CURRENT TOPIC

Evolution of the Placenta and Fetal Membranes Seen in the Light of Molecular Phylogenetics

A. M. Carter[a]

Department of Physiology and Pharmacology, University of Southern Denmark, Winsloewparken 21, DK-5000 Odense, Denmark

Recent analyses of nucleotide sequence data suggest that living placental mammals belong to one of four superorders. The early divergence of these groups was followed by long periods of geographical isolation, due to the break up of continental land masses, allowing for convergent evolution of similar traits in different superorders. As an example, the transition from epitheliochorial to haemochorial placentation occurred independently in bats, rodents, anthropoid primates, armadillos and others. A group of ancient African mammals is suggested by the molecular data, but is not fully supported by morphological evidence. The hypothesis is, however, consistent with some of the data on fetal membranes, suggesting that it would be worthwhile to study the early development of tenrecs, golden moles and elephant shrews. Analyses of fetal membrane traits that group the tarsiers with anthropoid primates, and separate them from the lemurs, are challenged by the molecular data. Other relatives of the primates seem to include tree shrews and flying lemurs, and little is known about the fetal membranes of the latter group. Comparative studies of placental function normally are confined to primates, rodents, lagomorphs and domestic animals: the biological diversity represented by mammals that evolved in ancient Africa and South America is not represented. Therefore, future comparative studies should strive to include species such as the rock hyrax and the armadillo. © 2001 Harcourt Publishers Ltd
Placenta (2001), **22**, 800–807

INTRODUCTION

Fetal membranes and placentation have often been seen as a guide to the phylogeny of placental mammals (Hill, 1932; Mossman, 1937; Luckett, 1993). It now seems pertinent to reverse the process and review current concepts of placental development in the light of modern phylogenetics, which can establish interrelationships between mammalian orders with some certainty. Of particular note are two recent analyses of large data sets, based on the nucleotide sequences of nuclear and mitochondrial genes from many species (Madsen et al., 2001; Murphy et al., 2001). These studies resolve the placental mammals into four superordinal clades, as shown in Figure 1. Divergence of these groups occurred in the Cretaceous era, about 100 million years ago, well before the Cretaceous/ Tertiary (K/T) boundary that marks the demise of the dinosaurs. Geographical isolation between groups then occurred with the breakup of the continents (Hedges et al.,

1996). This laid the ground for a remarkable degree of parallel evolution as the mammals expanded into ecological niches vacated by the dinosaurs. The tendency to convergent evolution is reflected in placental development, with haemochorial placentation evolving independently in each of the four superorders.

ANCESTRAL FORMS

The importance of defining ancestral or primitive features is that they underpin the findings arrived at by the cladistic approach to phylogenetics. It is the sharing of derived or advanced characters between species that indicates a shared phylogenetic relationship; the retention of an ancestral state does not (Ridley, 1986). An example of a primitive or ancestral feature is the choriovitelline placenta, formed by fusion of the yolk sac and chorion. This is the definitive placenta in all marsupials (except bandicoots). However, in eutherian mammals, a choriovitelline placenta occurs only as a temporary state of development, for its functions are assumed by a chorioallantoic placenta. Thus the choriovitelline placenta is an

[a] To whom correspondence should be addressed at: Department of Physiology and Pharmacology, University of Southern Denmark, Winsloewparken 21, DK-5000 Odense, Denmark. Fax: 45-6613-3479; E-mail: acarter@health.sdu.dk
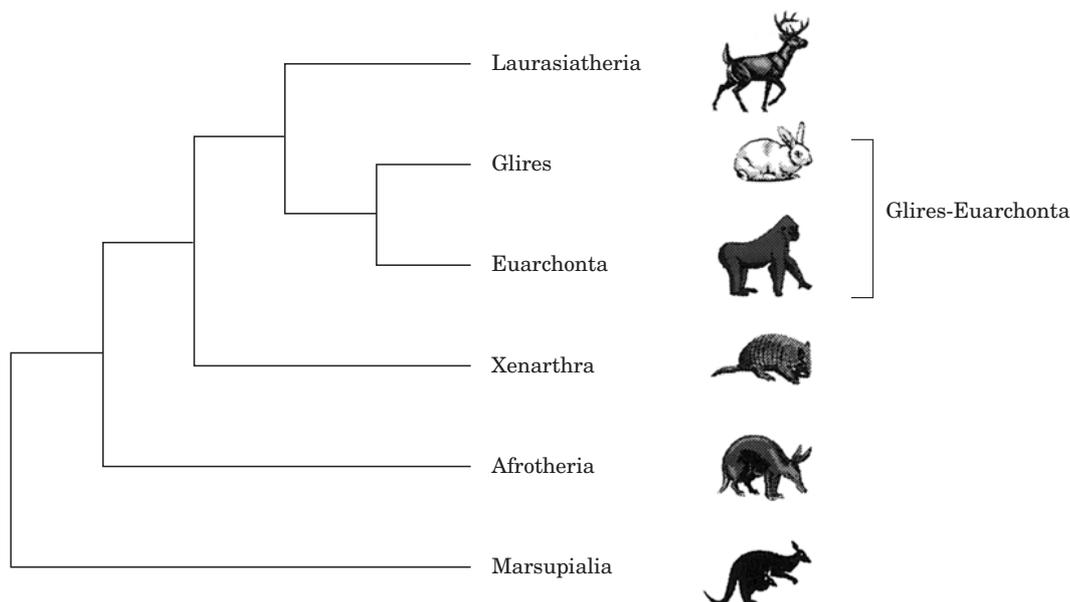
Figure 1. Four superorders of mammals are supported by analysis of nucleotide sequence data with marsupials as an outgroup to anchor the tree (Madsen et al., 2001; Murphy et al., 2001). Separation of these superorders occurred in the Cretaceous era with the break up of the continents, first into Laurasia (present day Europe, Asia and North America) and Gondwanaland (present day Africa and South America), and then with separation of Africa from South America. Glires, the rodents and lagomorphs, and Euarchonta, which includes primates, are sister taxa in the superorder Glires-Euarchonta.

ancestral feature and its absence is regarded as an advanced feature (Luckett, 1976).

As first suggested by Huxley (1880), the earliest eutherians may have been insectivore-like creatures. These ancestral forms likely would have had diffuse epitheliochorial placentation, a large allantoic vesicle and an amnion formed by folding rather than cavitation (Luckett, 1976). Implantation would have been paraembryonic and noninvasive. Early in development, a large vascular yolk sac would have been present and participated in the formation of a choriovitelline placenta. However, the yolk sac would have been reduced in later stages (Luckett, 1993).

A DIVERSE GROUP: LAURASIATHERIA

The primitive traits of the putative ancestral stock are best preserved in the Laurasiatherians. This superorder is one of two that occupied the northern supercontinent of Laurasia following its separation from the southern supercontinent of Gondwanaland. It includes the whales, artiodactyls, perissodactyls, carnivores, pangolins, bats and core insectivores. Within this clade, only the bats show many advanced characters in their placentation (see below).

Grouping of whales and porpoises with artiodactyls (cloven-hoofed mammals) as Cetartiodactyla is strongly supported by the molecular data and consistent with a morphological analysis of skeletal features in extant and fossil forms (Novacek, 1992). Whales and porpoises have diffuse, epitheliochorial placentation. Likewise, artiodactyls have epitheliochorial placentae of the diffuse (e.g. domestic pig, hippopotamus, llama) or cotyledonary type (e.g. sheep, giraffe, antelopes). An advanced feature in ruminants is fusion of fetal binucleate cells with uterine epithelial cells to form syncytial plaques, a condition referred to as synepitheliochorial (Wooding et al., 1993).

The perissodactyls (horses, tapirs and rhinos) and pangolins or scaly anteaters also have diffuse, epitheliochorial placentae. However, in equids, girdle cells of fetal origin invade the uterine epithelium to form endometrial cup cells (Enders and Liu, 1991). Mossman (1987) noted the resemblance in definitive yolk sac placentation between whales, artiodactyls, perissodactyls and pangolins, but grouped them together with some non-laurasiatherians.

Carnivores

There are terrestrial and aquatic carnivores (sealions, walruses and seals). Most have zonary or circumferential endotheliochorial placentae (Mossman, 1987), although the hyena develops haemochorial placentation late in pregnancy (Wynn et al., 1990). The fetal membranes of carnivores share many of the primitive characters seen in cetartiodactyls and perissodactyls. Indeed, Mossman (1937) once considered the carnivore type of fetal membrane to be the most primitive among extant eutherians, because both the yolk sac and allantoic sac are large and persist until term.

Bats

There has been much debate about a possible polyphyletic origin for megabats (fruit-eating bats) and microbats, with

the megabats at one time characterized as flying primates (Pettigrew, 1986). This dispute seems now to be settled in favour of bat monophyly. Megabats retain an epitheliochorial placenta, with amniogenesis by cavitation as their only advanced developmental feature. Meanwhile, as befits a widely diversified adaptive group of mammals (Enders et al., 1998), microbats have evolved a multiplicity of endotheliochorial and haemochorial placental types (Badwaik and Rasweiler, 2000) and exhibit many other advanced features of membrane development (Luckett, 1993).

Core insectivores

Included among laurasiatherians are the core insectivores: moles, shrews and hedgehogs (Eulipotyphla). Since divergence between the superorders likely occurred at the insectivore stage, it is perhaps not surprising that such forms have persisted in three of the superorders. Thus tenrecs and golden moles are found in Afrotheria and tree shrews in Glires-Euarchonta. The core insectivores have similar yolk sac placentation (Mossman, 1987), but vary greatly in the nature of their definitive placenta, which is epitheliochorial in moles, endotheliochorial in shrews and haemochorial in hedgehogs. Hedgehogs have some additional advanced features, such as amnion formation by cavitation (Luckett, 1993).

OF MICE AND MEN: GLIRES AND EUARCHONTA

This is the second of the superorders associated with the Laurasian supercontinent. In contrast to laurasiatherians, most mammals in this group display haemochorial placentation, though this has been independently evolved at least four times: in flying lemurs, tarsiers, anthropoid primates, and in rodents and lagomorphs.

Rodents and lagomorphs

Mossman (1937, 1987) argued for a close relationship between rodents and lagomorphs (rabbits and pikas) based on a persist-ent, inverted yolk sac placenta and small to absent allantoic sac. His interpretation was controversial at the time, but it receives strong support from molecular phylogenetics, which groups rodents and lagomorphs together in the cohort Glires (Murphy et al., 2001). Rodents and lagomorphs have haemochorial placentae of the labyrinthine type, though different degrees of thinning result in mono-, di- or trihaemochorial placentation (Enders, 1965). With regard to fetal membrane development, the most advanced features are found in the hystricognaths, which include New and Old World porcupines, guinea pigs and chinchillas. Squirrels have mostly primitive features, with voles, mice and rats being intermediate. The fetal membranes of lagomorphs resemble those of squirrels, as was noted by

Mossman (1937), and squirrels are the rodents most closely related to rabbits and pikas according to nucleotide sequence analysis (Murphy et al., 2001).

Primates

The association of Glires with primates, tree shrews and flying lemurs, collectively referred to as Euarchonta (Madsen et al., 2001), receives strong support from the recent phylogenetic analyses, but is not definitive. Grouping of monkeys, apes and man (anthropoids) with lemurs, lorises and tarsiers remains likely on this analysis and is supported by morphological data (Purvis, 1995).

The position of the tarsiers has long been debated (Le Gros Clark, 1962; Purvis, 1995) and has important implications for placental phylogeny (Carter, 1999). Some features of the skeleton and soft tissues, as well as the palaeontological record, suggest that the tarsiers and the lemurs are closely related (Le Gros Clark, 1962). However, on the evidence of the fetal membranes and placenta, Luckett (1976) grouped primates in two suborders: strepsirhine (lemurs and lorises) and haplorhine (tarsiers, monkeys and apes). In thus separating the lemurs from the tarsiers, he followed the lead of Hill (1932). The views of these two eminent placentologists are, however, contradicted by the molecular phylogeneticists, who present strong evidence for a deep divergence between lemurs and tarsiers and the other primates.

Lemurs and lorises have epitheliochorial placentation, but tarsiers have a discoid, haemochorial placenta. Thus, the evidence from molecular phylogenetics suggests that haemo-chorial placentation evolved separately in tarsiers and monkeys, as indeed was conceded by Hill (1932).

Tree shrews and flying lemurs

Tree shrews have led an itinerant existence, being classified both as insectivores and as primates. They have a quite distinctive form of endotheliochorial placentation, involving twin discoidal attachments to special pads developed on the lining of the uterus (Luckett, 1969). Conservative features of their fetal membranes include retention of a large allantoic vesicle and a large yolk sac (Luckett, 1969). Tree shrews are now grouped in the Euarchonta together with, but separate from, the primates. There is strong support from the molecular studies for a sister grouping of tree shrews with flying lemurs, which exhibit haemochorial placentation. Flying lemurs have some additional, derived features, such as amnio-genesis by cavitation and implantation involving the embryonic pole (Luckett, 1993).

ENDEMIC SOUTH AMERICAN MAMMALS: XENARTHRA

Two superorders of mammals are thought to have evolved on the southern supercontinent of Gondwanaland. One of these,

Xenarthra, comprises the sloths, New World anteaters and armadillos. Based on morphological evidence, they were previously grouped with the pangolins as Edentata. However, this hypothesis is not supported by a detailed analysis of skeletal characters (Rose and Emry, 1993) or by the molecular data.

Sloths, anteaters and armadillos

Sloths and New World anteaters are united by phylogenetic analysis in the suborder Piloda, with armadillos as a sister group (Murphy et al., 2001). Luckett (1993) grouped sloths, anteaters and armadillos together based on a cladistic analysis of their fetal membranes and cranioskeletal features. Their shared, derived features include discoid placentae, which are endotheliochorial in sloths and haemomonochorial in anteaters and armadillos. Similarities between the fetal membranes of these mammals and primates, including the nature of yolk sac placentation, led Mossman (1987) into considering a possible phylogenetic relationship, but this controversial idea is not supported by analysis of bones and teeth (Luckett, 1993) or by molecular data (Murphy et al., 2001).

ANCIENT AFRICAN MAMMALS: AFROTHERIA

This superordinal clade was first proposed on the basis of molecular evidence (Springer et al., 1997) and is strongly supported by the most recent analyses. Following the breakup of Gondwanaland, Africa separated from South America, and remained geographically isolated until it connected with Europe (Hedges et al., 1996). There was thus a window of opportunity from the Late Cretaceous to the Early Caenozoic for the diversification of its fauna. This explains why there is a separate group of African frogs (Hedges et al., 1996) and it underpins the hypothesis of a mammalian superorder Afrotheria. Additionally, representatives of this group first appear in the fossil record in Africa (Springer et al., 1997). Nevertheless, there is a lack of morphological evidence for the clade as a whole (Asher, 1999). They do share some primitive traits in their fetal membranes, such as the temporary appearance of a choriovitelline placenta and retention of a large allantoic vesicle. However, shared ancestral traits are not the best guide to phylogenetic relationships (Ridley, 1986).

Sea cows, elephants and hyraxes

There is good support from skeletal and soft tissue morphology for grouping the elephants with the sea cows (manatees and dugongs) and hyraxes as Paenungulata (Shoshani and McKenna, 1998; Liu et al., 2001). Mossman (1987) also grouped them together because of the similarity of their definitive yolk sacs. Elephants and manatees form a nested group within the paeungulates (Tethytheria) and have endotheliochorial placentation. The hyraxes, or Biblical conies, are small herbivores that occupy similar niches to rabbits (Young, 1962). They were Africa's dominant small- to medium-sized terrestrial herbivores during the Oligocene (Madsen et al., 2001). The extant forms have haemochorial placentation.

Tenrecs, golden moles, elephant shrews and the aardvark

Tenrecs are African insectivores resembling European hedgehogs. Together with the South African golden moles, they were once classified in the insectivore order, but are now included with the afrotherians. They have haemochorial placentation, as do the elephant shrews (Cutler et al., 1998). Interestingly, Mossman (1987) grouped the tenrecs with the elephant shrews because they shared several traits, including a free definitive yolk sac and a medium sized allantoic sac. The aardvark has a rather similar definitive yolk sac and endotheliochorial placentation.

PERSPECTIVES FOR PLACENTAL RESEARCH

Placental characteristics have been used to aid classification ever since Huxley (1864) distinguished between mammals with deciduate and non-deciduate placentae. Later, Mossman (1937) stressed the importance of considering all available data on the fetal membranes and placenta, not just the nature of the definitive placenta. This approach enabled him correctly to deduce a close relationship between the rodents and lagomorphs and to group tenrecs with elephant shrews. However, Mossman (1937, 1987) also proposed some controversial phylogenetic relationships that are not supported by other morphological criteria or by modern molecular analyses. In large part this resulted from his opinion that convergent evolution was less likely to occur in fetal membranes than in skeletal or dental traits. The contrary view, that individual characters of the fetal membranes and placenta have undergone convergent evolution several times (Luckett, 1976), harmonizes better with the findings of molecular phylogenetics.

Characters that are prone to convergent evolution are a poor guide to phylogenetics. The advantage of reducing the number of layers in the interhemal membrane is clearly great enough for such adaptations to have been selected many times. Haemochorial placentation is therefore found in many groups (Table 1), although it should be noted that Enders et al. (1998) instanced five different types of haemochorial placentation. Moreover, haemochorial placentation is achieved by quite different developmental pathways in, for example, rodents, primates and armadillos (Enders and Welsh, 1993). Convergent evolution of haemochorial placentation extends to trophoblast invasion of maternal vessels as, for example, in bats (Badwaik and Rasweiler, 2001) and hystricomorph rodents (Carter et al., 1998).

Table 1. A mammalian classification based on the findings of molecular phylogenetics. The placentae of ancestral forms are thought to have been epitheliochorial. Convergent evolution is indicated by the separate development of haemochorial placentation at least once in each of the four superorders. A temporary yolk sac is the ancestral form with complete inversion of the yolk sac regarded as a derived character

Group	Definitive Chorioallantoic Placenta	Definitive Yolk Sac Placenta[a]
Superorder Laurasiatheria		
Whales, porpoises, cloven-hoofed mammals	Epitheliochorial or synepitheliochorial (ruminants)	Usually temporary, small if retained
Horses, tapirs, rhinos	Epitheliochorial	Usually temporary, small if retained
Carnivores	Endotheliochorial or haemomonochorial (hyenas)	Permanent, large, T-shaped
Pangolins or scaly anteaters	Epitheliochorial	Permanent, small, attached
Bats		
Microbats	Endothelio- or haemochorial[b]	Permanent and free or incompletely inverted
Megabats (Asian fruit bats)	Haemomono- or haemodiochorial	Permanent, free, glandular
Hedgehogs, shrews, moles	Epithelio-, endothelio- or haemochorial and labyrinthine	Permanent, incompletely inverted
Superorder Glires-Euarchonta		
Rodents	Haemomono- or haemotrichorial, labyrinthine[c]	Permanent and incompletely or completely inverted
Lagomorphs	Haemodichorial, labyrinthine	Permanent, incompletely inverted
Primates		
Monkeys, apes, man	Haemomonochorial, villous	Temporary
Lemurs, tarsiers	Epitheliochorial (lemurs) or haemochorial (tarsiers)	Temporary
Flying lemurs	Haemochorial, labyrinthine	Uncertain
Tree shrews	Endotheliochorial	Permanent, large, free
Superorder Xenarthra		
Sloths, anteaters, armadillos	Endotheliochorial (sloths) or haemomonochorial and villous (anteaters, armadillos)	Temporary (sloths) or permanent with complete inversion but avascular (armadillos)
Superorder Afrotheria		
Elephants, sea cows	Endotheliochorial	Temporary
Hyraxes or conies	Cellular, haemomonochorial, labyrinthine	Temporary
Tenrecs, golden moles	Haemochorial, labyrinthine	Permanent and free (tenrecs) or trilaminar (golden moles)
Aardvark	Endotheliochorial	Rudimentary
Elephant shrews	Haemochorial, labyrinthine	Permanent, free

[a]Data from Mossman (1987).
[b]There is great diversity in the placentation of the microbats (Enders et al., 1998; Badwaik and Rasweiler, 2000).
[c]The kangaroo rat (*Dipodomys*) and Cape spring hare (*Pedetes*) have endotheliochorial placentation (Tibbits and King, 1975; Fischer and Mossman, 1969).

Other fetal membrane characters are more highly conserved and offer a more reliable guide to phylogeny than does the nature of the interhemal membrane. This is exemplified in Table 1 by the definitive form of the yolk sac placenta. A temporary yolk sac is the ancestral form with complete inversion of the yolk sac regarded as a derived character (Luckett, 1976). However, the yolk sac placentation of many species exhibits advanced features that cannot be accommodated in this scheme (King and Enders, 1993). Moreover, the inverted yolk sac of the armadillo is avascular and it clearly subserves different functions than the highly vascularized inverted yolk sac of rodents (Enders, personal communication).

As emphasized by Luckett (1993), it is hazardous to draw conclusions based on only one type of data, be it fetal membranes, dentition or nucleotide sequences. The two most recent studies are based on large data sets. Murphy et al. (2001) examined 18 gene segments totalling 9779 base pairs. Madsen et al. (2001) used a set of 5708 base pairs for their primary analysis and one of 2947 base pairs for hypothesis testing. Their conclusions are largely supported by a recent meta-analysis of over 300 morphological and molecular data sets (Liu et al., 2001; Springer and de Jong, 2001). However, although the molecular data are extensive, they are not intrinsically better than morphological data. It is pertinent to ask if developmental traits contradict the more controversial conclusions of the molecular studies or can add support to the weaker of their associations.

African insectivores

That there is a superordinal clade Afrotheria is a hypothesis based entirely on molecular data. There is sound anatomical support for grouping elephants, sea cows and hyraxes in the taxon Paenungulata (Shoshani and McKenna, 1998) and this association is consistent with the palaeontological record (Colbert, 1961). A further similarity between these mammals is

Table 2. Evidence in support of inclusion of the tenrecs in a clade of African mammals (Afrotheria) or in an insectivore clade (Lipotyphla)

	Supports inclusion in Afrotheria	Supports inclusion in Lipotyphla	Reference
Cranial, dental and postcranial skeletal characters	−	+	Asher (1999)
Nucleotide sequence data	+	−	Madsen et al. (2001); Murphy et al. (2001); Stanhope et al. (1998)
Protein sequence signatures	+	−	van Dijk et al. (2001)
Yolk sac placentation	+	−	Mossman (1987)
Chorioallantoic placentation	−	−	Cf. Table 1
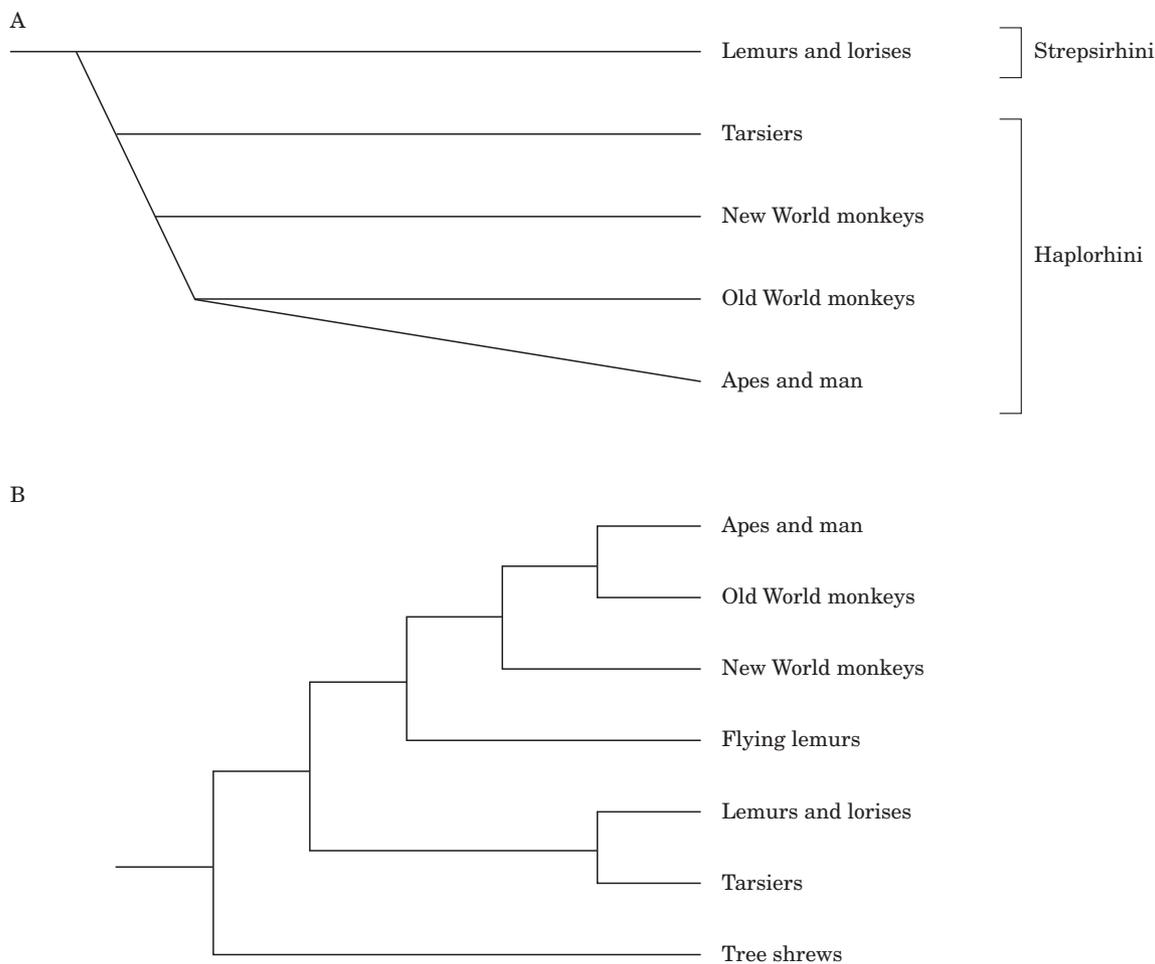
Figure 2. Contrasting phylogenies of primate superfamilies are yielded by cladistic analysis of fetal membranes and nucleotide sequences. **A.** Analysis of fetal membrane characters by Luckett (1976) separated the lemurs and lorises (Strepsirhini) from other primates, including the tarsiers (Haplorhini). **B.** An analysis based on sequence data from nuclear and mitochondrial genes grouped tarsiers with lemurs and separated them from New and Old World monkeys and great apes (Murphy et al., 2001). Orders shown in B comprise the Euarchonta, as seen in Figure 1. The position of the flying lemurs is uncertain: some analyses suggest flying lemurs and tree shrews are sister taxa.

the nature of their definitive yolk sacs (Mossman, 1987). Anatomical data also provide some evidence that aardvarks and elephant shrews may be related to paenungulates (Springer et al., 1997). More controversial is the inclusion of the insectivorous tenrecs and golden moles in the same superorder (Table 2). A recent study of living and fossil insectivores, based on characters from the cranium, dentition and post-cranial skeleton, found no support for inclusion of tenrecs and golden moles in an African clade of mammals (Asher, 1999). On the other hand, unique combinations of amino acid replacements in three proteins provide strong, independent evidence for the Afrotheria clade (van Dijk et al., 2001). Therefore, it is significant that Mossman (1987) grouped tenrecs with elephant shrews on the basis of derived features in

their yolk sac placentation. There is no recent literature on the fetal membranes of golden moles, tenrecs or aardvark and Mossman's (1987) comprehensive bibliography lists few papers of earlier date. The elephant shrews have fared a little better, although the two recent studies deal only with the definitive placenta (Cutler et al., 1998; Oduor-Okelo, 1984). There is a strong case for re-examining the fetal membranes of these mammals in relation to other members of the putative superorder Afrotheria.

Far relations of the primates

The phylogeny of the primates is still far from resolved (Figure 2). The separation of tarsiers from lemurs, argued from anatomical evidence, including placentation (Luckett, 1976), is not supported by the molecular evidence (Murphy et al., 2001). Nor, however, do the data consistently support primate monophyly. Depending on the method of analysis applied, anthropoids appear more closely related to flying lemurs than to lemurs and tarsiers. Mossman (1987) noted that little is known about the fetal membranes of flying lemurs and there are no recent studies to rectify this deficiency. Yet this is an area where placental studies could make a significant contribution to phylogenetics, since there is strong disagreement between morphologists (Lemelin, 2000) and molecular biologists (Madsen et al., 2001; Murphy et al., 2001) on the relationship between flying lemurs and primates.

Comparative functional studies

Rodents are widely used for functional studies of the placenta. Because most gene knockout and transgenic models are developed in mice, this trend will continue. It is often argued that the haemochorial placentation of rodents makes them an excellent model for the human placenta, especially where the placenta is of the haemomonochorial type, as in the guinea pig. It is conveniently overlooked that haemochorial placentation has evolved separately in rodents and primates (Luckett, 1969), and that there are developmental and functional differences between placentae of the labyrinthine and villous types. Comparative studies of placental function usually include different morphological types. Thus haemochorial placentae are often contrasted with epitheliochorial placentae from pigs (diffuse) and horses (microcotyledonary), the syn-epitheliochorial, cotyledonary placenta of sheep, and the endotheliochorial, zonary placenta of the mink.

All these examples are drawn from just two superorders. The Gondwanan lineages that led to Afrotheria and Xenarthra are not represented. If we truly wish to exploit the full genetic diversity represented by placental types, comparative studies should include species such as the rock hyrax (Oduor-Okelo et al., 1983) and armadillo (Enders, 1960; Nelson et al., 1997). Because these two lineages diverged early in mammalian history, their living representatives may well have some conserved characters that could provide the missing links in many areas of placental study.

REFERENCES

Asher RJ (1999) A morphological basis for assessing the phylogeny of the 'Tenrecoidea' (Mammalia, Lipotyphla). *Cladistics*, **15**, 231–252.

Badwaik NK & Rasweiler JJ (2000) Pregnancy. In *Reproductive Biology of Bats* (Ed.) Chrichton EG, pp. 221–293. London: Academic Press.

Badwaik NK & Rasweiler JJ (2001) Altered trophoblastic differentiation and increased trophoblastic invasiveness during delayed development in the short-tailed fruit bat, *Carollia perspicillata*. *Placenta*, **22**, 124–144.

Carter AM (1999) J. P. Hill on placentation in primates. *Placenta*, **20**, 513–517.

Carter AM, Tanswell B, Thompson K & Han VKM (1998) Immunohistochemical identification of epithelial and mesenchymal cell types in the chorioallantoic and yolk sac placentae of the guinea-pig. *Placenta*, **19**, 489–500.

Colbert EH (1961) *Evolution of the Vertebrates*. New York: John Wiley and Sons.

Cutler JB, Dumas A & Wynn RM (1998) Immunohistochemical analysis of the interhemal membrane of the elephant shrew. *Gynecol Obstet Invest*, **46**, 46–48.

Enders AC (1960) Development and structure of the villous hemochorial placenta of the nine-banded armadillo. *J Anat (Lond)*, **94**, 34–45.

Enders AC (1965) A comparative study of the fine structure of the trophoblast in several hemochorial placentas. *Am J Anat*, **116**, 29–68.

Enders AC, Blankenship TN, Lantz KC & Enders SS (1998) Morphological variations in the interhemal areas of chorioallantoic placentas. In *The Maternal–Fetal Interface* (Ed.) Carter AM, Dantzer V & Jansson T. *Trophoblast Res*, **12**, 1–19.

Enders AC & Liu IK (1991) Trophoblast-uterine interactions during equine chorionic girdle cell maturation, migration, and transformation. *Am J Anat*, **192**, 366–381.

Enders AC & Welsh AO (1993) Structural interactions of trophoblast and uterus during hemochorial placenta formation. *J Exp Zool*, **266**, 578–587.

Fischer TV & Mossman HW (1969) The fetal membranes of *Pedetes capensis*, and their taxonomic significance. *Am J Anat*, **124**, 89–115.

Hedges SB, Parker PH, Sibley CG & Kumar S (1996) Continental breakup and the ordinal diversification of birds and mammals. *Nature*, **381**, 226–229.

Hill JP (1932) The developmental history of the primates. *Phil Trans Roy Soc B*, **221**, 45–178.

Huxley TH (1864) *Lectures on the Elements of Comparative Anatomy*. London: John Churchill and Sons.

Huxley TH (1880) On the application of the laws of evolution to the arrangement of the Vertebrata and more particularly of the Mammalia. *Proc Zool Soc Lond*, **1880**, 649–662.

King BF & Enders AC (1993) Comparative development of the mammalian yolk sac. In *The Human Yolk Sac and Yolk Sac Tumors* (Ed.) Nogales FF, pp. 1–32. Berlin: Springer.

Le Gros Clark WE (1962) *The Antecedents of Man*. Edinburgh: Edinburgh University Press.

Lemelin P (2000) Micro-anatomy of the volar skin and interordinal relationships of primates. *J Hum Evol*, **38**, 257–267.

Liu FG, Miyamoto MM, Freire NP, Ong PQ, Tennant MR, Young TS & Gugel KF (2001) Molecular and morphological supertrees for eutherian (placental) mammals. *Science*, **291**, 1786–1789.

Luckett WP (1969) Evidence for the phylogenetic relationships of the tree shrews (Tupaiidae) based on the placenta and foetal membranes. *J Reprod Fert Suppl*, **6**, 419–433.

Luckett WP (1976) Cladistic relationships among higher primate categories: Evidence of the fetal membranes and placenta. *Folia Primatol (Basel)*, **25**, 245–276.

Luckett WP (1993) Uses and limitations of mammalian fetal membranes and placenta for phylogenetic reconstruction. *J Exp Zool*, **266**, 514–527.

Madsen O, Scally M, Douady CJ, Kao DJ, DeBry RW, Adkins R, Amrine HM, Stanhope MJ, de Jong WW & Springer MS (2001) Parallel adaptive radiations in two major clades of placental mammals. *Nature*, **409**, 610–614.

Mossman HW (1937) Comparative morphogenesis of the fetal membranes and accessory uterine structures. *Carnegie Instit Contrib Embryol*, **26**, 129–246.

Mossman HW (1987) *Vertebrate Fetal Membranes*. New Brunswick, New Jersey: Rutgers University Press.

Murphy WJ, Eizirik E, Johnson WE, Zhang YP, Ryder OA & O'Brien SJ (2001) Molecular phylogenetics and the origins of placental mammals. *Nature*, **409**, 614–618.

Nelson DM, Swanson PE, Davison BB, Baskin GB & Enders AC (1997) Ontogenetic and phylogenetic evaluation of the presence of fibrin-type fibrinoid in the villous haemochorial placenta. *Placenta*, **18**, 605–608.

Novacek MJ (1992) Mammalian phylogeny: shaking the tree. *Nature*, **356**, 121–125.

Oduor-Okelo D (1984) Histology of the chorioallantoic placenta of the golden-rumped elephant shrew (*Rhynchocyon chrysopygus* Gunther, 1881). *Anat Anz*, **157**, 395–407.

Oduor-Okelo D, Musewe VO & Gombe S (1983) Electron microscopic study of the chorioallantoic placenta of the rock hyrax (*Heterohyrax brucei*). *J Reprod Fertil*, **68**, 311–316.

Pettigrew JD (1986) Flying primates? Megabats have the advanced pathway from eye to midbrain. *Science*, **231**, 1304–1306.

Purvis A (1995) A composite estimate of primate phylogeny. *Philos Trans R Soc Lond B Biol Sci*, **348**, 405–421.

Ridley M (1986) *Evolution and Classification: The Reformation of Cladism*. Harlow: Longman Group.

Rose KD & Emry RJ (1993) Relationships of Xenarthra, Pholidota, and fossil 'edentates': The morphological evidence. In *Mammal Phylogeny: Placentals* (Ed.) Szalay PS, Novacek MJ & McKenna MC, pp. 81–102. New York: Springer.

Shoshani J & McKenna MC (1998) Higher taxonomic relationships among extant mammals based on morphology, with selected comparisons of results from molecular data. *Mol Phylogenet Evol*, **9**, 572–584.

Springer MS, Cleven GC, Madsen O, de Jong WW, Waddell VG, Amrine HM & Stanhope MJ (1997) Endemic African mammals shake the phylogenetic tree. *Nature*, **388**, 61–64.

Springer MS & de Jong WW (2001) Phylogenetics. Which mammalian supertree to bark up? *Science*, **291**, 1709–1711.

Stanhope MJ, Waddell VG, Madsen O, de Jong W, Hedges SB, Cleven GC, Kao D & Springer MS (1998) Molecular evidence for multiple origins of Insectivora and for a new order of endemic African insectivore mammals. *Proc Natl Acad Sci USA*, **95**, 9967–9972.

Tibbitts FD & King BF (1975) The fine structure of the trophospongial layer of the kangaroo rat placenta. *Anat Rec*, **183**, 567–578.

Wooding FB, Hobbs T, Morgan G, Heap RB & Flint AP (1993) Cellular dynamics of growth in sheep and goat synepitheliochorial placentomes: an autoradiographic study. *J Reprod Fertil*, **98**, 275–283.

Wynn RM, Hoschner JA & Oduor-Okelo D (1990) The interhemal membrane of the spotted hyena: an immunohistochemical reappraisal. *Placenta*, **11**, 215–221.

van Dijk MA, Madsen O, Catzeflis F, Stanhope MJ, de Jong WW & Pagel M (2001) Protein sequence signatures support the African clade of mammals. *Proc Natl Acad Sci USA*, **98**, 188–193.

Young JZ (1962) *The Life of Vertebrates*. Oxford: The Clarendon Press.