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Evolutionary Affinities of the Order Perissodactyla and the Phylogenetic Status of the Superordinal Taxa Ungulata and Altungulata

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Contrary to morphological claims, molecular data indicate that the order Perissodactyla (e.g., horses, rhinoceroses, and tapirs) is neither part of the superordinal taxon Paenungulata (Sirenia, Proboscidea, and Hyracoidea) nor an immediate outgroup of the paenungulates. Rather, Perissodactyla is closer to Carnivora and Cetartiodactyla (Cetacea + Artiodactyla) than it is to the paenungulates. Therefore, two morphologically defined superordinal taxa, Altungulata (Proboscidea, Sirenia, Hyracoidea, and Perissodactyla) and Ungulata (Altungulata and Cetartiodactyla), are invalidated. Perissodactyla, Carnivora, and Cetartiodactyla are shown to constitute a rather tight trichotomy. However, a molecular analysis of 36 protein sequences with a total concatenated length of 7885 aligned amino acids indicates that Perissodactyla is closer to Cetartiodactyla than either taxa is to Carnivora. The relationships among Paenungulata, Primates, and the clade consisting of Perissodactyla, Carnivora, and Cetartiodactylaa could not be resolved on the basis of the available data.

INTRODUCTION

In most contemporary morphological phylogenetic schemes (e.g., Novacek, 1992), horses and their relatives (order Perissodactyla) are positioned either as the closest outgroup to the superorder Paenungulata, which includes three extant orders, Proboscidea (elephants), Hyracoidea (hyraxes), and Sirenia (sea cows and manatees), or as nearest neighbors of the hyraxes, and, therefore, nested within the Paenungulata (Prothero *et al.*, 1988; Fisher and Tassy, 1993; Prothero, 1993). Molecular analyses, on the other hand, indicate that Perissodactyla may be closely related to Artiodactyla, Cetacea, and Carnivora (e.g., Irwin *et al.*, 1991; Ma *et al.*, 1993; Krettek *et al.*, 1995; Queralt *et al.*, 1995; Zolzer and von Hagen, 1995). In the following, we use proteins for which orthologous sequence data exist for members of Paenungulata, Perissodactyla, Artiodactyla, Cetacea, Carnivora, and Primates, as well as noneutherian outgroups, to test different evolutionary schemes and identify the phylogenetic position of Perissodactyla within the eutherian tree. We also test the phylogenetic validity, i.e., the monophyly, of the following proposed superorders: (1) Altungulata (Proboscidea, Sirenia, Hyracoidea, and Perissodactyla) (Prothero and Schock, 1988) and (2) Ungulata (Perissodactyla, Cetartiodactyla, Proboscidea, Sirenia, and Hyracoidea) (McKenna, 1975).

DATA AND METHODS

Proteins have been collected by using Release 11 of the HOVERGEN (Duret *et al.*, 1994) and Release 46.0 of the PIR (George *et al.*, 1994) databases. The orders Cetacea and Artiodactyla were treated as a single taxon, Cetartiodactyla (Montgelard *et al.*, in press), since either they are very closely related sister taxa (Novacek, 1992) or the Cetacea are nested within the Artiodactyla (Graur and Higgins, 1994; for review, see Milinkovitch, 1995). The protein sequences were aligned by using the CLUSTAL W program (Thompson *et al.*, 1994). Ambiguous parts in the alignments (as judged by visual inspection), as well as gaps, have been removed from further analysis. In each analysis, sequences were used only if they were available for all the taxa in question. If a certain taxon was represented in a protein data set by two or more species, we constructed a neighbor-joining phylogenetic tree and selected the sequence with the shortest branch length to represent the order in question. The list of proteins and the organisms from which they were obtained are given in Table 1. Implicit in this procedure is the assumption that each taxon dealt with in this study is monophy-

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TABLE 1

List of Protein Sequences and the Organisms from which They Were Derived

Protein	CET	CAR	HYR	PER	PRI	PRO	SIR	MYO	OUT
1. Nuclearly encoded proteins									
αA-crystallin	Cdro	Cfam	Pcap	Tind	Lful	Lafr	Tinu	Mmus	Mruf
Hemoglobin-β	Rtar	Pvit	Pcap	Csim	Pcyn	Emax	Tinu	Rnor	Mruf
Hemoglobin-α	Chir	Aful	Pcap	Ecab	Cape	Emax	Tinu	Mmar	Mgig
von Willebrand factor	Sscr	Cfam	Pcap	Csim	Hsap	Lafr	Ddug	Spol	—
Insulin	Btau	Cfam	—	Ecab	Hsap	Lafr	—	Maur	Ggal
Prolactin	Sscr	Fcat	—	Ecab	Hsap	Lafr	—	Maur	Ggal
Interleukin-2	Sscr	Fcat	—	Ecab	Mnem	—	Tman	Mung	—
Myoglobin	Sscr	Llut	—	Ecab	Mfas	Emas	—	Sleu	Dvir
Growth hormone	Sscr	Vvul	—	Ecab	Hsap	Lafr	—	Maur	Ggal
Insulin-like growth factor I	Sscr	Cfam	—	Ecab	Hsap	—	—	Rnor	Ggal
β-chorionic gonadotropin	Sscr	Cfam	—	Easi	Pham	—	—	Rnor	Ccot
Phospholipase A-2	Sscr	Cfam	—	Ecab	Hsap	—	—	Rnor	Bmul
CD44 antigen	Btau	Cfam	—	Ecab	Pham	—	—	Maur	—
Na,K-ATPase α1 subunit	Oari	Cfam	—	Ecab	Hsap	—	—	Rnor	Ggal
Serum albumin	Sscr	Cfam	—	Ecab	Hsap	—	—	Rnor	Ggal
Atrial natriuretic polypeptide	Sscr	Cfam	—	Ecab	Hsap	—	—	Rnor	Ggal
γ-interferon	Oari	Cfam	—	Ecab	Hsap	—	—	Mung	—
Pancreatic polypeptide	Btau	Clup	—	Tpin	Hsap	—	—	Mmus	Dvir
Tumor necrosis factor α	Sscr	Fcat	—	Ecab	Pham	—	—	Mmus	—
Colipase	Sscr	Cfam	—	Ecab	Hsap	—	—	Rnor	—
Cytochrome c	Lgua	Cfam	—	Easi	Mmul	—	—	Mmus	Mgig
Plasminogen	Btau	Cfam	—	Ecab	Hsap	—	—	Mmus	—
SRY protein	Oari	Hgry	—	Ecab	Ppyg	—	—	Hall	Smac
2. Mitochondrially encoded proteins									
Cytochrome b	Sscr	Pvit	—	Egre	Hsap	Lafr	—	Rnor	Mdom
NADH dehydrogenase 1	Btau	Pvit	—	Ecab	Hsap	—	—	Mmus	Dvir
NADH dehydrogenase 2	Btau	Pvit	—	Ecab	Hsap	—	—	Mmus	Dvir
NADH dehydrogenase 3	Btau	Pvit	—	Ecab	Hsap	—	—	Rnor	Dvir
NADH dehydrogenase 4	Btau	Pvit	—	Ecab	Hsap	—	—	Rnor	Dvir
NADH dehydrogenase 5	Btau	Pvit	—	Ecab	Hsap	—	—	Mmus	Dvir
NADH dehydrogenase 6	Btau	Pvit	—	Ecab	Hsap	—	—	Mmus	Dvir
NADH dehydrogenase 4L	Btau	Pvit	—	Ecab	Hsap	—	—	Mmus	Dvir
Cytochrome c oxydase I	Btau	Pvit	—	Ecab	Hsap	—	—	Mmus	Dvir
Cytochrome c oxydase II	Btau	Hgry	—	Ecab	Tban	—	—	Mmus	Dvir
Cytochrome c oxidase III	Bmus	Hgry	—	Ecab	Hsap	—	—	Rnor	Dvir
ATPase subunit 6	Btau	Pvit	—	Ecab	Hsap	—	—	Mmus	Dvir
ATPase subunit 8	Btau	Pvit	—	Ecab	Hsap	—	—	Mpen	Dvir

Note. Abbreviations: CET, Cetartiodactyla; Bmus, *Balaenoptera musculus;* Btau, *Bos taurus;* Cdro, *Camelus dromedarius;* Chir, *Capra hircus;* Lgua, *Lama guanicoe;* Oari, *Ovis aries;* Rtar, *Rangifer tarandus;* Sscr, *Sus scrofa;* CAR, Carnivora; Aful, *Ailurus fulgens;* Cfam, *Canis familiaris;* Clup, *Canis lupus;* Fcat, *Felis catus;* Hgry, *Halichoerus grypus;* Llut, *Lutra lutra;* Pvit, *Phoca vitulina;* Vvul, *Vulpes vulpes;* HYR, Hyracoidea; Pcap, *Procavia capensis;* PER, Perissodactyla; Csim, *Ceratotherium simum;* Ecab, *Equus caballus;* Egre, *Equus grevyi;* Easi, *Equus asinus;* Tind, *Tapirus indicus;* Tpin, *Tapirus pinchaque;* PRI, Primates; Cape, *Cebus apella;* Hsap, *Homo sapiens;* Lful, *Lemur fulvus;* Mnem, *Macaca nemestrina;* Mfas, *Macaca fascicularis;* Mmul, *Macaca mulatta;* Pcyn, *Papio cynocephalus;* Pham, *Papio hamadryas;* Ppyg, *Pongo pygmaeus;* Tban, *Tarsius bancanus;* PRO, Proboscidea; Emax, *Elephas maximus;* Lafr, *Loxodonta africana;* SIR, Sirenia; Ddug, *Dugong dugon;* Tinu, *Trichechus inunguis;* Tman, *Trichechus manatus;* MYO, Myomorpha; Mmus, *Mus musculus;* Rnor, *Rattus norvegicus;* Spol, *Spalax polonicus;* Sleu, *Spalax leucodon ehrnbergi;* Mmar = *Marmota marmota;* Maur, *Mesocricetus auratus;* Mung, *Meriones unguiculatus;* Hall, *Hylomyscus alleni;* Mpen, *Microtus pennsylvanicus;* OUT, Noneutherian outgroup; Bmul, *Bungarus multicinctus;* Ccot, *Coturnix coturnix;* Dvir, *Didelphis virginiana;* Ggal, *Gallus gallus;* Mgig, *Macropus giganteus;* Mruf, *Macropus rufus;* Mdom, *Monodelphis domestica;* Smac, *Sminthopsis macroura.*

letic, and, therefore, valid. Genetic distances were computed by correcting for multiple hits (Kimura, 1983). Phylogenetic trees were constructed by using three reconstruction methods: neighbor joining (Saitou and Nei, 1987) by means of the CLUSTAL W program, maximum parsimony with the PROTPARS program in the PHYLIP package (Felsenstein, 1989), and maximum likelihood with PROTML (Adachi and Hasegawa, 1992). Reliability of internal branches of neighbor-joining trees was ascertained by 1000 bootstrap replicates (Felsenstein, 1985). To evaluate the extent to which a maximum likelihood tree is a significantly better representation of the true tree than the alternative possible trees, we estimated the bootstrap probability by the resampling of the estimated log-likelihood method with 10,000 replicates (Kishino *et al.*, 1990).

For purposes of maximum utilization of the molecular data, we address each question in this study by using the smallest possible number of taxa.

RESULTS

In the first stage of the analysis, we checked whether Perissodactyla is nested within the Paenungulata, i.e., closer to hyraxes than either is to sirenians and proboscideans, as advocated by Prothero and colleagues (1988; Prothero, 1993). Four protein sequences, αA crystallin, hemoglobin α, hemoglobin β, and exon 28 of von Willebrand factor, are available for Sirenia, Proboscidea, Hyracoidea, Perissodactyla, and Primates. The length of the aligned concatenated sequence was 826 amino acids. With four ingroup taxa and an outgroup (Primates), there are 15 possible phylogenetic trees (Table 2). Trees 1–3 are consistent with paenungulate monophyly, whereas trees 4–12 indicate that Perissodactyla should be included within Paenungulata. Trees 13–15 are inconsistent with paenungulate monophyly even if Perissodactyla is included within this superorder. By using the neighbor-joining method we obtained tree 2. Judging by the bootstrap value for the clustering of Hyracoidea and Proboscidea to the exclusion of Sirenia (394/1,000), however, none of the three possible internal arrangements for the three paenungulate orders (trees 1–3) is significantly better than the other two. The Hyracoidea–Proboscidea–Sirenia clade, on the other hand, is supported by all 1000 bootstrap replicates. Trees 1 and 3 emerge as equally parsimonious, each requiring 399 amino acid replacements. Tree 2 requires 400 amino acid replacements and is therefore equally likely. Trees in which the Paenungulata are rendered paraphyletic by Primates or Perissodactyla require 24–34 additional amino acid replacements. Topology 3 turned out to be the maximum likelihood tree. A comparison among the 15 alternative trees by the maximum likelihood method is shown in Table 2. The combined bootstrap probability for trees 1–3 is 100%, as opposed to a combined probability of zero for all the other trees. Therefore, the molecular data indicate conclusively that Perissodactyla is not nested within the Paenungulata.

TABLE 2

Comparison among 15 Possible Alternative Phylogenetic Trees for Primates (Pri), Perissodactyla (Per), Sirenia (Sir), Proboscidea (Pro), and Hyracoidea (Hyr) by the Maximum Likelihood Method

Tree topology	Log-likelihood difference from the maximum likelihood tree (±SE)	Bootstrap probability of tree being the ML tree from among 15 possible trees (%)
1 (Pri, (Per, (Hyr, (Sir, Pro))))	−2.44 ± 9.78	28.87
2 (Pri, (Per, (Pro, (Hyr, Sir))))	−3.10 ± 9.55	25.19
3 (Pri, (Per, (Per, (Hyr, Pro))))	Maximum likelihood tree	45.94
4 (Pri, (Pro, (Per, (Hyr, Sir))))	−69.92 ± 21.72	0.00
5 (Pri, (Pro, (Sir, (Hyr, Per))))	−88.66 ± 22.31	0.00
6 (Pri, (Pro, (Hyr, (Sir, Per))))	−90.84 ± 21.93	0.00
7 (Pri, (Hyr, (Per, (Sir, Pro))))	−75.52 ± 21.84	0.00
8 (Pri, (Hyr, (Sir, (Per, Pro))))	−90.55 ± 22.00	0.00
9 (Pri, (Hyr, (Pro, (Sir, Per))))	−95.47 ± 21.28	0.00
10 (Pri, (Sir, (Per, (Hyr, Pro))))	−67.55 ± 19.76	0.00
11 (Pri, (Sir, (Hyr, (Per, Pro))))	−83.65 ± 22.61	0.00
12 (Pri, (Sir, (Pro, (Per, Hyr))))	−84.50 ± 22.53	0.00
13 (Pri, ((Pro, Per), (Sir, Hyr)))	−69.77 ± 21.69	0.00
14 (Pri, ((Sir, Per), (Pro, Hyr)))	−74.88 ± 18.26	0.00
15 (Pri, ((Pro, Sir), (Per, Hyr)))	−73.98 ± 15.49	0.00

TABLE 3

Comparison among 15 Possible Alternative Phylogenetic Trees for Primates (Pri), Perissodactyla (Per), Carnivora (Car), Paenungulata (Pae), and Cetartiodactyla (Cet) by the Maximum Likelihood Method

Tree topology	Log-likelihood difference from the maximum likelihood tree (±SE)	Bootstrap probability of tree being the ML tree from among 15 possible trees (%)
1 (Pri, (Pae, (Per, (Cet, Car))))	−9.25 ± 13.92	24.09
2 (Pri, (Pae, (Car, (Cet, Per))))	Maximum likelihood tree	73.21
3 (Pri, (Pae, (Cet, (Car, Per))))	−20.60 ± 11.88	0.90
4 (Pri, (Cet, (Car, (Pae, Per))))	−60.81 ± 22.15	0.01
5 (Pri, (Car, (Cet, (Pae, Per))))	−48.45 ± 21.39	0.55
6 (Pri, ((Pae, Per), (Car, Cet)))	−46.88 ± 22.87	0.39
7 (Pri, (Per, (Cet, (Car, Pae))))	−66.08 ± 20.99	0.00
8 (Pri, (Per, (Pae, (Cet, Car))))	−53.31 ± 22.20	0.04
9 (Pri, (Per, (Car, (Pae, Cet))))	−53.91 ± 23.19	0.41
10 (Pri, (Cet, (Per, (Pae, Car))))	−76.71 ± 19.61	0.00
11 (Pri, (Cet, (Pae, (Per, Car))))	−71.18 ± 19.64	0.00
12 (Pri, (Car, (Per, (Cet, Pae))))	−52.24 ± 21.27	0.30
13 (Pri, (Car, (Pae, (Cet, Per))))	−48.19 ± 16.08	0.06
14 (Pri, ((Car, Per), (Pae, Cet)))	−58.46 ± 21.45	0.04
15 (Pri, ((Pae, Car), (Per, Cet)))	−53.62 ± 15.30	0.00

Next, we tested the phylogenetic integrity of Altungulata and Ungulata. In this analysis, the three paenungulate orders were treated as a single taxon, and their phylogenetic affinities to Perissodactyla, Cetartiodactyla, and Carnivora (a nonungulate taxon) were reconstructed, with Primates as an outgroup. In this case we base our reconstruction on 10 proteins: insulin, prolactin, αA crystallin, interleukin-2, myoglobin, hemoglobin α, hemoglobin β, cytochrome b, growth hormone, and exon 28 of von Willebrand factor. The length of the aligned concatenated sequence consisting of these proteins is 1908 amino acids. Again, we deal with 15 possible topologies (Table 3). Trees 4–6 are consistent with altungulate monophyly; tree 5 is consistent with the superorder Ungulata. In all the other possible trees, the altungulates are paraphyletic. The neighbor-

joining method yields tree 1. However, phylogenies 2 and 3 cannot be excluded on the basis of the bootstrap value (622/1000) for the clustering of Cetartiodactyla and Carnivora to the exclusion of Perissodactyla. In contrast, the branch separating the Paenungulata from the Perissodactyla–Carnivora–Cetartiodactyla clade is supported by 983 of 1000 bootstrap replicates. Tree 2 emerges as the most parsimonious arrangement, with a total length of 942 amino acid replacements. It cannot, however, be shown to be significantly better than tree 1 with 949 amino acid replacements. Tree 3, on the other hand, with 955 replacements, is significantly lengthier than trees 1 and 2. The trees in which Paenungulata clusters with Perissodactyla to the exclusion of the other three taxa (trees 4–6) require 29–32 additional amino acid replacements. Other trees require up to 43 more replacements than the most parsimonious tree. Topology 2 also turned out to be the maximum likelihood tree (Table 3). The combined bootstrap probability for trees 1–3 is 98.2%, as opposed to a negligible combined probability of 0.95% for the three trees (4–6) in which Perissodactyla is a sister group of Paenungulata. Altungulata and Ungulata, therefore, do not seem to constitute monophyletic clades.

Next, with the aim of determining whether the paenungulates are closer to the clade that includes Perissodactyla, Cetartiodactyla, and Carnivora or to Primates, we added to the phylogenetic analysis a noneutherian outgroup. Eight sequences (insulin, prolactin, growth hormone, αA crystallin, myoglobin, hemoglobin α, hemoglobin β, and cytochrome b) with a total concatenated length of 1426 aligned amino acids were available for analysis. With any of the three methods of phylogenetic reconstruction, we were unable to resolve the trichotomy among Primates, Paenungulata, and the Perissodactyla–Carnivora–Cetartiodactyla clade. The trichotomy remained unresolved with all methods of reconstruction even after treating Perissodactyla, Carnivora, and Cetartiodactyla as a single clade, thereby reducing the number of taxa in the analyses. Since myomorph rodents are now generally believed to be basal to the above ingroup lineages, and since they are closer evolutionarily to the ingroup than either avians or marsupials, we repeated the previous analyses by using myomorphs as outgroup. Nine protein sequences (cytochrome b, insulin, prolactin, αA-crystallin, myoglobin, α and β globin, growth hormone, and exon 28 of von Willebrand factor) with a total concatenated length of 1778 aligned amino acids were available. The neighbor-joining and maximum parsimony analyses yielded a clustering of Paenungulata and the Perissodactyla–Carnivora–Cetartiodactyla clade. However, the branch connecting this clade was not supported by bootstrap. The maximum likelihood analysis supported a clustering of the Paenungulata with Primates to the exclusion of the Perissodactyla–Carnivora–Cetartiodactyla clade. However, the bootstrap probability of this tree was only 74.59%.

Finally, we attempted to disentangle the Perissodactyla–Carnivora–Cetartiodactyla trichotomy by using 36 protein sequences: insulin-like growth factor I, insulin, β chorionic gonadotropin, prolactin, phospholipase A-2, CD44 antigen, Na^+,K^+-ATPase α1-subunit, serum albumin, atrial natriuretic polypeptide, αA-crystallin, γ-interferon, interleukin-2, pancreatic polypeptide, tumor necrosis factor α, colipase, myoglobin, cytochrome c, plasminogen, β-globin, α-globin, growth hormone, SRY protein, exon 28 of von Willebrand factor protein, and all the 13 proteins encoded by the mitochondria: NADH dehydrogenase subunits 1, 2, 3, 4, 4L, 5, and 6, cytochrome c oxydase subunits 1–3, ATPase subunits 6 and 8, and cytochrome b. The length of the concatenated sequence was 7885 aligned amino acids. Primates was used as the outgroup. There are three possible trees (Table 4). The neighbor-joining method yields phylogeny 1, an arrangement supported by 978/1000 bootstrap replicates. Tree 1 also emerged as the most parsimonious arrangement, with a total length of 3206 amino acid replacements. Trees 2 and 3 required 3221 and 3216 amino acid replacements, respectively. Tree 1 also turned out to be the maximum likelihood tree, with a bootstrap probability of 85.42%. This tree is therefore significantly better than the other two alternative trees. The length of the internal branch is only about a quarter the values of the terminal branches leading to Perissodactyla and the Artiodactyla + Cetacea clade, and, therefore, the Perissodactyla–Carnivora–Artiodactyla + Cetacea trichotomy seems to be rather tight. Nevertheless, the currently available data indicate that Perissodactyla clusters with the Artiodactyla + Cetacea clade to the exclusion of Carnivora.

DISCUSSION

In this study, we present molecular evidence for the evolutionary relationships of Perissodactyla relatively

TABLE 4

Comparison among Three Possible Alternative Phylogenetic Trees for Perissodactyla (Per), Carnivora (Car), and Cetartiodactyla (Cet), with Primates (Pri) as Outgroup, by the Maximum Likelihood Method

Tree topology	Log-likelihood difference from the maximum likelihood tree (±SE)	Bootstrap probability of tree being the ML tree from among three possible trees (%)
1 (Pri, (Car, (Cet, Per)	Maximum likelihood tree	85.42
2 (Pri, (Cet, (Per, Car)	−40.71 ± 31.18	8.30
3 (Pri, (Per, (Cet, Car)	−42.92 ± 30.99	6.28

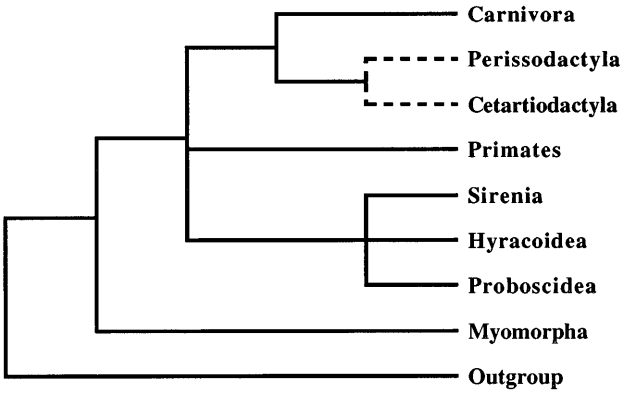

FIG. 1. Schematical relationships among eight eutherian taxa deduced from separate analyses of distinct sets of protein sequences. Only the order of branchings in the tree is significant; branch lengths do not indicate evolutionary distances. Trichotomies indicate unresolved branching order. The dashed line indicates a tentative relationship.

to other mammalian orders. The ordinal relationships emerging from this study is schematically summarized in Fig. 1. We show conclusively that horses are closely related to the clade consisting of artiodactyls and cetaceans, and more distantly to carnivores, and do not exhibit any particular affinity to the paenungulate taxa. This finding invalidates the superordinal taxa Altungulata (Proboscidea, Sirenia, Hyracoidea, and Perissodactyla) and Ungulata (Altungulata + Artiodactyla + Cetacea). The relationships among Paenungulata, Primates, and the clade consisting of Perissodactyla, Carnivora, and Cetartiodactyla could not be resolved on the basis of the available data.

Taken in its entirety, our present study illustrates that, as far as mammalian ordinal phylogeny is concerned, there is little congruence between morphological and molecular data. To date, several higher-order taxa within Mammalia, which had been defined according to morphological criteria, have been invalidated by molecular studies. These taxa are Rodentia (Graur *et al.*, 1991, 1992; D'Erchia *et al.*, 1996), Glires (Lagomorpha + Rodentia) (Graur *et al.*, 1996), both Volitantia (Chiroptera + Dermoptera) and Archonta (Primates + Scandentia + Chiroptera + Dermoptera) (Bailey *et al.*, 1992; Stanhope *et al.*, 1992, 1996; Goodman *et al.*, 1994; Porter *et al.*, 1996), both Anagalidia and Paenungulata (de Jong *et al.*, 1993; Madsen *et al.*, 1996), and Theria (Eutheria + Metatheria) (Janke *et al.*, 1996). Clearly, superordinal morphological cladograms, such as the one by Novacek (1992, 1993), are challenged by the molecular data.

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