Evolution of the Nutritional Components in Milk

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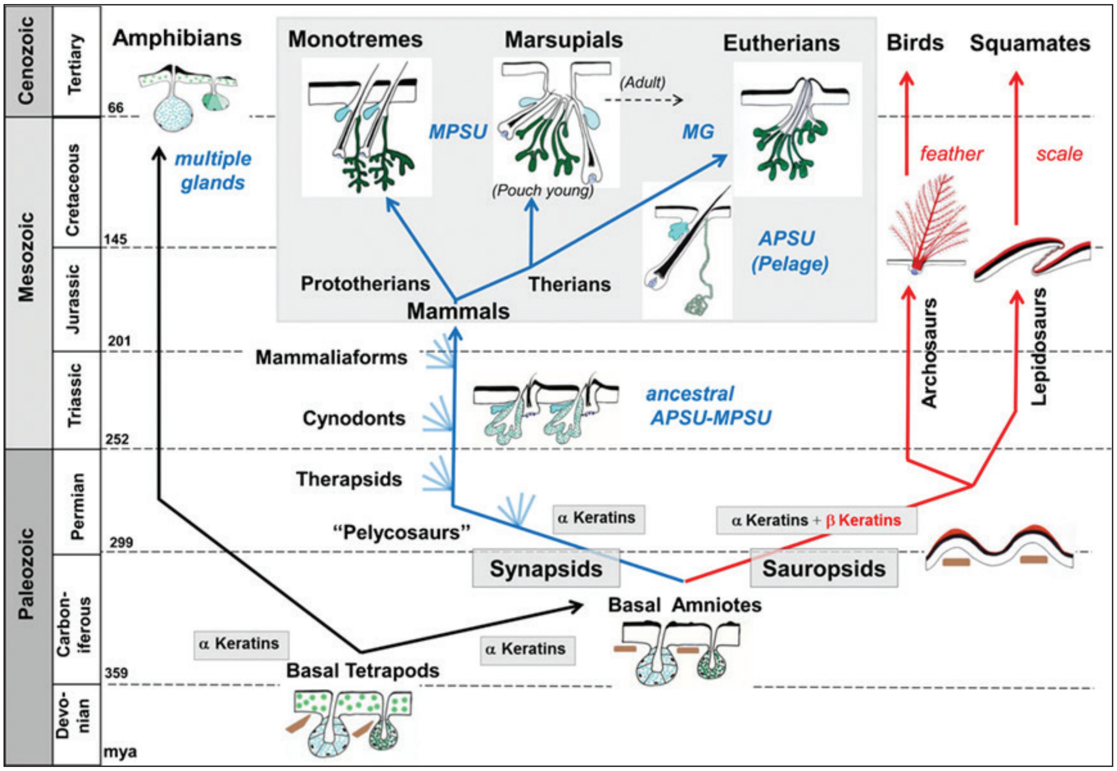
Lactation is a defining and uniquely mammalian trait, providing the massive transfer of nutrients and bioactive components to young via milk and permitting offspring immaturity at birth. To achieve this transfer, the mother's diet is transformed, stored, balanced, and simplified. Lactation is complex and species-specific, and represents a profound evolutionary achievement that involved the long co-evolution of both milk production and offspring development. We can look to past modifications of developmental signalling pathways and morphogenesis (evo-devo) and the molecular evolution of specific milk constituents.

The Evolution of Lactation

Mammary glands—which appear to have derived from apocrine-like glands—initially secreted onto the skin surface and likely provided moisture, protective constituents, and elemental nutrients to eggs and/or hatchlings long before mammals evolved **(Figure 1)**.[1] Synapsids, the ancestors of mammals, laid parchment-shelled eggs that permitted the uptake of exogenous moisture and simple nutrients.[2,3] However, very little is known about apocrine gene expression, secretory products, or development.

Several key steps were required to transform this initial secretion into a nutrient-dense fluid[4]: 1) conversion of an antimicrobial constituent (c-lysozyme) into a regulator of sugar synthesis (α-lactalbumin), giving rise to lactose and a large variety of lactose-based oligosaccharides; 2) transformation of mineralization protein(s) into large Ca- and P-transporting casein micelles; and 3) incorporation of constituents involved in cellular immunity into the fat globule membrane, so that fat secretion can be greatly upregulated without damage to secretory cells. Nutrient-dense

Figure 1. Mammary evolution.[1]



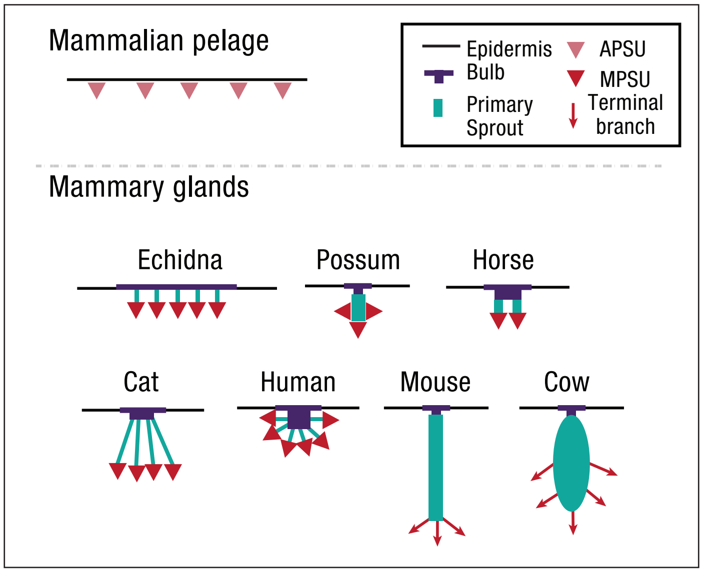
milk evolved prior to the Triassic miniaturization of mammalian ancestors more than 210 million years ago. The ancestral mammalian pattern of hatching from an egg followed by a prolonged developmental period dependent on milk persists in living monotremes, such as the platypus and echidnas.[2] The echidna secretes milk onto its skin (no nipples), which is believed the be the ancestral form of lactation, before the development of placental mammals.

Species-specific Lactation

The process of mammary development varies greatly among species, including evidence of the role of triads of mammary hair follicle–sebaceous units (MPSUs) in mammary morphogenesis **(Figure 2)**.[1] These MPSUs likely derived from apo-pilo-sebaceous units (APSUs; **Figure 1**).

Mammals that give birth to highly altricial (undeveloped) offspring typically exhibit great changes in milk constituents, including oligosaccharides, over the course of lactation, presumably to accommodate changes in functional development of the offspring. Eutherian milks are thus extremely diverse in composition, whether in terms of water, fat, protein, sugars, or energy.

Figure 2. Mammary gland development.[1]



Human Milk Is Uniquely Evolved for Human Infants

Human babies are born with a low functional ability and slow development to independence, but human milk is adapted to meet the needs of these infants. The cost of human lactation is low compared with other mammals if you look at the energy cost per day, but not when you look at it as a whole process. Upright posture required a reconfigured pelvis and limited birth canal size, which resulted in immature infants at birth. Human milk has a high water/low energy content associated with frequent nursing, which facilitates social bonding. Sugars and other nutrients in milk help to support the development and metabolism of a large brain. Protein corresponds to a very low proportion of the milk energy (6%; compared with 13% in old-world monkeys and 19% in new-world monkeys), which relates to the slow rate of infant growth. The oligosaccharide diversity of human milk is greater than that of any other mammal, facilitating the growth of beneficial gut microbes, and the predominance of type I oligosaccharides is unique to human milk.[5] Together with antimicrobial constituents, the milk oligosaccharides help to mitigate the dangers of pathogen exposure that result from increased sociality compared with other primates.

Human milk has many characteristics in common with the milk of other primates, but in many ways is distinctive. Although milk production is highly species-specific, the relationship between developmental maturity and the provision/utilization of nutrients is still not well understood across species.

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