Ref. (51)	
		Time	CI	Time	Time	CI	Time	CI	Time	CI
1	104.7	104.7	115–96	101.6	105.0	118–92	104.5	122–90	-	-
2	103.3	103.3	114–95	-	-	-	-	-	-	-
3	97.4	97.4	106–90	-	92.0	95–89	92.5	105–81	-	-
4	91.0	91.0	99–84	89.0	90.8	95–87	85.5	98–76	88.8	73–101
5	89.1	89.1	97–82	-	85.9	109–63	78.0	88–70	87.9	73–100
6	87.2	87.2	93–82	-	-	-	81.5	91–74	-	-
7	86.4	86.4	94–80	74.6	-	-	74.0	89–62	85.7	71–98
8	86.2	-	-	-	-	-	-	-	86.2	71–98
9	84.6	84.6	80–90	-	83.0	91–75	78.0	85–72	-	-
10	84.2	84.2	89–79	-	74.0	85–63	-	-	-	-
11	82.5	82.5	87–78	-	-	-	-	-	-	-
12	79.8	79.8	85–75	-	-	-	74.0	81–67	-	-
13	77.8	77.8	86–70	79.9	-	-	89.0	104–75	-	-
14	75.1	75.1	83–67	-	-	-	80.0	96–67	-	-
15	73.0	73.0	81–65	-	-	-	85.0	100–71	-	-
16	64.2	64.2	73–56	-	-	-	79.0	94–65	-	-
17	61.1	61.1	70–53	-	-	-	-	-	-	-

Note: Node times in the timetree are from ref. (37). Results from independent molecular data sets are included: a large mitochondrial + nuclear DNA sequence data set (36), mitochondrial protein-coding genes (41), a large data set of nuclear proteins (39), and two large nuclear gene amino acid alignments (43). For ref. (43), midpoint of the ranges were taken to generate a point estimates. Different partitions of the data set in ref. (36) have been used in other molecular divergence time studies, with overlapping taxon and gene sampling, and produce similar divergence times (see 22, 40–42, 44, 47).

and South America and supports hypotheses that claim a role for continental breakup in the early history of Placentalia (13–15, 17, 39, 40). In contrast, most relaxed clock studies that include multiple members of each mammalian order support divergences within orders in the Cenozoic, although some evolutionary divergences within Xenarthra, Eulipotyphla, Primates, and Rodentia are found to extend into the late Cretaceous (>66 Ma) (37–51). Molecular divergence times therefore imply that the early diversification of placental mammals occurred in the Cretaceous, where they potentially existed at the feet of the dinosaurs as mostly small-bodied, insectivorous forms. The combination of current molecular and paleontological evidence indicates that the derived features of extant crown-group orders, including large body size and extreme morpho-ecological diversity, did not evolve until after the Cretaceous–Paleogene extinction event that marked the demise of the dinosaurs.

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