

ORIGINS AND
RELATIONSHIPS
OF THE MAJOR
EXTANT CLADES

THE RISE OF PLACENTAL MAMMALS

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MOLECULAR EVIDENCE FOR MAJOR PLACENTAL CLADES

SUCH FEATURES OF MAMMALIAN ANATOMY as the skeleton, muscular system, and reproductive system have long supplied systematists with evidence for proposing and testing hypotheses of supraordinal relationships. The ongoing challenge is to distinguish between homologous and homoplastic characters. Morphological phylogenies often support competing hypotheses (e.g., the placement of pholidotans as the sister taxon to either Xenarthra or Carnivora), but there remain recurrent hypotheses that pervade morphological studies of placental mammal phylogeny. Examples include Tethytheria (Proboscidea + Sirenia), Paenungulata (Tethytheria + Hyracoidea), Altungulata (Paenungulata + Perissodactyla), Ungulata (Paenungulata + Perissodactyla + Artiodactyla + Cetacea + Tubulidentata), Glires (Lagomorpha + Rodentia), Anagalida (Glires + Macroscelidea), Volitantia (Chiroptera + Dermoptera), Archonta (Volitantia + Primates + Scandentia), and Epitheria (all living placentals except Xenarthra). Against this backdrop of a priori hypotheses, the advent of molecular data provides an opportunity to evaluate morphologically based groups that reflect homology vs. homoplastic similarity.

Early molecular data sets included immunological distances (Goodman, 1975; Shoshani, 1986) and amino acid sequences for one or more proteins (Goodman, 1975; de Jong et al., 1981; Shoshani et al., 1985; Kleinschmidt et al., 1986; Miyamoto and Goodman, 1986). These studies failed to provide a well-resolved tree for the orders of placental mammals, but in some cases, provided support for a paenungulate clade, with or without the inclusion of aardvarks (de Jong et al., 1981; Kleinschmidt et al., 1986; Miyamoto and Goodman, 1986; Shoshani, 1986). Subsequently, protein

sequences supported an association of elephant shrews with aardvarks and paenungulates (de Jong et al., 1993). In addition, early studies challenged the naturalness of such groups as Archonta (Goodman, 1975), Edentata (Shoshani, 1986), and Ungulata (Shoshani, 1986).

In the past decade, DNA studies have been at the forefront of molecular investigations into placental phylogeny. Initially, these studies were based on segments of single genes and met with limited success (Stanhope et al., 1992, 1993, 1996; Springer and Kirsch, 1993; Lavergne et al., 1996; Porter et al., 1996; Springer et al., 1997a). Nevertheless, they provided robust support for Paenungulata, as well as for an expanded clade that joined aardvarks and elephant shrews with paenungulates. DNA data sets that increased taxon sampling and included both mitochondrial and nuclear genes suggested that the paenungulate-aardvark-elephant shrew clade also included the insectivore families Chrysochloridae and Tenrecidae (Springer et al., 1997b; Stanhope et al., 1998a,b). Stanhope et al. (1998b) proposed the name Afrotheria for the clade that includes Hyracoidea, Proboscidea, Sirenia, Macroscelidea, Tubulidentata, and Afrosoricida—the latter a newly proposed order for chrysochlorids and tenrecids. This hypothesis met resistance among morphologists, both because morphological synapomorphies for Afrotheria were not forthcoming (Asher, 1999) and because this hypothesis challenged the monophyly of lipotyphlan insectivores (MacPhee and Novacek, 1993), rendering this group polyphyletic.

Large data sets, including both longer gene segments of individual genes (*BRCA1*; Madsen et al., 2001; Scally et al., 2001) and concatenated data sets incorporating segments from multiple genes (Eizirik et al., 2001; Madsen et al., 2001; Murphy et al., 2001a,b; Scally et al., 2001; Delsuc et al., 2002; Amrine-Madsen et al., 2003; Springer et al., in press), provided for increased resolution and divided placental mammals into four major groups: Afrotheria, Xenarthra, Laurasiatheria, and Euarchontoglires. The largest concatenations of DNA sequences, which range from 16.4 to 17.3 kb (Murphy et al., 2001b; Amrine-Madsen et al., 2003; Springer et al., in press), allow for only local rearrangements in the placental tree (e.g., the paenungulate trifurcation is not satisfactorily resolved) when they are analyzed with maximum likelihood and Bayesian methods (Fig. 4.1). It is worth noting that these data sets are dominated by nuclear exons, which have more resolving power than do mitochondrial protein-coding genes for investigating deep-level placental relationships (Springer et al., 2001a). The emerging view of higher-level placental relationships that has resulted from nuclear data sets, with or without the addition of mitochondrial rRNA genes, is partially corroborated by other lines of evidence, including rare genomic changes (see below), analyses of complete rRNA + tRNA gene sequences from the mitochondrial genome (Hudelot et al., 2003), and to a lesser extent, by mitochondrial protein-coding sequences (Árnason et al., 2002; Lin et al., 2002). At the same time, there have been important challenges to the growing consensus that there are four major clades of placental mam-

mals. The analysis by Árnason et al. (2002) of mitochondrial protein-coding sequences suggests that Laurasiatheria is diphyletic and that Euarchontoglires, Glires, and Rodentia are all paraphyletic taxa near the base of the placental tree. Another feature of these authors' topology is that Afrotheria and Xenarthra are deeply nested in the placental tree rather than basal or near-basal, as we have recovered in our analyses (e.g., Madsen et al., 2001; Murphy et al., 2001a,b; Amrine-Madsen et al., 2003). Asher et al. (2003) performed maximum parsimony analysis with a molecular concatenation that included 19 nuclear segments and three mitochondrial genes under 12 different optimization alignment settings that employed different character transformation weights. They recovered paraphyletic Rodentia, Glires, and Euarchontoglires at the base of Placentalia in six of 12 analyses. Rodent paraphyly at the base of Placentalia, with a basal split between murids and other placentals, also resulted in three of 12 analyses in the total evidence analyses by Asher et al. (2003) that included both molecular and morphological data. In analyses with depauperate taxon sampling, Misawa and Janke (2003) have suggested that Glires is paraphyletic and that lagomorphs are more closely related to primates and artiodactyls than to rodents. The possibility that rodents, Glires, and Euarchontoglires are paraphyletic at the base of Placentalia has profound consequences for the early biogeographic history of Placentalia and the deployment of morphological and genomic changes in this group.

For paleontologists who are primarily concerned with morphological data, choosing between disparate molecular views of placental relationships may seem daunting. We argue later in the chapter that a robust solution for placental relationships is already in place and allows for only local rearrangements. Some molecular studies that challenge this view, principally by altering the placement of the placental root, are compromised by limited taxon sampling and/or inadequate methods of phylogenetic analysis. Below, we review evidence for the major features of the phylogeny depicted in Figure 4.1, with the view that congruence from fundamentally different types of data is a guiding principle in systematics (Patterson, 1982). We also review problems associated with analyses that place rodents at the base of the placental tree, often as a paraphyletic taxon. Next, we provide a molecular timescale for placental evolution and discuss implications of placental phylogeny and divergence times for understanding the biogeographic history of Placentalia. Finally, we offer a brief prospectus on integrating molecular and morphological data, including data for fossil taxa.

MAJOR CLADES OF PLACENTAL MAMMALS

Maximum likelihood and Bayesian analyses of data sets that emphasize concatenated nuclear genes provide robust support for four major groups of placental mammals:

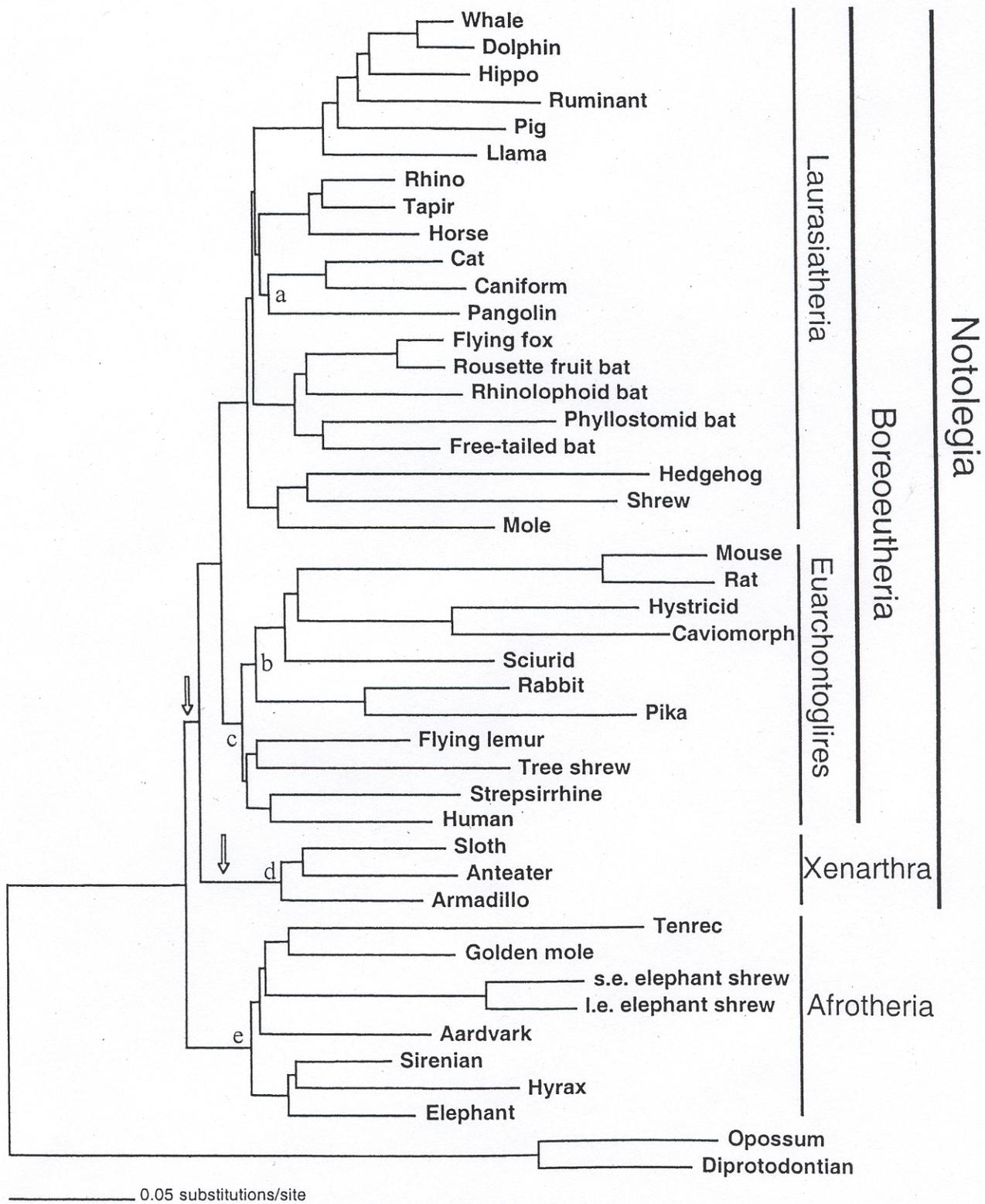


Fig. 4.1. Molecular phylogeny of placental mammals, based on the concatenated DNA sequence data set of Murphy et al. (2001b). Branch lengths are drawn to scale, indicating the proportional magnitude of molecular change per lineage. Major clades are indicated on the right. Arrows denote the two alternative positions for the root. Letters indicate additional lines of evidence supporting adjacent nodes: a, Carnivora + Pholidota (deletion in *apolipoprotein B* gene; osseus tentorium); b, Glires (morphological synapomorphies); c, Euarchoptoglires (deletions in two different genes); d, Xenarthra (morphological synapomorphies; deletion in the *aA-crystallin* gene); e, Afrotheria (deletions in two different genes; presence of unique SINE elements).

Xenarthra, Afrotheria, Laurasiatheria, and Euarchontoglires (Madsen et al., 2001; Murphy et al., 2001a,b; Scally et al., 2001; Delsuc et al., 2002; Amrine-Madsen et al., 2003; Springer et al., in press) (Table 4.1). Furthermore, there is robust support for Boreoeutheria; that is, a clade comprised of Laurasiatheria and Euarchontoglires. Of these clades, only Xenarthra is supported by morphological data. The absence of morphological evidence for Afrotheria, Laurasiatheria, Euarchontoglires, and Boreoeutheria suggests that synapomorphies for these clades were never present, have been eroded in the subsequent evolutionary history of these taxa, or remain to be discovered, possibly among morphological characters that are not confederated with diet and locomotion. Even in the absence of morphological evidence for these clades, rare genomic changes have been discovered that support Xenarthra, Afrotheria, Euarchontoglires, and possibly Laurasiatheria. Xenarthra is supported by a three-amino-acid deletion in the eye lens protein α -crystallin (van Dijk et al., 1999). Rare genomic changes supporting Afrotheria include a 9 bp deletion in *BRCA1* (Madsen et al., 2001; Scally et al., 2001), a 237–246 bp deletion in the *apolipoprotein B* alignment of Amrine-Madsen et

al. (2003), and a family of short interspersed nuclear elements (SINE) called AfroSINES that is unique to this group (Nikaido et al., 2003). In addition, chromosome painting studies now reveal two potential genomic characters (associations or shared synteny) supporting the monophyly of representative afrotherians (elephants and armadillos; Froenicke et al., 2003). Rare genomic changes supporting Euarchontoglires include an 18-amino-acid deletion in exon 8 of the *SCA1* gene, and a 6 bp deletion in the *PRNP* gene (Poux et al., 2002; de Jong et al., 2003). Thomas et al. (2003) identified several indels, including transposon insertions, that occur in primates and rodents but not in carnivores, artiodactyls, or non-mammalian vertebrates that were sampled. These indels are consistent with the monophyly of Euarchontoglires, but will require additional taxon sampling within Placentalia to confirm that they are true synapomorphies. Finally, and with less certainty because of alternate alignment possibilities, we have discovered a putative deletion in *PLCB4* that supports Laurasiatheria (Fig. 4.2).

Given the monophyly of Xenarthra, Afrotheria, and Boreoeutheria, there are only three possible locations for the root of the placental tree. The first is between Xenarthra

Table 4.1 Bootstrap percentages and posterior probabilities for the major clades of placental mammals

Method	Data Set	Reference	Clade				
			Xenarthra	Afrotheria	Euarchontoglires	Laurasiatheria	Boreoeutheria
ML ^a	<i>BRCA1</i> (2,947 bp)	Madsen et al. (2001)	100, 100	100, 100	100, 100	100, 100	100, 100
ML ^a	6 gene concatenation (5,708 bp)	Madsen et al. (2001)	Not applicable	100, 100	44, 66	99, 99	45, 64
ML	18 gene concatenation (9,779 bp)	Murphy et al. (2001a)	100	99	85	99	79
ML	22 gene concatenation (16,397 bp)	Murphy et al. (2001b)	100	100	100	100	100
ML	3 gene concatenation (4,350 bp)	Delsuc et al. (2002)	100	100	98	100	98
ML	<i>APOB</i> (1,342 bp)	Amrine-Madsen et al. (2003)	98	77	100	100	94
ML	23 gene concatenation (17,736 bp)	Amrine-Madsen et al. (2003)	100	100	100	100	100
Bayesian	22 gene concatenation (16,397 bp)	Murphy et al. (2001b)	1.00	1.00	1.00	1.00	1.00
Bayesian	3 gene concatenation (4,350 bp)	Delsuc et al. (2002)	1.00	1.00	1.00	1.00	1.00
Bayesian	<i>APOB</i> (1,342 bp)	Amrine-Madsen et al. (2003)	1.00	1.00	1.00	1.00	1.00
Bayesian	23 gene concatenation (17,736 bp)	Amrine-Madsen et al. (2003)	1.00	1.00	1.00	1.00	1.00
Bayesian	Mt tRNA + rRNA genes (3,571 bp)	Hudlot et al. (2003)	1.00	1.00	1.00	0.96	0.96
Bayesian	Concatenation of UTRs from 4 genes (1,762 bp)	Springer et al. (in press)	1.00	1.00	1.00	1.00	1.00
Bayesian	Concatenation of protein-coding segments from 15 genes (12,988 bp)	Springer et al. (in press)	1.00	1.00	1.00	1.00	1.00

^aDuplicate maximum likelihood (ML) values in cells across these rows are for analyses without an allowance for rate-heterogeneity (first value in double-valued clade column entries) and with a gamma distribution of rates (second value).

<i>Didelphis</i>	CATGGAGAATAGAT--GAGTTC-CACATTTTCAGTTTTAACATTTT
<i>Macropus</i>	CATGGAGAACACGTAAGAGTTA-GATATTTTCAGTTTTAACATTTT
<i>Choloepus</i>	CACAGAGACTTAGAATGA-TAA-CATAC-TCCTTTTGAGCATTT-
<i>Amblysomus</i>	CATAGAGACTTGGAAATGACTTA-CATGC-TTCTATTTAACATTTT
<i>Trichechus</i>	CATAGACTTGGAAATGACTTA-CATAT-TTCTGTTTAACTTTC
<i>Orycteropus</i>	CATAGAGACTTGGAAATGACTTA-CATA--TTCTATTTAACATTTT
<i>Tamias</i>	CACAAAGACGTGGAATGAC--A-CATAC-TTCTATTTATCAGTTT
<i>Mus</i>	CACATGGACTGGGGATGACCAAACGCCTCTTATATTTAACAAATTT
<i>Cavia</i>	CACAGAGACTGGGGATGACTTA-TGTAC-TTCGATTTAACGGTTC
<i>Sylvilagus</i>	CGGAGAGACTTGTA-TGACCTA-CGTAC-ATATCTTTACCAGTTG
<i>Cynocephalus</i>	CACAGAGACTTGGGATGACTTA-CATAC-TTCAGTTTAACTTTC
<i>Tupaia</i>	CACAGCGACATGGAACAATTTA-TATGC-TTCTCTTTAGCAGTTT
<i>Homo</i>	CAGAGAGACTTGGAAATGTCTGA-CTGAC-TTCTATTTAACAGCTT
<i>Erinaceus</i>	CACAGAAAC-----TTA-CATAC-TTCTATTTAACATTTT
<i>Sorex</i>	CACCGAAAC-----GTA-CATAC-TTCTATTTAATGTTTT
<i>Artibeus</i>	CACAGA-C-----TAA-CATGC-TTCTACTTCANGT---
<i>Rousettus</i>	CACAGA-T-----TTA-CATACCTTTTGTTCACATTTT
<i>Megaptera</i>	CACAGAGAC-----TTA-CGTAC-TTCTCTTAAATGTTTT
<i>Hippopotamus</i>	CACAGAGAC-----TTA-CGTAC-TTCTCTTAAACATTTT
<i>Tragelaphus</i>	CACAGAGAT-----GTAC-TTCTCTTAAACATTTCT
<i>Equus</i>	CACAGAGAT-----TTA-----ACCTTTG
<i>Ceratotherium</i>	CACAGAGAT-----TTA-CATAC-TTCTCTTTAACATCTT
<i>Tapirus</i>	CACAGAGAT-----TTA-CATAC-TTCTCTTTAACATTTT
<i>Felis</i>	CACCGAGAC-----TTA-CATAT-TTCTATTTAACATTTT
<i>Manis</i>	CACAGAGAC-----TTA-CATAC-TTCTACTTAACTTTC

Fig. 4.2. Putative deletion for Laurasiatheria in the 3' UTR of the *PLCB4* gene. Representative sequences are from Murphy et al. (2001a,b). The sequence for *Homo* corresponds to positions 165–207 of GenBank sequence AY011788.

and Epitheria, which is consistent with some morphological studies (McKenna, 1975). The second possibility, which is favored by several molecular studies (Murphy et al., 2001b; Amrine-Madsen et al., 2003), is between Afrotheria and other placental mammals (i.e., Notolegia; Springer et al., in press). The final possibility is between Atlantogenata (i.e., Xenarthra + Afrotheria; Waddell et al., 1999) and Boreoeutheria. Swofford-Olsen-Waddell-Hillis (SOWH) tests (Swofford et al., 1996) reported by Murphy et al. (2001b) rejected the first and third possibilities in favor of a rooting between Afrotheria and other placentals. However, Buckley (2002) has shown that SOWH tests can give overconfidence in a topology when the assumptions of a model of sequence evolution are violated. Given the small likelihood differences that separate these three rooting positions, resolving the trifurcation at the base of Placentalia will require additional data, including more genes and improved taxon sampling to mitigate against long branches. Delsuc et al. (2002) have shown that locating the placental root is sensitive to taxon sampling among the basal groups. Improved models of sequence evolution may also prove important in resolving the placental root. Other a priori positions for the placental root, including those on the erinaceomorph and murid edges, are firmly rejected by both SOWH and Kishino and Hasegawa (KH; 1989) tests (Sally et al., 2001). The KH test is more conservative than the SOWH test in rejecting alternative hypotheses.

RELATIONSHIPS WITHIN THE MAJOR CLADES

Within Xenarthra, molecular analyses suggest an association of anteaters and sloths, to the exclusion of armadillos (see Fig. 4.1). This result agrees with morphological evidence

and with a recent molecular study that included most living xenarthran genera (Delsuc et al., 2002).

The basal split in Afrotheria is between Fossoromorpha (i.e., aardvarks, elephant shrews, afrosoricidans; Springer et al., in press) and Paenungulata, with elephant shrews and afrosoricidans clustering together in the former group. The paenungulate trifurcation is not satisfactorily resolved by our data. Other molecular studies also attest to the difficulty of resolving relationships within Paenungulata (Amrine and Springer, 1999). In contrast, the total evidence of Asher et al. (2003), which combines molecular and morphological data, finds strong support for Tethytheria. Arguing against Tethytheria is a newly discovered AfroSINE that hyracoids and sirenians share to the exclusion of proboscideans (Nishihara et al., 2003), consistent with the maximum likelihood and Bayesian results of Murphy et al. (2001b).

The basal split within Laurasiatheria is between Eulipotyphla and other taxa (i.e., Variamana = Chiroptera + Perissodactyla + Cetartiodactyla + Pholidota + Carnivora; Springer et al., in press). The name Variamana reflects the highly divergent manus that occurs in members of this group. Within Variamana, there is some support for a monophyletic Fereuungulata (i.e., Perissodactyla + Cetartiodactyla + Pholidota + Carnivora; Waddell et al., 1999). Within Fereuungulata, an association of Carnivora and Pholidota is strongly supported by primary sequence analyses (see Fig. 4.1) and a 363 bp deletion in the *apolipoprotein B* alignment of Amrine-Madsen et al. (2003). Morphological evidence for this clade includes an osseous tentorium (Shoshani and McKenna, 1998). Within Chiroptera, microbats are paraphyletic and Yinpterochiroptera (i.e., megabats + non-nycterid rhinolophoids; Springer et al., 2001b; Teeling et al., 2002) is supported.

In contrast to some mitochondrial studies (Árnason et al., 2002; Hudelot et al., 2003), which support an association of

Scandentia and Lagomorpha, our data divide Euarchontoglires into Glires and Euarchonta. Molecular support for Glires adds to morphological evidence (e.g., Meng et al., 2003) favoring this hypothesis (e.g., Asher et al., 2003). Within Euarchontoglires, chromosome data also support Glires monophyly (Murphy et al., 2001c; Stanyon et al., 2003). Similarly, strong molecular support for rodent monophyly corroborates morphological evidence for this clade (Luckett and Hartenberger, 1993). Euarchonta includes Primates, Dermoptera, and Scandentia and is similar to the morphological Archonta hypothesis but with bats now excluded. With the removal of bats from Archonta, presumed morphological synapomorphies for Volitantia (Simmons and Quinn, 1994; Simmons and Geisler, 1998) must now be viewed as homoplastic in bats and flying lemurs. At the same time, ad hoc explanations for the absence of archontan tarsal specializations in bats (e.g., Szalay and Drawhorn, 1980) are no longer necessary.

LONG BRANCHES AND THE PATHOLOGIC BEHAVIOR OF PARSIMONY

Long branch attraction occurs when convergent changes on long branches outnumber synapomorphic changes on shorter, internal branches. This problem can be most acute when outgroup sequences are highly divergent relative to ingroup sequences (Swofford et al., 1996). Felsenstein (1978) demonstrated that parsimony is more susceptible to long branch attraction than is maximum likelihood. As mentioned above, some molecular analyses root the placental tree within Rodentia or between representative rodents and other taxa. Rooting within Rodentia is common in studies with limited taxon sampling, especially with parsimony, and this result is a candidate for long branch attraction. An example is provided by one of our own data sets—*BRCA1*. Fig. 4.3 shows an unrooted parsimony tree based on the *BRCA1* data set of Madsen et al. (2001). It is evident from this tree that long branches include terminal branches leading to *Hystrix*, *Elephantulus*, *Erinaceus*, *Lepus*, *Rhynchocyon*, *Scalopus*, *Tonatia*, and *Tupaia*, and internal branches leading to hyraxes, murids, and tenrecids. In analyses that included a marsupial outgroup (*Vombatus*), the most parsimonious trees (four at 10,867 steps) all rooted on the branch leading to *Hystrix*, which renders Rodentia, Glires, and Euarchontoglires paraphyletic. When *Hystrix* is removed from the analysis, the most parsimonious trees (four at 10,376 steps) root on the murid branch. Again, Rodentia, Glires, and Euarchontoglires are all rendered paraphyletic. Continued pruning of the tree, now with deletion of both murids (*Mus*, *Rattus*) from the analysis, results in four trees (9,965 steps), all of which root on the internal branch leading to the tenrecids (*Echinops*, *Tenrec*). This renders Rodentia, Glires, and Euarchontoglires monophyletic, but Afrotheria paraphyletic. Subsequent deletion of the tenrecids results in a single most parsimonious tree (8,958 steps) that roots on

Tupaia. When *Tupaia* is subsequently deleted, two most parsimonious trees (8,664 steps) are recovered, both of which root on *Erinaceus*. Deletion of *Erinaceus* results in two most parsimonious trees (8,304 steps) that root on *Scalopus*. Finally, deletion of *Scalopus* results in rooting the placental tree on *Tonatia* (two trees at 8,004 steps), rendering Chiroptera paraphyletic and suggesting that the ancestral placental mammal was capable of powered flight! Clearly, the placental root is highly unstable, sensitive to taxon sampling, and jumps from one long branch to another in parsimony analyses with the *BRCA1* data set of Madsen et al. (2001). Parsimony analyses of the Murphy et al. (2001a) data set produced similar rooting artifacts that were not observed with other tree building methodologies. This behavior is a hallmark feature of long branch attraction. Asher et al. (2003) performed analyses with a molecular data set that included 49 extant taxa and 22 genes from Murphy et al. (2001b). As noted above, the resulting root was between murid rodents and other taxa in six of 12 analyses. In the remaining analyses, the root was attracted to *Erinaceus* or elephant shrews. Murids, hedgehogs, and elephant shrews derive from three of the four major clades of placental mammals. In addition, these taxa consistently exhibit long branches on molecular topologies (e.g., Fig. 4.1), which may explain the attraction of the marsupial outgroup to these taxa in parsimony analyses. In view of these observations, as well as statistical tests that corroborate the occurrence of long branch attraction in parsimony analyses of such gene segments as *BRCA1* (Madsen et al., 2001; Scally et al., 2001), we dismiss these anomalous results as phylogenetic artifacts.

In contrast, maximum likelihood and Bayesian analyses with taxonomically diverse data sets and multiple nuclear genes consistently place the placental root between Xenarthra and Epitheria, Afrotheria and Notolegia, or Atlantogenata and Boreoeutheria (Madsen et al., 2001; Murphy et al., 2001a,b; Scally et al., 2001; Delsuc et al., 2002; Huchon et al., 2002; Amrine-Madsen et al., 2003; Springer et al., in press). Waddell et al. (2001) have shown that posterior probabilities of clade support may be inflated in some cases, but bootstrap analyses with maximum likelihood also constrain the root of the placental tree to one of these three locations. Furthermore, rare genomic changes are incompatible with rooting the placental tree within Rodentia, Glires, Euarchontoglires, Laurasiatheria (contingent on the *PLCB4* deletion), or Afrotheria.

TIMESCALE FOR PLACENTAL MAMMAL EVOLUTION

A timescale for placental diversification is of considerable importance for unraveling the early biogeographic history of this taxonomic group. Archibald and Deutschman (2001) reviewed three competing models for placental diversification. The Explosive Model postulates that both inter- and intraordinal divergences occurred after the K/T boundary.

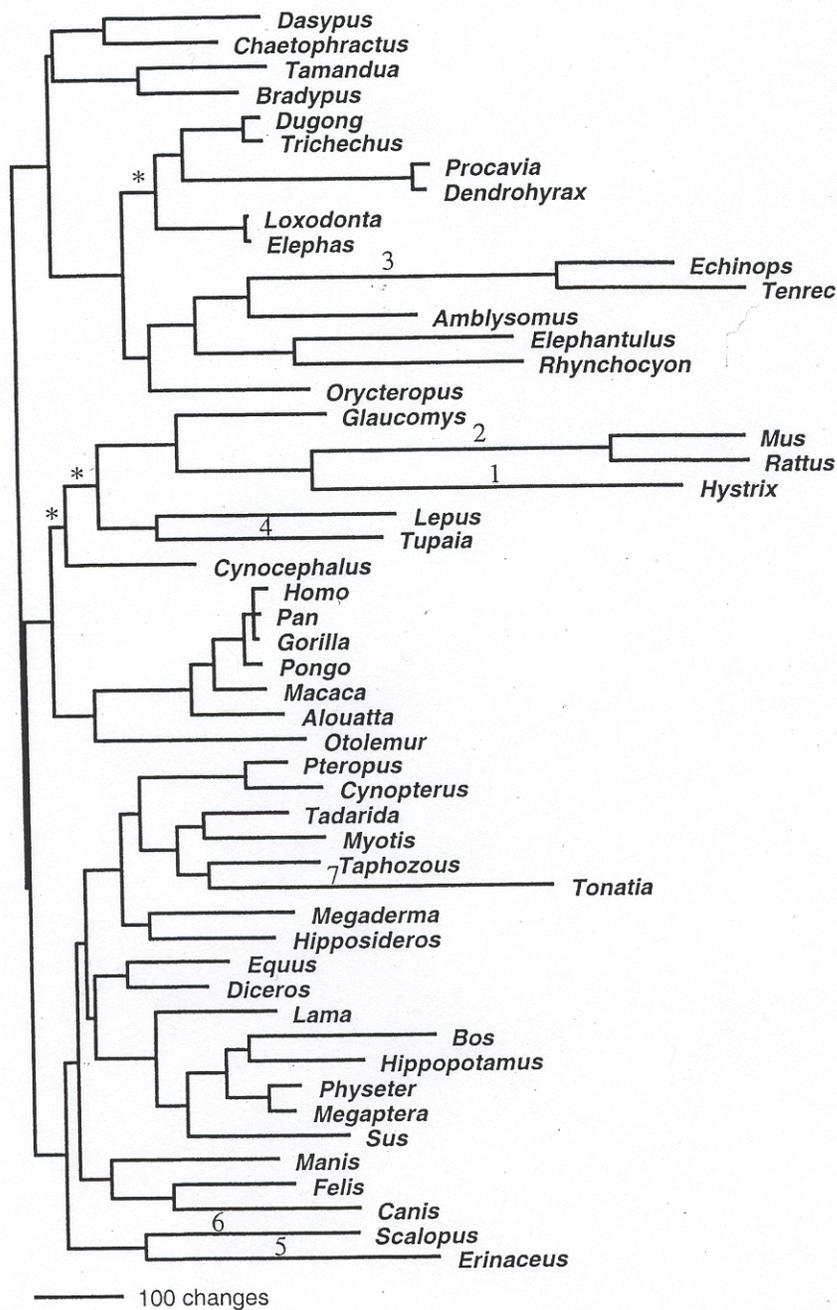


Fig. 4.3. One of four most parsimonious unrooted trees (accelerated transformation branch lengths) for the BRCA1 data of Madsen et al. (2001). Asterisks denote branches that collapse on the strict consensus tree. The basal split is arbitrarily shown between Atlantogenata and Boreoeutheria. When the outgroup taxon *Vombatus* is included in the analysis, the placental root occurs on the terminal branch leading to *Hystrix*, which is labeled 1 in the figure. Numbers 2-7 correspond to successive rooting positions as placental taxa are sequentially deleted from maximum parsimony analyses.

This model is preferred by some paleontologists (Gingerich, 1977; Carroll, 1997; Benton, 1999; Foote et al., 1999). At the other extreme, the Short Fuse Model postulates inter- and some intraordinal cladogenesis well back in the Cretaceous, including splits within Rodentia as old as 112-125 million years (Janke et al., 1997; Springer, 1997; Kumar and Hedges, 1998; Huelsenbeck et al., 2000). The Long Fuse Model is intermediate between these hypotheses and postulates Cretaceous interordinal and Cenozoic intraordinal divergences, although with an allowance for limited intraordinal diversification near the end of the Cretaceous (e.g., Eulipotyphla). In their analysis of the placental record, Archibald and Deutschman (2001) rejected the Short Fuse Model but could not discriminate between the Explosive and Long

Fuse Models. Some cladistic analyses support the Long Fuse Model by including 85- to 90-million-year-old zalambdalestids and zhelestids in crown group Eutheria (Archibald et al., 2001).

Virtually all molecular studies agree that interordinal diversification began well back in the Cretaceous (Springer, 1997; Kumar and Hedges, 1998; Penny et al., 1999; Eizirik et al., 2001). In our own recent work, we have employed both linearized trees and quartet dating and have estimated the base of Placentalia at approximately 103 million years (Murphy et al., 2001b). Our recent analysis using the relaxed clock method of Thorne et al. (1998) and Kishino et al. (2001) recovered dates in the range of 97-109 million years for the base of Placentalia and is generally consistent with

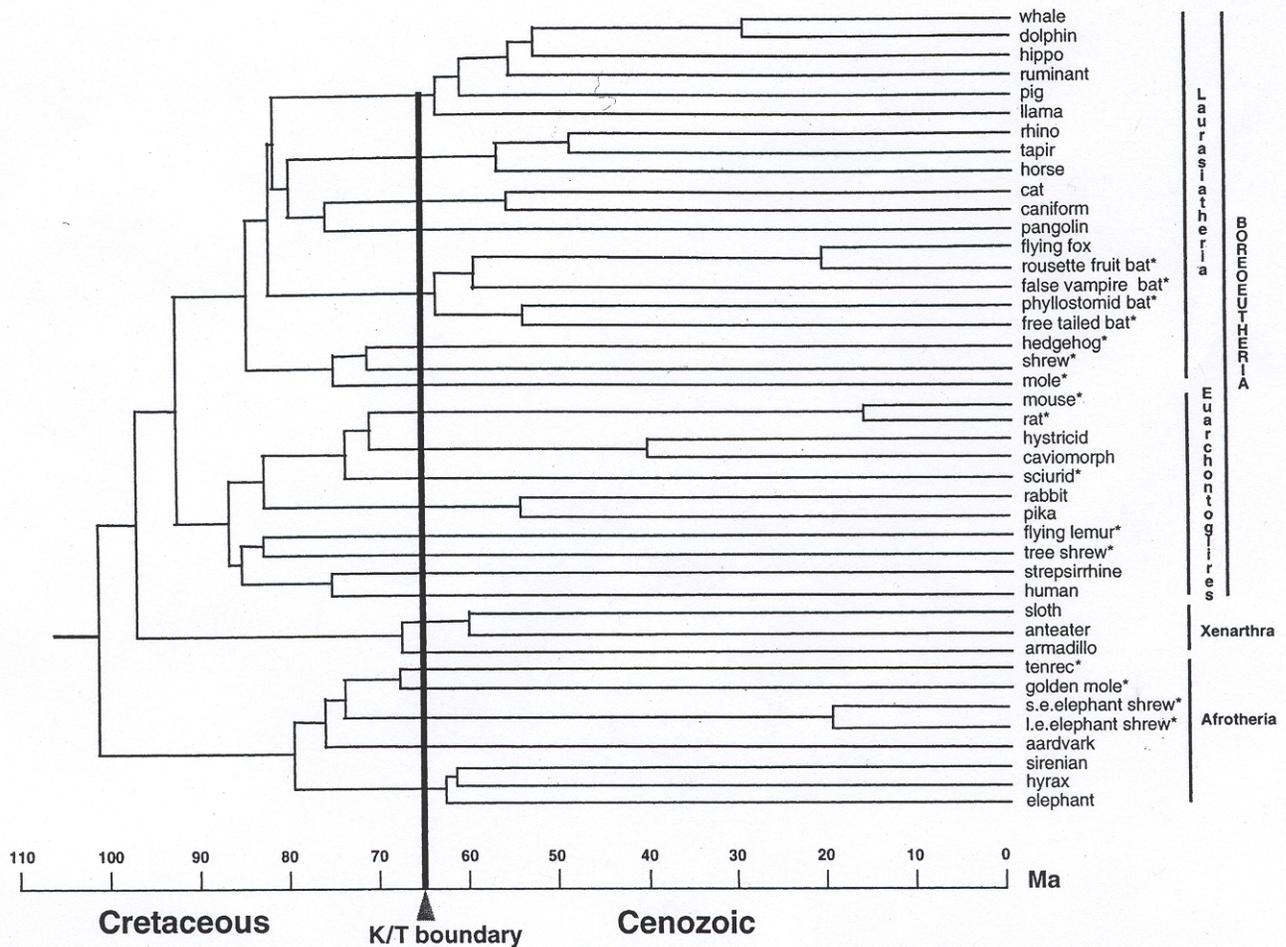


Fig. 4.4. Molecular timescale for the diversification of placental orders, based on the Murphy et al. (2001b) data set (PNOG segment excluded) and the *multidivtime* program of Thorne and Kishino (2002). Each of 18 different gene segments (AZAB, ADORA, ADRB2, APP, ATP7A, BDNF, BMI1, BRCA1, CNR1, CREM, EDG1, IRBP, PLCB4, RAG1, RAG2, TYR, vWF, ZFX) was allowed to have its own parameters under the F84 model of sequence evolution, with an allowance for a gamma distribution of nucleotide substitution rates among sites. We used 13 fossil constraints following Springer et al. (2003). It was necessary to exclude PNOG because marsupial sequences are lacking for this segment. Asterisks denote placental taxa included in the "K/T body size" taxon set of Springer et al. (2003), which was used to test the hypothesis that molecular estimates of Cretaceous divergence times are an artifact of increased body size subsequent to the K/T boundary. In those analyses, Springer et al. (2003) found that interordinal divergences remained in the Cretaceous.

the Long Fuse Model of diversification (Springer et al., 2003). Similar results were obtained by Douady and Douzery (2003). Although the original implementation of the Thorne/Kishino method did not allow for distinct process partitions of heterogeneous molecular data, the multidivtime program of Thorne and Kishino (2002) allows different models of sequence evolution for individual gene segments. We employed this methodology with the Murphy et al. (2001b) data set and recovered divergence estimates that were generally within one to two million years of the values reported in Springer et al. (2003). These results are shown in Fig. 4.4 and Table 4.2. Ninety-five percent credibility intervals for all of the nodes in Figure 4.4 are given in Table 4.2.

We have further suggested that the separation of Xenarthra and Afrotheria at approximately 100–110 million years ago may have resulted from the vicariant separation of South America and Africa at 100–120 million years ago (Smith et al., 1994; Hay et al., 1999). This hypothesis ascribes an important role for both plate tectonic events and Gondwana in the early history of placental mammals.

Following the Murphy et al. (2001b) phylogeny, which roots between Afrotheria and other placentals, we suggested the possibility of a Gondwanan origin for Placentalia. According to this model, the basal split between Afrotheria and Notolegia corresponds to the vicariant event that separated South America and Africa. This hypothesis also requires subsequent dispersal to Laurasia, which had separated from Gondwana by 160–170 million years ago (Smith et al., 1994). In contrast, Archibald (2003) suggested that the agreement of molecular dates for the Xenarthra-Afrotheria split and geologic dates for the South America-Africa separation is mere coincidence, and that Xenarthra and Afrotheria represent separate dispersals to these continents from the Northern Hemisphere. Archibald (2003) further argued that a Laurasian origin for Placentalia, with subsequent dispersals to South America and Africa, is more parsimonious than a Gondwanan origin. Such exercises are sensitive to how higher-level taxa are coded for their place of origin. In contrast to Archibald (2003), we coded Xenarthra and Afrotheria as Gondwanan, and Laurasiatheria and Euarchontoglires

Table 4.2 Bayesian estimates of divergence dates for placental nodes

Node	Date (My)	95% Credibility Intervals
Sirenian to Hyrax	60.8	56.3, 63.9
Base of Paenungulata	62.9	58.9, 64.9
<i>Macroselides</i> to <i>Elephantulus</i>	18.2	15.0, 21.9
Base of Afrosoricida	67.9	62.2, 73.2
Afrosoricida to Macroscelidea	73.9	68.7, 78.7
Base of Fossoromorpha	75.6	70.6, 80.3
Base of Afrotheria	78.8	74.0, 82.9
Strepsirrhine to human	75.2	70.3, 80.0
Dermoptera to Scandentia	83.1	78.5, 88.0
Base of Euarchonta	85.2	80.9, 89.8
Rabbit to pika	52.9	47.9, 58.0
Hystricid to Caviomorph	40.1	35.5, 44.9
Mouse to rat	16.7	14.2, 19.6
Mouse-Rat to Hystricid-Caviomorph	71.6	66.8, 76.7
Base of Rodentia	74.9	70.3, 79.8
Base of Glires	82.3	77.8, 87.1
Base of Euarchontoglires	86.5	82.4, 91.0
Cat to Caniform	53.5	50.3, 57.7
Base of Ostentoria	74.6	71.3, 78.1
Rhino to tapir	48.3	44.6, 52.0
Base of Perissodactyla	56.1	54.1, 57.9
Ostentoria to Perissodactyla	77.9	75.1, 81.0
Mysticete to Odontocete	27.3	24.0, 30.6
Hippo to Cetacea	52.3	52.0, 53.3
Hippo-Cetacea to ruminant	55.2	53.5, 56.9
Pig to hippo-Cetacea-ruminant	59.7	57.6, 61.9
Base of Cetartiodactyla	62.3	59.9, 64.6
Base of Fereuungulata	79.4	76.5, 82.5
Flying fox to Rousette fruit bat	19.7	16.3, 23.1
Base of Yinpterochiroptera	59.5	58.2, 60.0
Phyllostomid to free-tailed bat	53.7	50.2, 57.4
Base of Chiroptera	63.1	61.2, 65.3
Base of Variamana	80.3	77.3, 83.4
Hedgehog to shrew	70.6	66.0, 75.4
Hedgehog-shrew to mole	75.6	71.7, 79.6
Base of Laurasiatheria	83.1	79.7, 86.8
Base of Boreoeutheria	91.8	87.7, 96.2
Sloth to anteater	59.0	53.6, 64.9
Base of Xenarthra	66.8	61.6, 72.4
Notolegia to Afrotheria	96.9	92.3, 101.8
Base of Placentalia	101.3	96.2, 106.5

Note: See also Fig. 4.4.

as Laurasian (Madsen et al., 2001). If we ignore presumed stem eutherian outgroups to Placentalia, the most recent common ancestor of placental mammals is reconstructed as having resided in Gondwana, with a single step representing dispersal to Laurasia (Fig. 4.5A). One of the other viable positions for the placental root, between Xenarthra and Epitheria, also recovers a Gondwanan placental root (Fig. 4.5B). The final alternative for the root, between Atlantogenata and Boreoeutheria, is equivocal for the geographic origin of Placentalia, as it allows for either Laurasia or Gondwana (Fig. 4.5C). However, such a root would still imply a strong biogeographic component for the early cladogenesis of Placentalia, suggesting an initial split be-

tween Gondwanan and Laurasian clades, followed in the former group by the divergence between Afrotheria (African) and Xenarthra (South American). In reconstructions that recognize the Laurasian fossil *Eomaia* as the oldest eutherian mammal (Ji et al., 2002), two of three reconstructions (Xenarthra-Epitheria, Afrotheria-Notolegia) are equivocal for the placental root (Figs. 4.5D,E) and the third (Atlantogenata-Boreoeutheria) favors a Laurasian origin (Fig. 4.5F). An additional complication for these reconstructions is the possibility that the oldest stem eutherians are from Gondwana rather than from Laurasia (Woodburne et al., 2003).

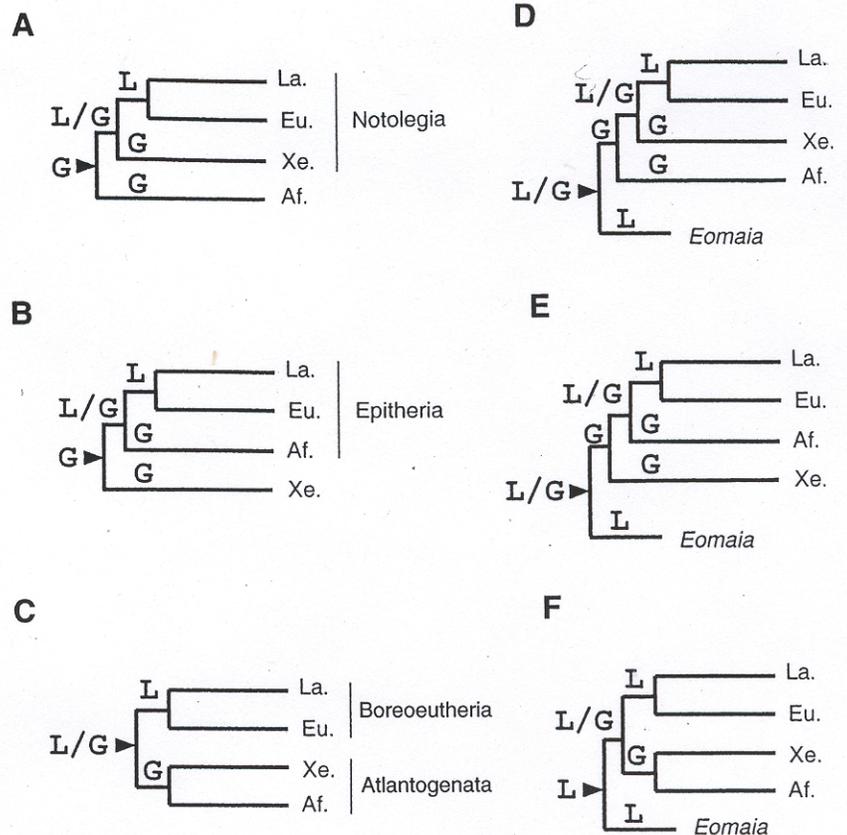
PROSPECTUS FOR FUTURE STUDIES

We stand on the threshold of a well-resolved molecular phylogeny for the extant orders of placental mammals (see Fig. 4.1). The major groups have been defined, and only local rearrangements remain to be resolved. Of these, resolving the trifurcation at the base of Placentalia is most significant and merits attention and resources. Beyond the living eutherian orders, the challenge of integrating molecular and morphological data (fossils included) into a comprehensive and accurate phylogeny for all eutherian orders is formidable. The total evidence analysis by Asher et al. (2003) is the first step in this direction, but, in our view, suffers from the methodological limitations of parsimony. Other methodological approaches should also be explored, including molecular scaffolds (Springer et al., 2001b) and Bayesian methods (Ronquist and Huelsenbeck, 2003) that allow molecular and morphological data partitions to have their own models of evolution.

SUMMARY

Maximum likelihood and Bayesian analyses of DNA sequences, principally derived from nuclear genes, provide a well-resolved phylogeny for the orders of placental mammals, with only local rearrangements resisting resolution. Placentalia is divided into four major groups: Afrotheria (Afrosoricida, Hyracoidea, Macroscelidea, Proboscidea, Sirenia, and Tubulidentata), Xenarthra, Laurasiatheria (Carnivora, Cetartiodactyla, Chiroptera, Eulipotyphla, Perissodactyla, and Pholidota), and Euarchontoglires (Dermoptera, Lagomorpha, Primates, Rodentia, and Scandentia). Of these, Laurasiatheria and Euarchontoglires are sister taxa that together make up Boreoeutheria. Rare genomic events corroborate Xenarthra, Afrotheria, Euarchontoglires, and possibly, Laurasiatheria. Molecular estimates of divergence times are generally consistent with the Long Fuse Model of diversification and place the root of the placental tree in the range of 97–109 million years. There are only three viable positions for this root: (1) between Xenarthra and Epitheria; (2) between Afrotheria and Notolegia; or (3) between Atlantogenata and Boreoeutheria. Each of these possibilities is consistent with a strong biogeographic component for

Fig. 4.5. Biogeographic reconstructions of the origin of Placentalia, as inferred from alternative rooting schemes given the relationships of extant major eutherian clades. Abbreviations: G., Gondwana; L., Laurasia; La., Laurasiatheria; Eu., Euarchontoglires; Xe., Xenarthra; Af., Afrotheria. Groups in (D), (E), and (F) are equivalent to those in (A), (B), and (C), respectively. The letters L and G on branches indicate the most parsimonious reconstruction of the geographic location at the origin of that lineage. Arrowhead indicates inferred geographic location at the placental root. Schemes in (D)–(F) include the fossil eutherian *Eomaia*.



the early history of Placentalia. Beyond the living eutherian orders, a major challenge ahead is integrating neontological and paleontological data into a comprehensive and robust phylogeny for all eutherian orders.

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REFERENCES

- Amrine, H. M., and M. S. Springer. 1999. Maximum likelihood analysis of the tethythere hypothesis based on a multigene data set and a comparison of different models of sequence evolution. *Journal of Mammalian Evolution* 6: 161–176.
- Amrine-Madsen, H., K.-P. Koepfli, R. K. Wayne, and M. S. Springer. 2003. A new phylogenetic marker, *apolipoprotein B*, provides compelling evidence for eutherian relationships. *Molecular Phylogenetics and Evolution* 28: 225–240.
- Archibald, J. D. 2003. Timing and biogeography of the eutherian radiation: Fossils and molecules compared. *Molecular Phylogenetics and Evolution* 28: 350–359.
- Archibald, J. D., A. O. Averianov, and E. G. Ekdale. 2001. Late Cretaceous relatives of rabbits, rodents, and other extant eutherian mammals. *Nature* 414: 62–65.
- Archibald, J. D., and D. Deutschman. 2001. Quantitative analysis of the timing of origin of extant placental orders. *Journal of Mammalian Evolution* 8: 107–124.
- Árnason, Ú., J. A. Adegoke, K. Bodin, E. W. Born, Y. B. Esa, A. Gullberg, M. Nilsson, R. V. Short, X. Xu, and A. Janke. 2002. Mammalian mitogenomic relationships and the root of the eutherian tree. *Proceedings of the National Academy of Sciences USA* 99: 8151–8156.
- Asher, R. J. 1999. A morphological basis for assessing the phylogeny of the “Tenrecoidea” (Mammalia, Lipotyphla). *Cladistics* 15: 231–252.
- Asher, R. J., M. J. Novacek, and J. H. Geisler. 2003. Relationships of endemic African mammals and their fossil relatives based on morphological and molecular evidence. *Journal of Mammalian Evolution* 10: 131–194.
- Benton, M. J. 1999. Early origins of modern birds and mammals: Molecules vs. morphology. *BioEssays* 21: 1043–1051.
- Buckley, T. R. 2002. Model misspecification and probabilistic tests of topology: Evidence from empirical data sets. *Systematic Biology* 51: 509–523.
- Carroll, R. L. 1997. *Patterns and Processes of Vertebrate Evolution*. Cambridge University Press, Cambridge.
- de Jong, W. W., J. A. M. Leunissen, and G. J. Wistow. 1993. Eye lens crystallins and the phylogeny of placental orders: Evidence for a macroscelidid-paenungulate clade? pp. 5–12 in F. S. Szalay, M. J. Novacek, and M. C. McKenna (eds.), *Mammal Phylogeny*. Volume 2. Placentals. Springer-Verlag, New York.
- de Jong, W. W., M. A. M. van Dijk, C. Poux, G. Kappe, T. van Rheede, and O. Madsen. 2003. Indels in protein-coding sequences of Euarchontoglires constrain the rooting of the

- eutherian tree. *Molecular Phylogenetics and Evolution* 28: 328–340.
- de Jong, W. W., A. Zweers, and M. Goodman. 1981. Relationship of aardvark to elephants, hyraxes and sea cows from alpha-crystallin sequences. *Nature* 292: 538–540.
- Delsuc, F., M. Scally, O. Madsen, M. J. Stanhope, W. W. de Jong, F. M. Catzeflis, M. S. Springer, and E. J. P. Douzery. 2002. Molecular phylogeny of living xenarthrans and the impact of character and taxon sampling on the placental tree rooting. *Molecular Biology and Evolution* 19: 1656–1671.
- Douady, C. J., and E. J. P. Douzery. 2003. Molecular estimation of eulipotyphlan divergence times and the evolution of "Insectivora." *Molecular Phylogenetics and Evolution* 28: 285–296.
- Eizirik, E., W. J. Murphy, and S. J. O'Brien. 2001. Molecular dating and biogeography of the early placental mammals. *Journal of Heredity* 92: 212–219.
- Felsenstein, J. 1978. Cases in which parsimony and compatibility methods will be positively misleading. *Systematic Zoology* 27: 401–410.
- Foote, M., J. P. Hunter, C. M. Janis, and J. J. Sepkoski, Jr. 1999. Evolutionary and preservational constraints on origins of biologic groups: Divergence times of eutherian mammals. *Science* 283: 1310–1314.
- Froenicke L., J. Wienberg, G. Stone, L. Adams, and R. Stanyon. 2003. Towards the delineation of the ancestral eutherian genome organization: Comparative genome maps of human and the African elephant (*Loxodonta africana*) generated by chromosome painting. *Proceedings of the Royal Society of London B* 270: 1331–1340.
- Gingerich, P. D. 1977. Patterns of evolution in the mammalian fossil record; pp. 469–500 in A. Hallam (ed.), *Patterns of Evolution as Illustrated by the Fossil Record*. Elsevier, Amsterdam.
- Goodman, M. 1975. Protein sequence and immunological specificity: Their role in phylogenetic studies of primates; pp. 219–248 in W. P. Luckett and F. S. Szalay (eds.), *Phylogeny of the Primates: A Multidisciplinary Approach*. Plenum, New York and London.
- Hay, W. W., R. M. DeConto, C. N. Wold, K. M. Wilson, S. Voigt, M. Schulz, A. R. Wold, W.-C. Dullo, A. B. Ronov, A. N. Balukhovskiy, and E. Soding. 1999. Alternative global Cretaceous paleogeography; pp. 1–48 in E. Barrera and C. C. Johnson (eds.), *Evolution of the Cretaceous Ocean-Climate System. Special Paper 332*. Geological Society of America, Boulder, Colorado.
- Huchon, D., O. Madsen, M. J. B. Sibbald, K. Ament, M. J. Stanhope, F. Catzeflis, W. W. de Jong, and E. J. P. Douzery. 2002. Rodent phylogeny and a timescale for the evolution of Glires: Evidence from an extensive taxon sampling using three nuclear genes. *Molecular Biology and Evolution* 19: 1053–1065.
- Hudelot, C., V. Gowri-Shankar, H. Jow, M. Rattray, and P. G. Higgs. 2003. RNA-based phylogenetic methods: Application to mammalian mitochondrial RNA sequences. *Molecular Phylogenetics and Evolution* 28: 241–252.
- Huelsenbeck, J. P., B. Larget, and D. Swofford. 2000. A compound process for relaxing the molecular clock. *Genetics* 154: 1879–1892.
- Janke, A., X. Xu, and Ú. Arnason. 1997. The complete mitochondrial genome of the wallaroo (*Macropus robustus*) and the phylogenetic relationship among Monotremata, Marsupialia, and Eutheria. *Proceedings of the National Academy of Sciences USA* 94: 1276–1281.
- Ji, Q., Z.-X. Luo, C. X. Yuan, J. R. Wible, J. P. Zhang, and J. A. Georgi. 2002. The earliest known eutherian mammal. *Nature* 416: 816–822.
- Kishino, H., and M. Hasegawa. 1989. Evaluation of the maximum likelihood estimate of the evolutionary tree topologies from DNA sequence data, and the branching order in Hominoidea. *Journal of Molecular Evolution* 29: 170–179.
- Kishino, H., J. L. Thorne, and W. J. Bruno. 2001. Performance of a divergence time estimation method under a probabilistic model of rate evolution. *Molecular Biology and Evolution* 18: 352–361.
- Kleinschmidt, T., J. Czelusniak, M. Goodman, and G. Braunitzer. 1986. Paenungulata: A comparison of the hemoglobin sequences from elephant, hyrax, and manatee. *Molecular Biology and Evolution* 3: 427–435.
- Kumar, S., and S. B. Hedges. 1998. A molecular timescale for vertebrate evolution. *Nature* 392: 917–920.
- Lavergne, A., E. Douzery, T. Stichler, F. M. Catzeflis, and M. S. Springer. 1996. Interordinal mammalian relationships: Evidence for paenungulate monophyly is provided by complete mitochondrial 12S rRNA sequences. *Molecular Phylogenetics and Evolution* 6: 245–258.
- Lin, Y.-H., P. A. McLenachan, A. R. Gore, M. J. Phillips, R. Ota, M. D. Hendy, and D. Penny. 2002. Four new mitochondrial genomes and the increased stability of evolutionary trees of mammals from improved taxon sampling. *Molecular Biology and Evolution* 19: 2060–2070.
- Luckett, W. P., and J.-L. Hartenberger. 1993. Monophyly or polyphyly of the order Rodentia: Possible conflict between morphological and molecular interpretations. *Journal of Mammalian Evolution* 1: 127–147.
- MacPhee, R. D. E., and M. J. Novacek. 1993. Definition and relationships of Lipotyphla; pp. 13–31 in F. S. Szalay, M. J. Novacek, and M. C. McKenna (eds.), *Mammal Phylogeny. Volume 2. Placentals*. Springer-Verlag, New York.
- Madsen, O., M. Scally, C. J. Douady, D. J. Kao, R. W. DeBry, R. Adkins, H. Amrine, M. J. Stanhope, W. W. de Jong, and M. S. Springer. 2001. Parallel adaptive radiations in two major clades of placental mammals. *Nature* 409: 610–614.
- McKenna, M. C. 1975. Toward a phylogenetic classification of the Mammalia; pp. 21–46 in W. P. Luckett and F. S. Szalay (eds.), *Phylogeny of the Primates: A Multidisciplinary Approach*. Plenum, New York and London.
- Meng, J., Y. Hu, and C. Li. 2003. The osteology of *Rhombomylus* (Mammalia, Glires): Implications for phylogeny and evolution of Glires. *Bulletin of the American Museum of Natural History* 275: 1–247.
- Misawa, K., and A. Janke. 2003. Revisiting the Glires concept—phylogenetic analysis of nuclear sequences. *Molecular Phylogenetics and Evolution* 28: 320–327.
- Miyamoto, M. M., and M. Goodman. 1986. Biomolecular systematics of eutherian mammals: Phylogenetic patterns and classification. *Systematic Zoology* 35: 230–240.
- Murphy, W. J., E. Eizirik, W. E. Johnson, Y. P. Zhang, O. A. Ryder, and S. J. O'Brien. 2001a. Molecular phylogenetics and the origins of placental mammals. *Nature* 409: 614–618.
- Murphy, W. J., E. Eizirik, S. J. O'Brien, O. Madsen, M. Scally, C. J. Douady, E. Teeling, O. A. Ryder, M. J. Stanhope, W. W. de Jong, and M. S. Springer. 2001b. Resolution of the early placental mammal radiation using Bayesian phylogenetics. *Science* 294: 2348–2351.

- Murphy, W. J., R. Stanyon, and S. J. O'Brien. 2001c. Evolution of mammalian genome organization inferred from comparative gene mapping. *Genome Biology* 2: 1-8.
- Nikaido, M., H. Nishihara, Y. Hukumoto, and N. Okada. 2003. Ancient SINEs from African endemic mammals. *Molecular Biology and Evolution* 20: 522-527.
- Nishihara, H., M. Nikaido, Y. Fukumoto, M. J. Stanhope, and N. Okada. 2003. Phylogenetic analysis among afrotherian mammals based on SINE insertions. *Society for Molecular Biology and Evolution Abstracts*, p. 84.
- Patterson, C. 1982. Morphological characters and homology; pp. 21-74 in K. A. Joysey and A. E. Friday (eds.), *Problems of Phylogenetic Reconstruction*. Systematics Association Special Volume 21. Academic Press, London and New York.
- Penny, D., M. Hasegawa, P. J. Waddell, and M. D. Hendy. 1999. Mammalian evolution: Timing and implications from using the logdeterminant transform for proteins of differing amino acid composition. *Systematic Biology* 48: 76-93.
- Porter, C. A., M. Goodman, and M. J. Stanhope. 1996. Evidence on mammalian phylogeny from sequences of exon 28 of the von Willebrand factor gene. *Molecular Phylogenetics and Evolution* 5: 89-101.
- Poux, C., T. Van Rheede, O. Madsen, and W. W. de Jong. 2002. Sequence gaps join mice and men: Phylogenetic evidence from deletions in two proteins. *Molecular Biology and Evolution* 19: 2035-2037.
- Ronquist, F., and J. P. Huelsenbeck. 2003. MRBAYES 3: Bayesian phylogenetic inference under mixed models. *Bioinformatics* 19: 1572-1574.
- Scally, M., O. Madsen, C. J. Douady, W. W. de Jong, M. J. Stanhope, and M. S. Springer. 2001. Molecular evidence for the major clades of placental mammals. *Journal of Mammalian Evolution* 8: 239-277.
- Shoshani, J. 1986. Mammalian phylogeny: Comparison of morphological and molecular results. *Molecular Biology and Evolution* 3: 222-242.
- Shoshani, J., M. Goodman, J. Czelusniak, and G. Braunitzer. 1985. A phylogeny of Rodentia and other eutherian orders: Parsimony analysis utilizing amino acid sequences of alpha and beta hemoglobin chains; pp. 191-210 in W. P. Luckett and J. L. Hartenberger (eds.), *Evolutionary Relationships among Rodents: A Multidisciplinary Analysis*. Plenum, New York.
- Shoshani, J., and M. C. McKenna. 1998. Higher taxonomic relationships among extant mammals based on morphology, with selected comparisons of results from molecular data. *Molecular Phylogenetics and Evolution* 9: 572-584.
- Simmons, N. B., and J. H. Geisler. 1998. Phylogenetic relationships of *Icaronycteris*, *Archaeonycteris*, *Hassianycteris*, and *Palaeochiropteryx* to extant bat lineages, with comments on the evolution of echolocation and foraging strategies in Microchiroptera. *Bulletin of the American Museum of Natural History* 235: 1-182.
- Simmons, N. B., and T. H. Quinn. 1994. Evolution of the digital tendon locking mechanism in bats and dermopterans: A phylogenetic perspective. *Journal of Mammalian Evolution* 2: 231-254.
- Smith, A. G., D. G. Smith, and B. M. Funnell. 1994. *Atlas of Cenozoic and Mesozoic Coastlines*. Cambridge University Press, Cambridge.
- Springer, M. S. 1997. Molecular clocks and the timing of the placental and marsupial radiations in relation to the Cretaceous-Tertiary boundary. *Journal of Mammalian Evolution* 4: 285-302.
- Springer, M. S., A. Burk, J. R. Kavanagh, V. G. Waddell, and M. J. Stanhope. 1997a. The interphotoreceptor retinoid binding protein gene in therian mammals: Implications for higher level relationships and evidence for loss of function in the marsupial mole. *Proceedings of the National Academy of Sciences USA* 94: 13754-13759.
- Springer, M. S., G. C. Cleven, O. Madsen, W. W. de Jong, V. G. Waddell, H. M. Amrine, and M. J. Stanhope. 1997b. Endemic African mammals shake the phylogenetic tree. *Nature* 388: 61-64.
- Springer, M. S., R. W. DeBry, C. Douady, H. Amrine, O. Madsen, W. W. de Jong, and M. J. Stanhope. 2001a. Mitochondrial versus nuclear gene sequences in deep-level mammalian phylogeny reconstruction. *Molecular Biology and Evolution* 18: 132-143.
- Springer, M. S., and J. A. W. Kirsch. 1993. A molecular perspective on the phylogeny of placental mammals based on mitochondrial 12S rDNA sequences, with special reference to the problem of Paenungulata. *Journal of Mammalian Evolution* 1: 149-168.
- Springer, M. S., W. J. Murphy, E. Eizirik, O. Madsen, M. Scally, C. J. Douady, E. C. Teeling, M. J. Stanhope, W. W. de Jong, and S. J. O'Brien. In press. A molecular classification for the living orders of placental mammals and the phylogenetic placement of primates; in M. Dagosto and M. Ravosa (eds.), *Primate Origins and Adaptations*. Plenum, New York.
- Springer, M. S., W. J. Murphy, E. Eizirik, and S. J. O'Brien. 2003. Placental mammal diversification and the Cretaceous-Tertiary boundary. *Proceedings of the National Academy of Sciences USA* 100: 1056-1061.
- Springer, M. S., E. C. Teeling, O. Madsen, M. J. Stanhope, and W. W. de Jong. 2001b. Integrated fossil and molecular data reconstruct bat echolocation. *Proceedings of the National Academy of Sciences USA* 98: 6241-6246.
- Stanhope, M. J., W. J. Bailey, J. Czelusniak, M. Goodman, J.-S. Si, J. Nickerson, J. G. Sgouros, G. A. M. Singer, and T. K. Kleinschmidt. 1993. A molecular view of primate supraordinal relationships from the analysis of both nucleotide and amino acid sequences; pp. 251-292 in R. D. E. MacPhee (ed.), *Primates and Their Relatives in Phylogenetic Perspective*. Plenum, New York.
- Stanhope, M. J., J. Czelusniak, J.-S. Si, J. Nickerson, and M. Goodman. 1992. A molecular perspective on mammalian evolution from the gene encoding interphotoreceptor retinoid binding protein, with convincing evidence for bat monophyly. *Molecular Phylogenetics and Evolution* 1: 148-160.
- Stanhope, M. J., O. Madsen, V. G. Waddell, G. C. Cleven, W. W. de Jong, and M. S. Springer. 1998a. Highly congruent molecular support for a diverse superordinal clade of endemic African mammals. *Molecular Phylogenetics and Evolution* 9: 501-508.
- Stanhope, M. J., M. R. Smith, V. G. Waddell, C. A. Porter, M. S. Shivig, and M. Goodman. 1996. Mammalian evolution and the interphotoreceptor retinoid binding protein (IRBP) gene: Convincing evidence for several superordinal clades. *Journal of Molecular Evolution* 43: 83-92.
- Stanhope, M. J., V. G. Waddell, O. Madsen, W. W. de Jong, S. B. Hedges, G. C. Cleven, D. Kao, and M. S. Springer. 1998b. Molecular evidence for multiple origins of Insectivora and

- for a new order of endemic African insectivore mammals. *Proceedings of the National Academy of Sciences USA* 95: 9967–9972.
- Stanyon, R., G. Stone, M. Garcia, and L. Froenicke. 2003. Reciprocal chromosome painting shows that squirrels, unlike murid rodents, have a highly conserved genome organization. *Genomics* 82: 245–249.
- Swofford, D. L., G. P. Olsen, P. J. Waddell, and D. M. Hillis. 1996. Phylogenetic inference; pp. 407–492 in D. M. Hillis, C. Moritz, and B. K. Mable (eds.), *Molecular Systematics*. Sinauer, Sunderland, Massachusetts.
- Szalay, F. S., and G. Drawhorn, 1980. Evolution and diversification of the Archonta in an arboreal milieu; pp. 133–169 in W. P. Luckett (ed.), *Comparative Biology and Evolutionary Relationships of Tree Shrews*. Plenum, New York.
- Teeling, E. C., O. Madsen, R. A. Van Den Bussche, W. W. de Jong, M. J. Stanhope, and M. S. Springer. 2002. Microbat paraphyly and the convergent evolution of a key innovation in Old World rhinolophoid microbats. *Proceedings of the National Academy of Sciences USA* 99: 1431–1436.
- Thomas, J. W., J. W. Touchman, R. W. Blakesley, et al. (68 other authors). 2003. Comparative analyses of multi-species sequences from targeted genomic regions. *Nature* 424: 788–793.
- Thorne, J. L., and H. Kishino. 2002. Divergence time and evolutionary rate estimation with multilocus data. *Systematic Biology* 51: 689–702.
- Thorne, J. L., H. Kishino, and I. S. Painter. 1998. Estimating the rate of evolution of the rate of molecular evolution. *Molecular Biology and Evolution* 15: 1647–1657.
- van Dijk, M.A.M., E. Paradis, F. Catzeflis, and W. W. de Jong. 1999. The virtues of gaps: Xenarthran (edentate) monophyly supported by a unique deletion in aA-crystallin. *Systematic Biology* 48: 94–106.
- Waddell, P. J., H. Kishino, and R. Ota. 2001. A phylogenetic foundation for comparative mammalian genomics. *Genome Informatics* 12: 141–154.
- Waddell, P. J., N. Okada, and M. Hasegawa. 1999. Towards resolving the interordinal relationships of placental mammals. *Systematic Biology* 48: 1–5.
- Woodburne, M. O., T. H. Rich, and M. S. Springer. 2003. The evolution of tribospheny and the antiquity of mammalian clades. *Molecular Phylogenetics and Evolution* 28: 360–385.