

# Chapter 16

## Molecular Phylogeny and Evolution in Primates

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### Abbreviations

K/T	Cretaceous/tertiary
Mya	Million years ago
NWM	New World monkey
OWM	Old World monkey
R	Purines (adenine and guanine)
rRNA	Ribosomal RNA
SINE	Short interspersed element
Y	Pyrimidines (cytosine and thymine)

### 16.1 Tree of Primates and Molecular Phylogenetic Problems in Primates

There are more than 350 species of extant primates in the world today (Groves 2005). Traditionally, the order Primates was classified into two suborders, the Prosimii (prosimians), which includes lemurs, lorises, and tarsiers, and the Anthroidea (anthropoids), which includes New World monkeys (NWMs), Old World monkeys

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(OWMs), and hominoids (humans and apes). However, there is another classification of Primates into two suborders, Strepsirrhini (lemurs and lorises), meaning “curved nose,” and the Haplorhini (tarsiers, NWMs, OWMs, and hominoids), meaning “simple nose,” based on the shape of the nose. Recent molecular studies revealed the monophyly of haplorhines (Schmitz et al. 2001; Matsui et al. 2009), supporting the latter classification. Moreover, NWMs and OWMs/hominoids are exactly equivalent to Platyrrhini, meaning “flat nose,” and Catarrhini, meaning “narrow nose,” respectively, in the latter classification.

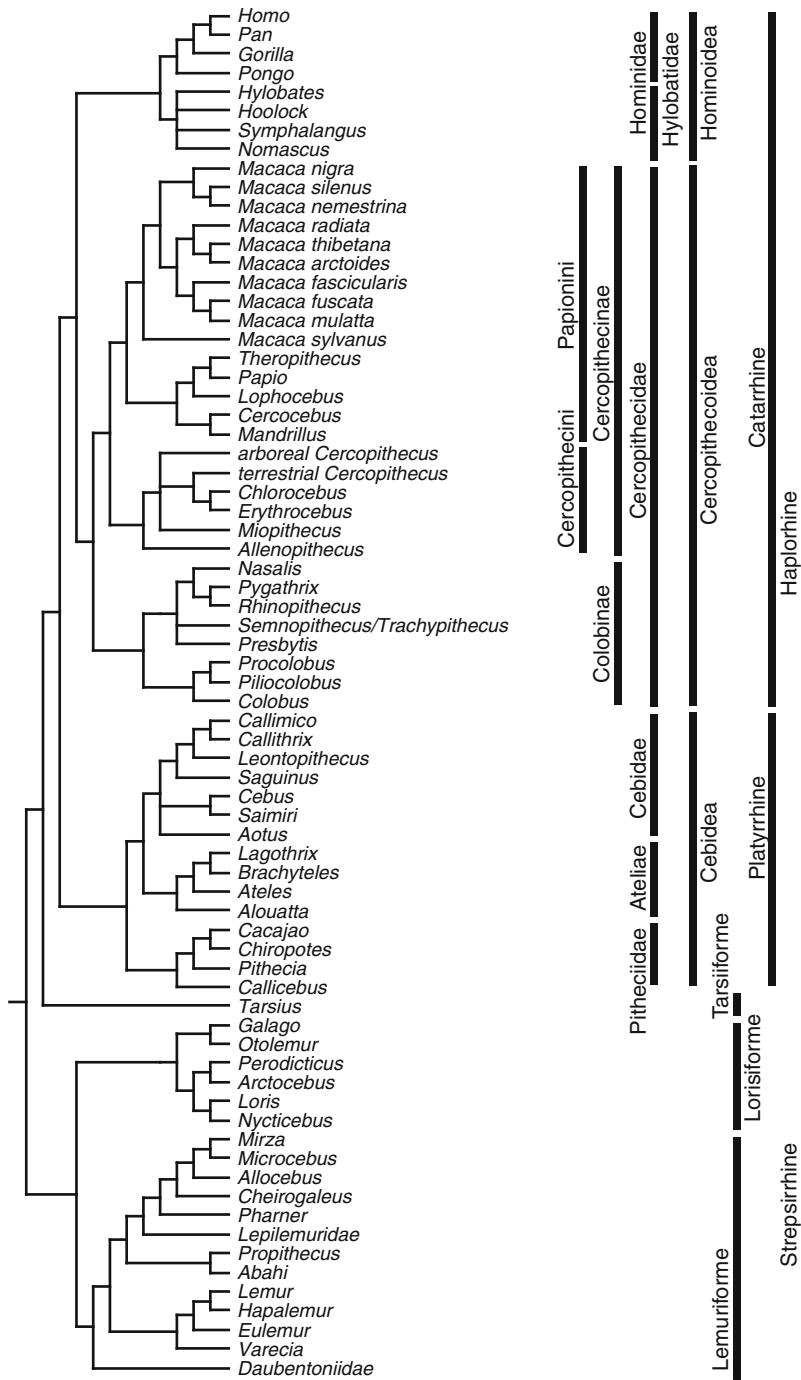
First, we show the simplified tree topology, which is a synthesized tree discussed in the following subsections, concerning the relationships among the main groups of living primates (Fig. 16.1).

### 16.1.1 *Lemurs (Lemuriformes)*

Lemurs are endemic to Madagascar and account for more than 15% of all extant primates in the world. In the lemuriforme clade, five extant families (Lemuridae, Cheirogaleidae, Daubentoniidae, Indriidae, and Lepilemuridae) are well defined. Nevertheless, the relationship among the four families, except for Daubentoniidae (containing only a single extant species, the aye-ayes), remains highly controversial and can be represented only as a multifurcation (Fig. 16.2a).

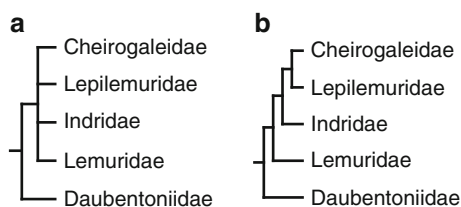
Previously, because of its morphological specializations, Daubentoniidae has sometimes been placed at the basal position of the strepsirrhine clade, thereby suggesting a diphyletic Lemuriformes (Groves 1989; Adkins and Honeycutt 1994) and even at the basal position of primates (Oxnard 1981). However, regardless of the data set used in molecular phylogenetics (Yoder 1994; Yoder et al. 1996; Porter et al. 1995; Pastorini et al. 2002; Poux and Douzery 2004) and by karyotype comparisons (Rumpler et al. 1988), the position of Daubentoniidae is well resolved as the sister group of all other Lemuriformes. Karanth et al. (2005) also suggested that Daubentoniidae represents the earliest offshoot in lemuriformes with additional analyses of ancient DNA from two subfossil lemur species.

As already mentioned, the phylogenetic relationships among the four families other than Daubentoniidae has been highly controversial. Pastorini et al. (2003) suggested that the Indriidae is the basal lineage among the problematic four families by using partial mitochondrial data, but they did not sufficiently resolve the relationships among the other three families (Lemuridae, Cheirogaleidae, and Lepilemuridae). Roos et al. (2004) suggested that the Lemuridae and Indriidae are sister relationships, but the positions of the other two families (Cheirogaleidae and Lepilemuridae) remain unresolved by analyses of SINE (short interspersed element) integrations. Using nuclear DNA data, Poux et al. (2005) proposed the following relationships: the Lemuridae is a sister lineage to the other three families, the Cheirogaleidae and Lepilemuridae form a sister clade, and the position of the Indriidae is sister to the Cheirogaleidae/Lepilemuridae. Horvath et al. (2008) strongly suggested the same relationships as those of Poux et al. (2005) by using a



**Fig. 16.1** Simplified tree topology: the synthesized tree discussed in Sect. 16.1, concerning the relationships among the main groups of living primates

**Fig. 16.2** (a) Multifurcation relationships among five families within the Lemuriformes. (b) Branching order within the Lemuriformes proposed by recent molecular phylogenetic studies



larger data set composed of mitochondrial and nuclear DNA (Fig. 16.2b). Furthermore, concerning the relationships among genera in the Lemuridae, *Varecia* is placed with a strong support at the most basal position in the family, *Lemur* and *Hapalemur* form a sister clade, and *Eulemur* is sister to the *Lemur*/*Hapalemur* clade (Pastorini et al. 2003; Horvath et al. 2008) (Fig. 16.1).

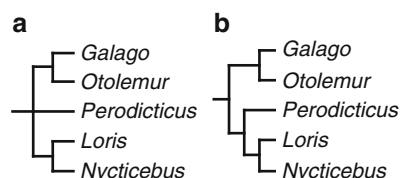
### 16.1.2 *Lorises (Lorisiformes)*

The Lorisiformes is classified into the African Galagidae and the African–Asian Lorisidae (Groves 2005). In the Lorisiformes, Galagidae is monophyletic, whereas the status of Lorisidae is controversial between morphological and molecular studies.

General morphological data (Schwartz 1992) support a monophyletic origin of Lorisidae. In contrast, Porter et al. (1997a, b) and Goodman et al. (1998) suggested Galagidae (*Otolemur*) and Asian Lorisidae (*Nycticebus*) grouped into one clade excluding African Lorisidae (*Perodicticus*) as an outgroup by using nuclear DNA data. Yoder et al. (2001) analyzed partial mitochondrial DNA and nuclear DNA data from three Lorisidae genera (*Nycticebus*, *Loris*, and *Perodicticus*) and found that the Asian Lorisidae (*Nycticebus* and *Loris*) formed a clade that was sister to the Galagidae, with African Lorisidae (*Perodicticus*) as the most basal taxon. Furthermore, by analyses of the molecular and morphological data, Masters et al. (2005) could not fully resolve the relationships among the Lorisiformes. Poux and Douzery (2004) discussed that the instability of the position of the potto (*Perodicticus*; African Lorisidae) might be caused by the slowest nucleotide substitution rate of the potto among Lorisiformes, and accordingly by the long-branch attraction (Felsenstein 1978) between Galagidae and Asian Lorisidae, by analyses of the nuclear gene encoding the interstitial retinoid-binding protein. These analyses suggest that Lorisidae is paraphyletic.

As already mentioned, the systematic relationships among the African–Asian lorises, particularly the position of the pottos, have been contentious in molecular studies. We also could not fully resolve the relationships among Lorisiformes, even with the whole mitochondrial genomes, because of the inconsistency of the position of pottos (Matsui et al. 2009). We detected three distinct lineages, African Lorisidae (potto, *Perodicticus*), Asian Lorisidae (*Loris* and *Nycticebus*), and monophyletic Galagidae (*Galago* and *Otolemur*), within the Lorisiformes (Fig. 16.3a).

**Fig. 16.3** (a) Trifurcation relationship composed of Galagidae, Asian Lorisidae, and African Lorisidae among the Lorisiformes. (b) Monophyly of the Lorisidae and Galagidae shown by molecular phylogenetic studies



Recently, Roos et al. (2004) suggested monophyly of the Lorisidae and of the Galagidae with three and six SINE integrations, respectively (Fig. 16.3b). Furthermore, several insertions suggested a common ancestry geologically of the African and Asian lorises. Masters et al. (2007) also suggested that the monophyly of the Lorisidae and of Galagidae using molecular and morphological data.

These results imply that the living Lorisidae is a monophyletic group and that two widespread geographic subclades in Asia and Africa have evolved in the fragmented area.

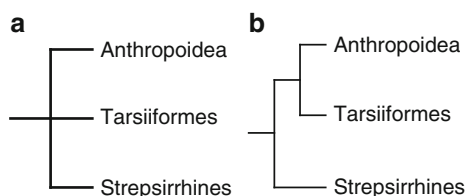
### 16.1.3 Tarsiers (*Tarsiiformes*)

One of the most controversial problems in primate phylogenetics at the intraordinal level is the position of tarsiers among primates. Tarsiers are the only surviving genus of formerly diverse ancestors in Tarsiiformes, which shares morphological characters of both Strepsirrhini and Anthropeidea. Practically, primates are divided into two suborders, of which the taxon content differs according to the phylogenetic position of tarsiers.

Several molecular studies suggested that tarsiers have a close relationship with Anthropeidea to form the Haplorhini (Schmitz et al. 2001; Poux and Douzery 2004; Gibson et al. 2005) or with Strepsirrhini to form the Prosimii (Eizirik et al. 2001; Murphy et al. 2001; Jow et al. 2002; Schmitz et al. 2002; Hudelot et al. 2003). Some data even suggested tarsiers to be a basal group of primates (Arnason et al. 2002). This incongruence is partly derived from the different data used for phylogenetic analyses. Nuclear DNA sequence comparisons tend to point toward a sister relationship of tarsiers and Anthropeidea, whereas mitochondrial DNA do not consistently support this affiliation or only marginally support it.

The base composition bias of mitochondrial DNA from several mammal species has been reported. Schmitz et al. (2002) compared the base composition of 26 mammalian mitochondrial genomes including the mitochondrial genome of *Tarsius bancanus*. They suggested that the overall nucleotide composition changed dramatically; decrease of T and A composition and increase of C composition on the lineage lead to higher primates at both silent and non-silent sites, and these changes of nucleotide composition have caused a change of amino acid composition.

**Fig. 16.4** (a) Trifurcation relationship among primates at intraordinal level concerning the position of tarsiers. (b) Monophyly of the Haplorhini (Anthropoidea and Tarsiiformes) and Strepsirrhini (*strepsirrhines*) shown by molecular phylogenetic studies



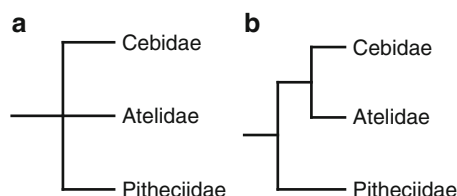
Furthermore, Gibson et al. (2005) carried out a comprehensive analysis of base composition in 69 mammalian mitochondrial genomes and examined whether the variation in base composition across genes and species affects the phylogenetic analysis. They found significant variation in T and C among these data, and they then tried to incorporate the effects in the phylogenetic reconstruction. As a result, they obtained the monophyly of Haplorhini.

Phillips and Penny (2003) mentioned the incongruence in the deep divergences of the mammalian tree obtained from mitochondrial genomes was caused by the difference of T and C frequencies among different species. The RY-coding [analyses using two nucleotide categories of purines (adenine and guanine: R) and pyrimidines (cytosine and thymine: Y)] was recently used to alleviate the bias caused by compositional differences in mammalian mitochondrial DNA sequences, and it was found to be effective in resolving some of the earliest branchings of the mammalian tree (Phillips and Penny 2003).

Therefore, we examined carefully the problematic characteristics of the mitochondrial genes and their effects on phylogenetic resolution of primates (Matsui et al. 2009). The position of tarsiers among primates could not be resolved by the maximum likelihood and neighbor-joining analyses with several data sets. Concerning the position of tarsiers, any of the three alternative topologies (monophyly of Haplorhini, monophyly of prosimians, and tarsiers being basal in primates) (Fig. 16.4a) could not be rejected at the significance level of 5%, neither at the nucleotide nor at the amino acid level. In addition, significant variations of C and T composition were observed across primate species. Furthermore, we used AGY data sets for phylogenetic analyses to remove the effect of different C/T (pyrimidines: Y) composition bias across species and to retain information from A/G (purines). These analyses provided a medium support for the monophyly of haplorhines, which might have been screened by the variation in base composition of mitochondrial DNA across species.

Recent studies of nuclear DNA seem to have established a consensus with respect to the phylogenetic position of tarsiers (Schmitz et al. 2001; Poux and Douzery 2004). By analyses of SINEs, Schmitz et al. (2001) found three Alu insertions at orthologous loci, suggesting the monophyly of Haplorhini (Anthropoidea and Tarsiiformes), and supported the monophyly of Strepsirrhini (Fig. 16.4b).

**Fig. 16.5** (a) Trifurcation relationship among the Ceboidea at family level. (b) Relationships of three monophyletic families among the Ceboidea by recent molecular phylogenetic studies

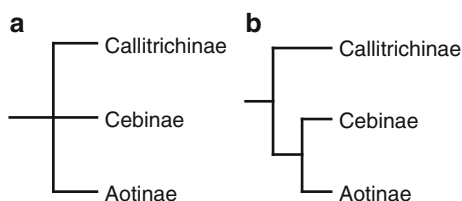


### 16.1.4 New World Monkeys (Ceboidea)

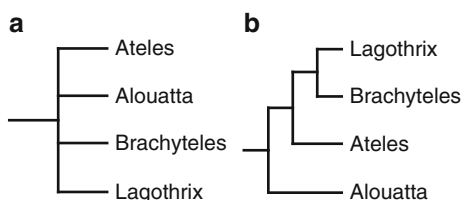
The extant NWMs constitute a monophyletic group, which is exactly equivalent to the infraorder Platyrrhini and the superfamily Ceboidea. They inhabit only South and Central America. Today, the Platyrrhini is divided, according to molecular studies, into three monophyletic families: the Atelidae, the Cebidae (or Callitrichidae), and the Pitheciidae (Goodman et al. 1998; Schneider 2000). Furthermore, six subgroups were recognized among Platyrrhini (Groves 1989; Schneider et al. 1993; Barroso et al. 1997): (1) the spider monkeys (*Ateles*), howler monkeys (*Alouatta*), marmosets (*Brachyteles*), and woolly monkeys (*Lagothrix*) subgroup; (2) the marmosets (*Callithrix*, *Cebuella*, *Callimico*) and tamarins (*Saguinus*, *Leontopithecus*) subgroup; (3) the capuchines (*Cebus*) and squirrel monkeys (*Saimiri*) subgroup; (4) the owl monkeys (*Aotus*) subgroup; (5) the saki monkeys (*Pithecia*, *Chiropotes*) and uakaris (*Cacajao*); and (6) the titi monkeys (*Callicebus*) subgroup. They are distributed into three monophyletic families as follows: the Atelidae [(1) *Ateles*, *Alouatta*, and *Brachyteles*], the Cebidae [(2) *Callithrix*, *Cebuella*, *Callimico*, *Saguinus*, and *Leontopithecus*; (3) *Cebus* and *Saimiri*; (4) *Aotus*], and the Pitheciidae [(5) *Pithecia*, *Chiropotes*, and *Cacajao*, and (6) *Callicebus*]. The following three phylogenetic problems still remain unresolved in Platyrrhini.

First, the relationships among three monophyletic families have not been sufficiently resolved (Fig. 16.5a). This issue has been extensively investigated using various molecular data. Several studies suggested that the Cebidae is basal and has a sister-group relationship with the Atelidae/Pitheciidae clade (Schneider et al. 1993; Harada et al. 1995; Porter et al. 1997a; Canavez et al. 1999a). Poux et al. (2006) suggested that Cebidae and Pitheciidae form a sister-group relationship. Conversely, some studies produced different topologies. Horovitz and Meyer (1995) proposed that the Pitheciidae is the first divergence from the Atelidae and Cebidae clade using mitochondrial sequences. From mitochondrial genome analysis, Hodgson et al. (2009) also found some support for a Cebidae/Atelidae clade with the Pitheciidae as a basal lineage. Recent studies using nuclear DNA data also suggested the same topology (Fig. 16.5b), although the support for the position of the Pitheciidae was not as strong and depends on the methods used in the analyses (von Dornum and Ruvolo 1999; Steiper and Ruvolo 2003; Prychitko et al. 2005; Opazo et al. 2006). Furthermore, Ray et al. (2005) provided robust support for the latter topology, which has a sister relationship between the Atelidae and Cebidae, by SINE analyses.

**Fig. 16.6** (a) Trifurcation relationship within the Cebidae at subfamily level. (b) Relationships of three monophyletic subfamilies among the Cebidae by recent molecular phylogenetic studies



**Fig. 16.7** (a) Unresolved relationships of four genera within the Atelidae. (b) Relationships of four genera among the Atelidae by recent molecular phylogenetic studies



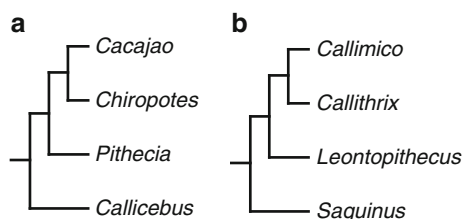
Second, there are problematic relationships among Callitrichinae (the marmosets and tamarins), Cebinae (the capuchins and squirrel monkeys), and Aotinae (the owl monkeys) at subfamily level within the Cebidae (Fig. 16.6a). In some studies, the position of Aotinae could not be fully resolved within the Cebidae (Schneider et al. 1993; von Dornum and Ruvolo 1999; Singer et al. 2003). Previous molecular studies suggested that Aotinae forms a sister clade with Callitrichinae (Harada et al. 1995; Porter et al. 1997a,b, 1999; Goodman et al. 1998) or that Aotinae is a basal lineage in Cebidae (Horovitz et al. 1998). Recent studies proposed a sister relationship between Aotinae and Cebinae, although with low support (Steiper and Ruvolo 2003; Opazo et al. 2006) (Fig. 16.6b). With SINE analyses, Ray et al. (2005) also provided a low support for this sister relationships between Aotinae and Cebinae by one insertion.

Third, a similar problem exists within Atelidae (*Ateles*, *Alouatta*, *Brachyteles*, and *Lagothrix*) (Fig. 16.7a). Early studies have suggested that *Brachyteles* have a close relationship to *Lagothrix* (Harada et al. 1995; Horovitz and Meyer 1995; Schneider et al. 1993, 1996; Porter et al. 1997a,b; Goodman et al. 1998; Canavez et al. 1999a; Meireles et al. 1999; von Dornum and Ruvolo 1999) (Fig. 16.7b). Based on mitochondrial and nuclear data, Collins (2004) proposed trichotomy among *Brachyteles*, *Lagothrix*, and *Ateles*. According to SINE analyses, Ray et al. (2005) presented a support for a closer relationship between *Lagothrix* and *Ateles* than either is to *Alouatta*. The relationships among these four genera in Atelidae, however, have remained unresolved.

At genus-level relationships among Pitheciidae, the branching order is well characterized as follows: *Callicebus* is a first-diverged species, and *Cacajao* and *Chiropotes* form a sister clade (Schneider et al. 1993; Harada et al. 1995; Porter et al. 1997a,b; Goodman et al. 1998; Horovitz et al. 1998; Canavez et al. 1999a; Meireles et al. 1999; Porter et al. 1999; von Dornum and Ruvolo 1999) (Fig. 16.8a).



**Fig. 16.8** (a) Phylogenetic relationships among the Pitheciidae at genus level. (b) Phylogenetic relationships among the subfamily Callitrichinae at genus level



The relationships among genera of the subfamily Callitrichinae have been agreed upon by most molecular studies (Canavez et al. 1999a, b; Chaves et al. 1999; von Dornum and Ruvolo 1999). *Saguinus* is a first-diverged species, *Leontopithecus* diverged next, and *Callimico* and *Callithrix* form a clade (Fig. 16.8b). Some molecular studies, however, suggested an alternative relationship, in which *Leontopithecus* and *Saguinus* form a clade (Schneider et al. 1993; Harada et al. 1995; Porter et al. 1997b, 1999; Goodman et al. 1998).

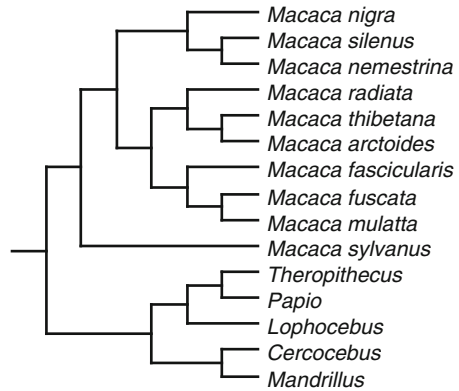
### 16.1.5 Old World Monkeys (*Cercopithecoidea*)

The extant OWMs constitute a monophyletic group, which is exactly equivalent to the superfamily Cercopithecoidea in the infraorder Catarrhini. Today, they widely inhabit Africa and Asia and are the most diverse group of primates. The superfamily Cercopithecoidea consists of the family Cercopithecidae. The Cercopithecidae is divided into two monophyletic subfamilies: the Cercopithecinae (cheek-pouched monkeys) and the Colobinae (leaf-eating monkeys) (Delson 1994; Raaum et al. 2005; Sterner et al. 2006; Groves 2005).

The subfamily Cercopithecinae consists of two tribes: the Papionini [mangabeys (*Cercocebus*, *Lophocebus*, and *Rungwecebus*), macaques (*Macaca*), baboons (*Papio*), drills and mandrills (*Mandrillus*), and geladas (*Theropithecus*)] and the Cercopithecini [patas monkeys (*Erythrocebus*), Allen's swamp monkeys (*Allenopithecus*), talapoin (*Miopithecus*), guenons (*Cercopithecus*), and vervet monkeys (*Chlorocebus*)] (Strasser and Delson 1987; Delson 1992, 1994; Disotell 2003; Groves 2005; Xing et al. 2005). The highland mangabey (kipunjis, *Rungwecebus*) was independently discovered by two research teams in 2003 and 2004, and recent molecular study assigned it to a new genus (Davenport et al. 2006). Most Cercopithecinae are distributed in sub-Saharan Africa. However, macaques exceptionally have wide distribution from eastern Asia to northern Africa (Fa 1989), and some small populations of baboons inhabit Arabia. Interestingly, it is well known that the Cercopithecini have colorful pelage patterns, although most Papionini have the grey or brown pelage.

Four issues in phylogeny of the subfamily Cercopithecinae remain unresolved at the tribe and subtribe level. The first question is whether the genus *Macaca* is a monophyletic group in the Papionini. Previous studies suggested the possibility that *Macaca* is a paraphyletic group consisting of two groups [barbary macaques

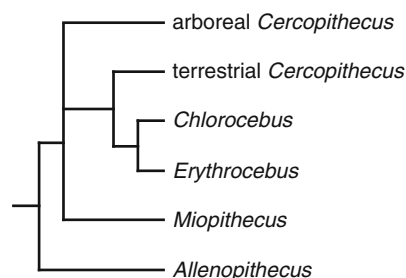
**Fig. 16.9** Phylogenetic relationships among the tribe Papionini at genus level (at species level in *Macaca*)



(*Macaca sylvanus*) and other *Macaca* species], based on morphological study (Groves 1989). However, molecular studies supported the monophyly of *Macaca* (Hayasaka et al. 1996; Morales and Melnick 1998; Tosi et al. 2000). Tosi et al. (2003) recently reinforced the monophyly of *Macaca* using gene sequences encoded on the Y chromosome. In addition, Xing et al. (2005) provided strong support for the *Macaca* monophyly by SINE analyses. They also presented monophyly of the subtribe Papionina as a sister clade to *Macaca*; *Papio* and *Theropithecus* form a monophyletic clade, which is a sister group to mangabeys (mentioned below) among Papionina (Fig. 16.9). Furthermore, the relationships within *Macaca* at genus level have not been well characterized in detail. Today, the genus *Macaca* is one of the most successful primates, and it is said that approximately 20–22 species exist in genus *Macaca*, although various definitions of species are proposed by different authors. The *Macaca* is classified into three to six species groups (Fooden 1976; Delson 1980; Groves 2005). Based on SINE analyses, Li et al. (2009) recently proposed that there are four monophyletic species groups within *Macaca*: the silenus group (*M. silenus*, *M. nemestrina*, and *M. nigra*), the sinica group (*M. radiata*, *M. thibetana*, and *M. arctoides*), the fascicularis group (*M. fascicularis*, *M. mulatta*, and *M. fuscata*), and the sylvanus group (*M. sylvanus*) as only one African clade. As for the relationships among these taxa, they suggested that the silenus group is a basal clade in the Asian macaques and that the sinica and fascicularis groups form a sister relationship (Fig. 16.9).

The second question is whether mangabeys (*Cercocebus* and *Lophocebus*) form a monophyletic group in the Papionini. Two genera in mangabeys have often been debated in morphological studies concerning their phylogenetic placement. Several morphological studies showed that the two mangabeys have similarities, suggesting their sister relationship (Szalay and Delson 1979; Strasser and Delson 1987). In contrast, however, others suggested that these mangabeys have diphyletic origins (Groves 1978; Fleagle and McGraw 1999). Molecular studies also suggested the diphyletic origin of mangabeys (Disotell 1994; Harris and Disotell 1998; Page and Goodman 2001) (Fig. 16.9). In addition, Tosi et al. (2003, 2005) recently proposed polyphyly of the mangabeys (*Cercocebus* and *Lophocebus*).

**Fig. 16.10** Phylogenetic relationships among the tribe Cercopithecini at genus level

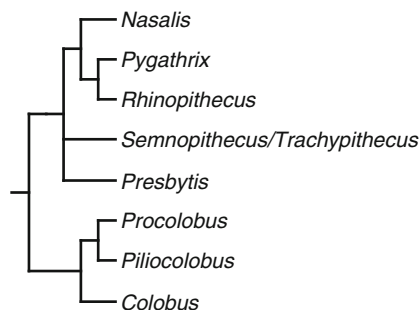


The third issue is whether guenons (*Cercopithecus*) form a monophyletic group in the Cercopithecini. The guenons (*Cercopithecus*) involve the arboreal species (arboreal *Cercopithecus*) and terrestrial species (*Cercopithecus aethiops* and *Cercopithecus lhoesti*). Many molecular studies suggested that the arboreal *Cercopithecus* within Cercopithecini form a monophyletic clade (Dutrillaux et al. 1988; Tosi et al. 2004). In contrast, the monophyly of the terrestrial species or guenons (*Cercopithecus*) has not been supported (Ruvolo 1988; Disotell and Raaum 2002; Tosi et al. 2002). However, Groves (1989) suggested that *C. aethiops* and *Erythrocebus patas* have a close relationship as a terrestrial species among the Cercopithecini. Concerning these problems, Tosi et al. (2003, 2005) proposed the paraphyly of *Cercopithecus* by analyses using a dataset of gene-encoded X- and Y chromosomes: *E. patas*, *C. aethiops*, and *C. lhoesti* form a monophyletic group (Fig. 16.10). Xing et al. (2005) supported the close relationship between terrestrial *Chlorocebus* and *Erythrocebus* by SINE analyses. These findings may imply two distinct clades composed of arboreal and terrestrial species, respectively, within the Cercopithecini.

The fourth issue is the phylogenetic position of *Allenopithecus* and *Miopithecus* in the subfamily Cercopithecinae. It has not been sufficiently resolved whether these species are involved in tribe Papionini or tribe Cercopithecini. Morphological studies by different authors suggested different affiliations of *Allenopithecus* and *Miopithecus* (Szalay and Delson 1979; Strasser and Delson 1987; Groves 1989). Some molecular studies showed that *Allenopithecus* and *Miopithecus* are involved in the tribe Cercopithecini (Disotell and Raaum 2002; Tosi et al. 2002) (Fig. 16.10). Recent molecular study also reported that the positions of *Allenopithecus* and *Miopithecus* fall into the tribe Cercopithecini (Fig. 16.10) (Tosi et al. 2003, 2005).

The subfamily Colobinae is roughly classified into two groups: the African clade [black and white colobuses (*Colobus*), red colobuses (*Procolobus*), and olive colobuses (*Piliocolobus*)] and the Asian clade [proboscis monkeys (*Nasalis*), snub-nosed monkeys (*Rhinopithecus*), douc langurs (*Pygathrix*), pigtailed langurs (*Simias*), surilis (*Presbytis*), gray langurs (*Semnopithecus*), and lutungs (*Trachypithecus*)] (Collura et al. 1996; Messier and Stewart 1997; Page et al. 1999; Disotell 2003; Groves 2005; Xing et al. 2005). Within the Asian clade there are two groups: the odd-nosed group (*Nasalis*, *Simias*, *Pygathrix*, and *Rhinopithecus*) and the langur and leaf monkeys group (*Presbytis*, *Semnopithecus*, and *Trachypithecus*) (Groves 1970; Jablonski

**Fig. 16.11** Phylogenetic relationships among the subfamily Colobinae at genus level



1998; Jablonski and Peng 1993; Xing et al. 2005). African colobuses have stub thumbs. The Colobinae species are usually arboreal and mainly eat leaves and hard fruits, have multi-chambered stomachs, and are also called leaf-eating monkeys (Chivers and Hladik 1980; Strasser and Delson 1987). Three phylogenetic issues of the subfamily Colobinae remain unresolved. The evolutionary relationships among Asian Colobinae especially remain contested and have not been fully demonstrated by molecular studies (Messier and Stewart 1997; Zhang and Ryder 1998).

The first question is whether the odd-nosed group is monophyletic within Asian Colobinae. Previously, several studies suggested that the odd-nosed group is not monophyletic (Bigoni et al. 2003, 2004; Jablonski 1998; Wang et al. 1995). Sterner et al. (2006), however, clearly showed their monophyly by using whole mitochondrial sequences (Fig. 16.11). This monophyletic relationship was strongly supported also by SINE analyses (Xing et al. 2005). Concerning the branching order within the odd-nosed group, they proposed that *Nasalis* is a first-diverged species and that *Pygathrix* and *Rhinopithecus* form a sister clade, although morphological studies by different authors suggested different relationships (Peng et al. 1993; Bigoni et al. 2003, 2004).

The second concern is the comprehensive relationships among the langur and leaf monkeys group. Different classifications for three genera (*Presbytis*, *Semnopithecus*, and *Trachypithecus*) have been proposed by different authors (Delson 2000; Groves 2005). The evolutionary relationships in these genera have not yet been resolved. Morphological studies suggested that *Semnopithecus* and *Trachypithecus* form a sister clade (Strasser and Delson 1987; Groves 2001). Recent mitochondrial genome analyses, however, suggested that *Presbytis* and *Trachypithecus* form a sister clade (Sterner et al. 2006). On the other hand, Ting et al. (2008) proposed that *Semnopithecus* and *Trachypithecus* are grouped into one clade, which is concordant with morphological analyses, using the dataset of genes encoded on the X chromosome. They statistically showed that the mitochondrial data set again supported a different topology from the X-chromosome data and that the position of *Presbytis* and odd-nosed groups among Asian Colobinae are quite different using mitochondrial data and X-chromosome data. Osterholz et al. (2008) also suggested the sister-group relationship of *Semnopithecus* and *Trachypithecus* by using the Y-chromosomal gene data, mitochondrial genes, and retroposon integrations. Now, the close relationship of *Semnopithecus* and *Trachypithecus* seems to

be supported by recent studies, as already mentioned (Fig. 16.11). Furthermore, there is disagreement about the relationships, particularly within the genus *Trachypithecus*. Gray langurs (*Semnopithecus*) are often called Hanuman langurs, and they inhabit all areas of the Indian subcontinent. *Trachypithecus* inhabit mainly Southeast Asia, and purple-faced langurs (*Trachypithecus vetulus*) and Nilgiri langurs (*Trachypithecus johnii*) live in south India, which is an area disconnected from Southeast Asia. In contrast, *Presbytis* inhabit only Southeast Asia. For this reason, the phylogenetic question is to which group these two species (purple-faced langurs and Nilgiri langurs) are more closely related, whether *Semnopithecus* in India or *Trachypithecus* in Southeast Asia (Fig. 16.11). Some molecular studies suggested that Hanuman langurs (*Semnopithecus*) and purple-faced langurs (*Trachypithecus*) form a sister clade as an Indian species clade and Southeast Asian *Trachypithecus* form another clade (Messier and Stewart 1997; Zhang and Ryder 1998). More recently, Karanth et al. (2008) also suggested these relationships using mitochondrial and nuclear datasets. They and Osterholz et al. (2008) mentioned that hybridization or introgression might have occurred between *Semnopithecus* and *Trachypithecus* clades during their evolutionary history in India. To solve these relationships, further research is required, and the relationship of *Presbytis*, *Semnopithecus*/*Trachypithecus*, and the odd-nosed group among Asian Colobinae should be treated as a trichotomy at present (Fig. 16.11). It might be necessary to change the current classification of *Semnopithecus* and *Trachypithecus* in the future.

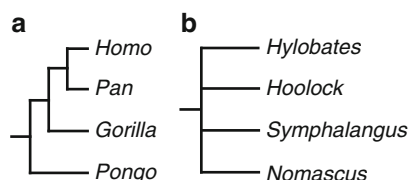
The third issue is that the branching order of the African Colobinae has not been fully resolved by molecular studies. There are three distinct clades among African Colobinae: black-and-white colobuses (*Colobus*), the olive colobuses (*Piliocolobus*), and the red colobuses (*Procolobus*). Ting (2008) showed that olive colobuses (*Piliocolobus*) and the red colobuses (*Procolobus*) are grouped into a sister clade, using mitochondrial data (Fig. 16.11), and analyzed the phylogeny of African Colobinae in detail. This relationship is concordant with previous studies of morphology and vocalizations.

### 16.1.6 Hominoids (*Hominoidea*)

The superfamily Hominoidea has two families: Hominidae (great apes) and Hylobatidae (gibbons, small apes).

The family Hominidae involves four extant genera [chimpanzees (*Pan*), gorillas (*Gorilla*), orangutans (*Pongo*), and humans (*Homo*)], and, except for humans, they inhabit only Africa and Asia. The relationships among the Hominidae have been extensively studied because of the direct relevance to human origins. Horai et al. (1995) proposed that humans have a sister relationship with chimpanzees among Hominidae, using whole mitochondrial sequences, and the phylogeny of the Hominidae has been established (Fig. 16.12a).

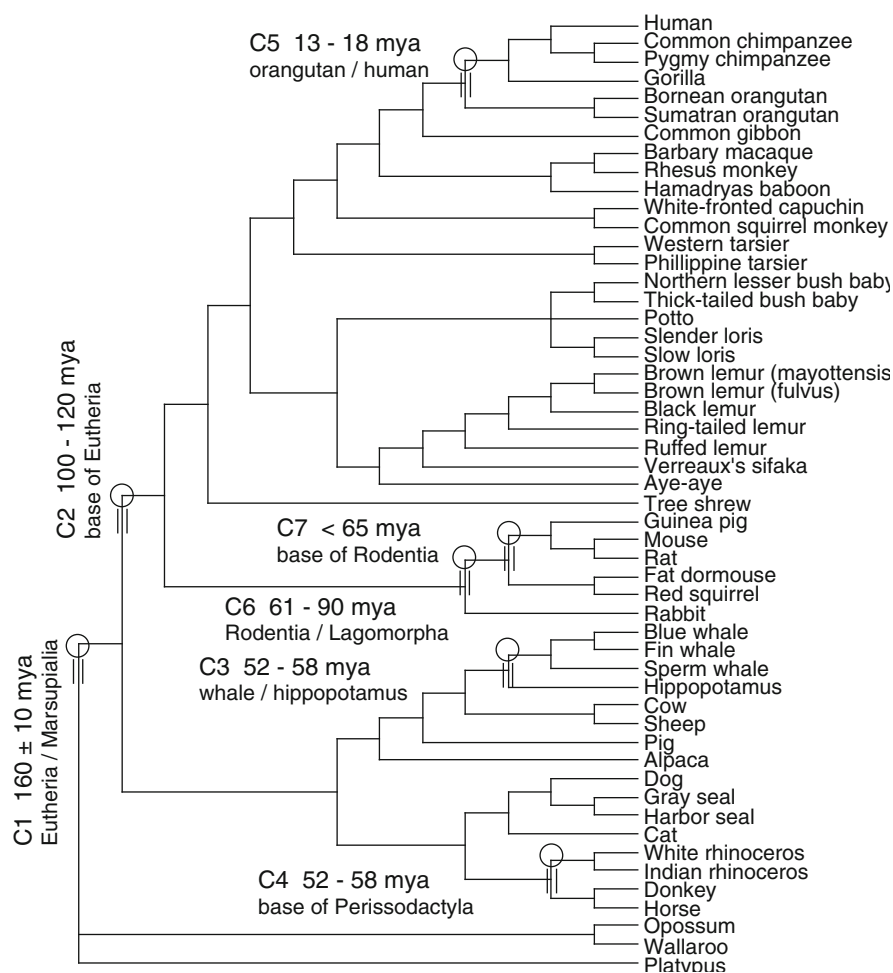
**Fig. 16.12** (a) Phylogenetic relationships among the family Hominidae. (b) Phylogenetic relationships among the family Hylobatidae proposed by recent molecular phylogenetic studies



The family Hylobatidae contains four genera (*Hylobates*, *Hoolock*, *Nomascus*, and *Symphalangus*) (Groves 2005; Mootnick and Groves 2005; Takacs et al. 2005). Each genus is a monophyletic group within the Hylobatidae. Previously, there was only one genus, *Hylobates*. However, recent molecular studies showed that the present four gibbon genera are more genetically diverged than are humans and chimpanzees and recommended that they should be treated as different genera (Brandon-Jones et al. 2004; Roos and Geissmann 2001). In addition, the genus *Bunopithecus* was recently changed to *Hoolock* for the hoolock gibbons (Mootnick and Groves 2005). Because gibbons (Hylobatidae) are relatively smaller than other apes, they are often called the lesser apes. They inhabit Southeast Asia (northeast India, southern China, Malay Peninsula, Java, Borneo, and Sumatra). Although the phylogeny of the Hominidae has been elucidated, the phylogenetic relationships among the four genera in Hylobatidae remain unresolved. Roos and Geissmann (2001) suggested that *Nomascus* first diverged and *Hoolock* (*Bunopithecus*) and *Hylobates* form a sister clade using control region (D-loop) data of mitochondrial DNA. On the other hand, Takacs et al. (2005) gave some support for either *Hoolock* (*Bunopithecus*) or *Nomascus* as the most basal genus and *Hylobates* to be most recently derived genus using a mitochondrial dataset. Recently, two studies using mitochondrial genome data suggested that *Nomascus* was a first-diverged genus and that *Hylobates* and *Symphalangus* form a sister clade, with high support value among these three genera (Matsudaira and Ishida 2010; Chan et al. 2010). However, the phylogenetic relationships among the four genera of Hylobatidae remain unclear by molecular studies (Thinh et al. 2010; Israfil et al. 2011) and should be further examined in future (Fig. 16.12b).

## 16.2 Divergence Times of Primates Estimated with Whole Mitochondrial Genome Data

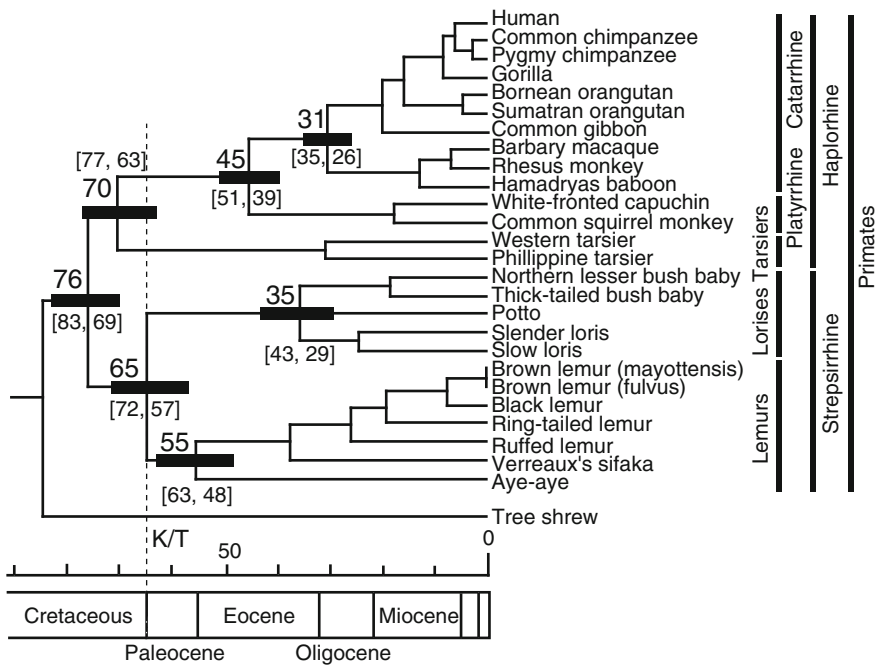
To estimate speciation dates within primates, we used the new complete mitochondrial genome data from 11 primates together with those from 15 primates that contained the mitochondrial genome sequence of sifakas determined by us from their feces samples (Matsui et al. 2007), and 26 non-primate mammals available in



**Fig. 16.13** Seven constraint points: *C1*, Eutheria/Marsupialia; *C2*, base of Eutheria (Boreoeutheria/Afrotheria/Xenarthra); *C3*, whale/hippopotamus; *C4*, base of perissodactyla (horse/rhinoceros); *C5*, orangutan/human; *C6*, base of Glires (Rodentia/lagomorph); *C7*, base of Rodentia (cavimorph/myomorph/sciurid)

public databases (Matsui et al. 2009). The significant rate of heterogeneity of mitochondrial DNA among eutherian lineages suggested that a variable rate clock has to be applied to estimate reliable divergence dates (Hasegawa et al. 2003). We analyzed the amino acid sequences of 12 proteins and nucleotide sequences of 2 ribosomal RNAs (rRNAs) encoded in mitochondrial DNA with a Bayesian method, which allows different rates on different branches, of Thorne and Kishino (Thorne et al. 1998; Thorne and Kishino 2002). Seven fossil-based divergence dates were used as constraints to calibrate the relaxed clock (Fig. 16.13). Only one constraint point chosen within the primates as the time of divergence between the orangutan





**Fig. 16.14** Phylogram of primates based on the amino acid sequences of the mitochondrial protein data set. Numbers on each node indicate the divergence dates estimated. Black bars on nodes represent 95% credibility interval for the divergence dates

and the human lineages (C5). The orangutan lineage first appeared in the fossil record as *Sivapithecus* about 12–13 million years ago (Mya) (Kelley 2002), but the fossil datings of *Sivapithecus* were once questioned (Pilbeam et al. 1990). Recent statistical analyses of cranial and postcranial characters (Begun et al. 1997; Ward 1997) suggested that the divergence between the *Sivapithecus*–orangutan and the African apes–human lineages occurred before 13 Mya (Ward 1997; Stewart and Disotell 1998), which is the current consensus among paleoanthropologists. Thus, we gave a constraint to the orangutan/human divergence at 13–18 Mya, in which the older bound of 18 Mya is the date of the connection between Africa and Eurasia (Waddell and Penny 1996). We further gave constraints to six nodes based on the paleontological records and previous research in mammal evolution, and the tree topology of non-primate mammals was adopted into our analyses from the mitochondrial protein analysis by Hasegawa et al. (2003). For the major nodes of primates, Fig. 16.14 depicts a time scale for placental mammal evolution based on the amino acid sequences of the mitochondrial DNA protein data set with the platypus as an outgroup. The estimated divergence dates are summarized in Table 16.1.

The divergence between Haplorhini and Strepsirrhini was estimated to be  $76.0 \pm 3.3$  (69.3–82.5, 95% credibility interval) Mya (protein)/ $80.9 \pm 4.4$  (72.4–89.6) Mya (rRNA) before the K/T (Cretaceous/Tertiary) boundary, which marked



**Table 16.1** Estimated dates with posterior standard deviations based on amino acid sequences (12H-strand encoded protein gene) and rRNA sequences of mitochondrial DNA

Branching among primates	Estimated dates (million years ago, Mya)		95% credibility interval	
	Protein (amino acid sequences)	rRNA	Protein (amino acid sequences)	rRNA
Haplorhini/Strepsirrhini	76.0±3.3	80.9±4.4	(69.3–82.5)	(72.4–89.6)
Anthropoidea/Tarsiiformes	70.1±3.4	76.8±4.8	(63.2–76.7)	(67.4–86.4)
Lemuriformes/Lorisiformes	64.5±3.7	69.3±4.8	(57.2–71.7)	(60.2–79.0)
The radiation of Lemuriformes	55.3±3.9	65.6±5.0	(47.7–63.0)	(56.3–75.5)
The radiation of Lemuridae	26.1±3.3	24.9±3.6	(20.0–32.6)	(18.5–32.5)
The radiation of Lorisiformes	35.4±3.7	31.5±3.9	(28.5–43.1)	(24.4–39.7)
<i>Tarsius bancanus</i> / <i>Tarsius syrichta</i>	30.8±3.9	20.2±3.3	(23.4–38.6)	(14.5–27.4)
Platyrrhini/Catarrhini	45.3±3.1	47.0±4.3	(39.4–51.3)	(39.1–55.7)
Hominoidea/Cercopithecoidea	30.5±2.5	33.1±3.3	(25.8–35.3)	(27.0–39.9)
Greater ape/small ape (gibbon)	19.9±1.7	21.3±2.2	(16.7–23.0)	(17.3–26.0)
Orangutan/human, chimpanzee, gorilla	15.8±1.3	14.9±1.3	(13.3–17.9) (13–18 <sup>a</sup> )	(13.1–17.6) (13–18 <sup>a</sup> )
Gorilla/human, chimpanzee	8.4±1.0	8.8±1.2	(6.6–10.3)	(6.8–11.4)
Human/chimpanzee	6.2±0.8	6.9±1.0	(4.7–7.8)	(5.1–9.1)
Bornean orangutan/Sumatran orangutan	4.7±0.7	3.8±0.7	(3.5–6.0)	(2.5–5.3)
Common chimpanzee/pygmy chimpanzee	3.0±0.5	2.3±0.5	(2.1–4.1)	(1.4–3.5)

For orangutan branching, constraints were given with <sup>a</sup> in parentheses

the extinction of the dinosaurs (Hedges et al. 1996). This result is in accord with the estimated dates of the previous studies concerning the interordinal diversification of placental mammals (Hasegawa et al. 2003; Springer et al. 2003). Hasegawa et al. (2003) and Springer et al. (2003) suggested that the Haplorhini/Strepsirrhini divergence was  $73.1 \pm 2.7$  Mya and approximately 77 Mya, respectively, at least several millions of years before the K/T boundary. Steiper and Young (2006) also suggested the origin of primates to be about 77.5 Mya using a large dataset of genome sequences. Although some recent molecular phylogenies assume that primates originated far earlier than the K/T boundary, the earliest fossil record suggests that primates began to diversify just after the K/T boundary, around 55 Mya (Ni et al. 2004). Divergence dates estimated with molecular data often predate the earliest recognized fossil representatives of the species studied, which has been explained

by the incompleteness of the fossil record of primates. The common ancestor of primates should be earlier than the oldest known fossils (Martin 1993), but adequate quantification is needed to interpret possible discrepancies between molecular and paleontological estimates. It is often said that the first small primates might have survived the K/T extinction event. Tavaré et al. (2002) estimated that living primates last shared a common ancestor 81.5 (72.0–89.6) Mya, based on a statistical analysis of the fossil record, which takes into account fossil preservation rate.

Subsequently, the split of Haplorhini in Anthropeidea and tarsiers was estimated to be 70.1 ± 3.4 (63.2–76.7) Mya (protein)/76.8 ± 4.8 (67.4–86.4) Mya (rRNA). Because of this deep branching of tarsiers, the position of tarsiers among primates might have to be resolved by the phylogenetic analyses.

The age of the last common ancestor of lorisiforms and lemuriforms was estimated to be approximately 64.5 ± 3.7 (57.2–71.7) Mya (protein)/69.3 ± 4.8 (60.2–79.0) Mya (rRNA). After the divergence of Strepsirrhini, Lemuriformes separated into Daubentonidae and other lemurs (Indriidae/Lemuridae) at the estimated date of 55.3 ± 3.9 (47.7–63.0) Mya (protein)/65.6 ± 5.0 (56.3–75.5) Mya (rRNA). In comparison with the previous results, Yoder et al. (1996), often referring to the Madagascar lemur study, proposed at least 62 Mya, 54 Mya, and 55 Mya, respectively, for the strepsirrhine, lemuriform, and lorisiform radiations. This analysis was, however, based on the calibration point (63 Mya) for the divergence between Strepsirrhini and Anthropeidea using partial mitochondrial sequences. In other words, the calibration point of the Yoder et al. (1996) analysis was a minimum value, and the actual date should be older, as mentioned earlier. Their recent study with the Bayesian method suggested 50–78 Mya for the diversification of Malagasy primates (Yoder et al. 2003). The radiation of Lemuridae was estimated to be 26.1 ± 3.3 (20.0–32.6) Mya (protein)/24.9 ± 3.6 (18.5–32.5) Mya (rRNA) because of the earliest divergence of *Varecia*.

The lorisiformes diverged at 35.4 ± 3.7 (28.5–43.1) Mya (protein)/31.5 ± 3.9 (24.4–39.7) Mya (rRNA) into Galagidae and Lorisidae. Because there is still no fossil record of the Madagascar lemur (Martin 2003) except for recent subfossils, the radiation of Lemuriformes, estimated to be 55.3 ± 3.9 (47.7–63.0) Mya (protein)/65.6 ± 5.0 (56.3–75.5) Mya (rRNA), cannot be confirmed by the fossil evidence. The estimated divergence date between Galagidae and Lorisidae within Lorisiformes is in agreement with fossils recently discovered by Seiffert et al. (2003) from the late middle Eocene, which suggested that the basal divergence between extant Galagidae and Lorisidae began at least 38–40 Mya.

Concerning these divergence times, Poux et al. (2005) suggested a younger date for the last common ancestor of Lorisiformes and Lemuriformes and the radiation of Lemuriformes, estimated to be about 60 Mya and 50 Mya, respectively using the nuclear DNA data set. On the other hand, Horvath et al. (2008) proposed older dates for these, about 75 Mya and 66 Mya, respectively, and the radiation of the Lorisiformes was estimated to be about 39 Mya using a large data set of genome sequences.

The estimated divergence times of Catarrhini/Platyrrhini and hominoids/OWMs are approximately 45.3 ± 3.1 (39.4–51.3) Mya (protein)/47.0 ± 4.3 (39.1–55.7) Mya (rRNA) and 30.5 ± 2.5 (25.8–35.3) Mya (protein)/33.1 ± 3.3 (27.0–39.9) Mya (rRNA),

respectively. The split of Catarrhini/Platyrrhini and hominoids/OWMs, often used as calibration points among primates, were at 35 Mya (Rosenberger et al. 1991) and at 25 Mya (Fleagle 1999), respectively. We, however, estimated both divergence dates to be earlier. Steiper and Young (2006) also suggested older divergence times of Catarrhini/Platyrrhini and hominoids/OWMs to be about 43 Mya and 31 Mya, respectively, using large genome sequences. Concerning NWMs, Poux et al. (2006) proposed that NWMs colonized in South America about 37 Mya and that the radiation of the NWMs occurred about 16.8 Mya. Recent studies also reported a similar estimation for NWMs. Hodgson et al. (2009) estimated that the most common ancestor of NWMs dates to about 19.5 Mya and proposed that extant NWMs are descendants of recent successive radiation in the South American primates.

The estimate for the divergence between humans and orangutans,  $15.8 \pm 1.3$  (13.3–17.9) Mya (protein)/ $14.9 \pm 1.3$  (13.1–17.6) Mya (rRNA), was also close to the paleontological estimate, 13 Mya (Ward 1997; Stewart and Disotell 1998), used as calibration ( $>13$  Mya). Steiper and Young (2006), in contrast, suggested the time of divergence between humans and orangutans to be about 18 Mya using large genome sequences. Our estimated dates for the (human, chimpanzee)/gorilla and great ape/small ape divergences were  $8.4 \pm 1.0$  (6.6–10.3) Mya (protein)/ $8.8 \pm 1.2$  (6.8–11.4) Mya (rRNA) and  $19.9 \pm 1.7$  (16.7–23.0) Mya (protein)/ $21.3 \pm 2.2$  (17.3–26.0) Mya (rRNA), respectively.

The estimate for the human/chimpanzee divergence date was  $6.2 \pm 0.8$  (4.7–7.8) Mya (protein)/ $6.9 \pm 1.0$  (5.1–9.1) Mya (rRNA), in accord with the widely accepted date. The currently accepted date of the chimpanzee–human split at about 6–7 Mya was initially proposed based on molecular estimates (Horai et al. 1995), which were much younger than fossil-based estimates at that time. This estimation is close to the ages of the recently discovered oldest hominid fossils (5.4–7.0 Mya) (Aiello and Collard 2001; Haile-Selassie 2001; Brunet et al. 2002).

By using molecular data accompanied with the fossil and geologic evidence, we should reexamine the biogeographic scenarios that have been proposed for the origin of the main lineages of primates and for their dispersal. The major questions in strepsirrhine evolution are when and how lemurs first arrived in Madagascar, and when and how lorises spread over Asia and Africa. The similar question has arisen for the NWMs in South America (when and how NWMs arrived at South America). Recently, estimation of divergence times and a supermatrix approach have been carried out with larger data sets than previously for primate phylogenetic analyses (Chatterjee et al. 2009; Fabre et al. 2009; Perelman et al. 2011). We hope to gain a better understanding of the speciation scenarios of primates by further studies.

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