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Phylogenetic Evidence for Early Hemochorial Placentation in Eutheria

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ABSTRACT

The eutherian placenta is remarkable for its structural and functional variability. In order to construct and test comparative hypotheses relating ecological, behavioral and physiological traits to placental characteristics it is first necessary to reconstruct the historical course of placental evolution. Previous attempts to do so have yielded inconsistent results, particularly with respect to the early evolution of structural relationships between fetal and maternal circulatory systems. Here, we bring a battery of phylogenetic methods – including parsimony, likelihood and Bayesian approaches – to bear on the question of placental evolution. All of these approaches are consistent in indicating that highly invasive hemochorial placentation, as found in human beings and numerous other taxa, was an early evolutionary innovation present in the most ancient ancestors of the living placental mammals.

1. Introduction

Modification of the amniote system of fetal membranes, specifically involving fusion of the chorion with the allantois or yolk sac [1], permits the fetal circulatory system to access the extra-embryonic maternal environment during gestation, and has resulted in multiple independent origins of placentation in a range of vertebrate taxa including squamate reptiles [2–5], chondrichthyans [6,7], eutherian mammals [1] and marsupials [8,9]. The "placental" mammals (Eutheria) are unusual among the vertebrates in being a relatively large clade in which chorioallantoic placentation is universal rather than a rarity; furthermore the placenta exhibits striking structural and functional diversity including adaptations apparently unique to eutherians [10–12] alongside evolutionary convergence with respect to vertebrate out-groups (i.e., Refs. [13,14]).

Grosser's tripartite classification of placentas as hemochorial, endotheliochorial or epitheliochorial [15] has with some minor extensions been regarded as an important framework for the description of eutherian placental diversity [1,16–19]. The scheme is based on variation in the interface of fetal and maternal tissues: in epitheliochorial placentation the fetal chorion is in contact with the epithelium of the uterus; in endotheliochorial placentation the fetal chorion is in contact with the endothelial wall of maternal blood vessels; and in hemochorial placentation the fetal chorion is directly bathed in maternal blood. The placental categories differ in the extent to which fetal tissues invade the wall and circulatory system of the uterus; placentas can thus be ranked in terms of placental invasiveness, with epitheliochorial placentation the least invasive form and hemochorial placentation the most invasive form [1]. The placental interface has further been categorized in terms of the interdigitation between fetal and maternal tissues (ranging along a continuum from the presence of simple unbranched villi to highly branched labyrinthine vasculature) and the shape of the placental attachment (ranging from highly localized discoid attachment to diffusely attached and cotyledonary forms; Table 1). Together these classification schemes describe variation in the intimacy and geometry of maternofetal contact.

The direct functional consequences of variation in placental form remain obscure, and the notion that some forms of placentation are in some way "more efficient" than others has been rejected by a number of recent authors [20,21]. Nevertheless, a body of evidence on fetal nutrition suggests that under invasive placentation the transport rate of some nutritional substances, such as free fatty acids, may be more responsive to the availability of such substances in the maternal circulatory system [20]; it has also been suggested that species with less invasive forms of placentation may be less likely to experience immune problems associated with the transfer of foreign cellular matter across the placenta during pregnancy [22], though this interpretation is challenged on molecular and comparative grounds [23,24].

Comparative approaches should help to identify functional aspects of placental evolution, to the extent that variation in

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Table 1
Examples of placental states found in the main eutherian clades. See Appendix for further details and references.

Interhemal membrane	Shape	Interdigitation	Examples
Afrotheria			
Endotheliochorial	Zonary	Labyrinthine	Aardvark, manatee, elephant, otter shrew
Endotheliochorial	Discoid	Labyrinthine	Sengi, hyrax, tenrec
Euarchontaglires			
Endotheliochorial	Bidiscoid	Labyrinthine	Tree shrew
Epitheliochorial	Diffuse	Villous	Lemur, loris, aye–aye
Hemochorial	Bidiscoid	Trabecular	Monkey
Hemochorial	Discoid	Labyrinthine	Murid rodent
Hemochorial	Discoid	Villous	Hominid
Laurasiatheria			
Endotheliochorial	Bidiscoid	Labyrinthine	European mole
Endotheliochorial	Zonary	Labyrinthine	Dog, cat, bear
Epitheliochorial	Diffuse	Oligocotyledonary	Deer
Epitheliochorial	Diffuse	Polycotyledonary	Cow
Epitheliochorial	Diffuse	Trabecular	Whale, pig, horse, pangolin
Epitheliochorial	Zonary	Villous	Eastern mole
Hemochorial	Zonary	Labyrinthine	Hyaena
Xenarthra			
Endotheliochorial	–	Labyrinthine	Armadillo
Hemochorial	Discoid	Villous	Anteater, sloth

placental characters can be associated with variation in mammalian life history, ecology, behavior and physiology [20,24–26]. A number of recent theoretical and empirical advances have provided critical information needed to help clarify the historical course of evolution in placental characteristics and thus provide a framework for comparative hypotheses. First, the advent of molecular phylogenetics and the collection of large comparative nucleotide sequence datasets offer estimates of mammalian systematics that are relatively robust with respect to differing cladistic methods and choice of data. A number of studies identify four principal eutherian clades (i.e., Refs. [27,28]), for each of which the range of placental characters is described in Table 1. Most importantly, molecular phylogeneticists have enjoyed considerable success in resolving the hierarchy of eutherian interordinal relationships, problems that have confounded traditional morphological methods and are of great importance for understanding patterns of early placental diversification [29–32]. Resolving the position of the eutherian root has been more problematic, with three configurations (basal Xenarthra, Afrotheria, or Afrotheria + Xenarthra) found to be equally likely [31–33]. Second, the development of methods for the combination of existing phylogenies into a consensus “supertree” permits the construction of extraordinarily large phylogenetic trees that are maximally consistent with molecular data and previous morphological studies and which span sufficient taxonomic diversity to cover all major evolutionary events involving eutherian placentation [34–37]. Finally, recent efforts to document placental type in species of phylogenetic interest, especially in Afrotheria and Xenarthra, are potentially illuminating since these basal species are the most informative with respect to ancient transformations of the placenta (though interpretation is difficult due to poor phylogenetic resolution of ordinal relationships within the former clade) [38–43].

Previous attempts to reconstruct placental characteristics of the common ancestor of extant eutherians (Table 2) have agreed on two points. First, epitheliochorial placentation is apparently a derived condition that evolved independently in Laurasiatheria, Primates and Lipotyphla, and was not present during very early evolution of the eutherian placenta. Second, the earliest crown eutherians were likely characterized by discoid, labyrinthine placentation, a condition found today widely dispersed among extant taxa (Table 1). There is, however, disagreement concerning the interhemal membrane of the ancestor of extant eutherians. Wildman’s group used parsimony and a one-parameter likelihood model to infer that the ancestor most likely exhibited hemochorial placentation [44], as did Elliot and Crespi [24] (who grouped endotheliochorial and epitheliochorial placentae into a single category); Mess and Carter [45] and Martin [21] inferred that the condition was, under linear maximum parsimony, indeterminate and either hemochorial or endotheliochorial (the latter reconstruction being favored by one version of the eutherian phylogeny but not by alternatives). Vogel [46], who grouped endotheliochorial and hemochorial placentae into a single category, reach the more limited conclusion that the ancestral eutherian was not epitheliochorial. Finally, Carter and Enders [47] favor the hypothesis of an endotheliochorial ancestral placenta but did not use a statistical approach.

The use of linear parsimony methods (which infer ancestral states by generating a reconstruction that minimizes the number of evolutionary transitions on a phylogenetic tree) is not the most efficient use of the large dataset available to comparative biologists. The existence of placental variation within otherwise homogenous clades (for example, the presence of endotheliochorial placentation in Heteromyidae within the hemochorial Rodentia, or of hemochorial placentation in Hyaenidae within the endotheliochorial Carnivora) has no effect on ancestral state reconstructions at nodes deeper than the ordinal level; similarly, the absence of variation within large clades (such as the uniformly epitheliochorial Cetartiodactyla) is not informative with respect to the frequency of evolutionary transitions across the tree as a whole. Under linear parsimony it is thus sufficient to consider only branches upon which transitions have occurred; such approaches therefore disregard a large proportion of the comparative data that might otherwise be used to distinguish between competing evolutionary hypotheses. Furthermore, linear parsimony estimates of character states at the root of a phylogenetic tree are highly dependent upon the character state found in the most basal taxa included in the study, especially when the tree is

Table 2
Previous reconstructions of the ancestral eutherian interhemal membrane.

Study	Data	Method	Root condition
Carter and Enders (2004)	13 taxa	–	Endotheliochorial
Vogel (2005)	21 taxa	Parsimony	Hemotrophic
Elliot and Crespi (2006)	88 taxa	Maximum likelihood (1 parameter)	Hemochorial
Mess and Carter (2006)	36 taxa	Linear parsimony	Endotheliochorial/hemochorial
Wildman et al (2006)	44 taxa	Parimony and maximum likelihood (1 parameter)	Hemochorial
Martin (2008)	18 taxa	Linear parsimony	Endotheliochorial (ordered) or Endotheliochorial/hemochorial (unordered)