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NOTES AND COMMENTS

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α -LACTALBUMIN AND THE ORIGINS OF LACTATION

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This note suggests a connection between a finding in molecular genetics, the molecular evolution of α -lactalbumin from lysozyme, and a problem that has been debated by evolutionary biologists for over a century, the evolution of milk production. All of the hypotheses for the evolution of lactation (reviewed by Long, 1969, 1972; Graves and Duvall, 1983) implicitly or explicitly rely on the following scenario, as expanded from that of Darwin (1872): 1) increased proximity of mother and newly laid eggs, perhaps with the maternal development of a vascularized, abdominal, incubation patch; 2) enhancement of offspring (egg or hatching) survivorship through secretion by maternal cutaneous glands; 3) accidental ingestion or absorption of maternal secretions by offspring and their subsequent use as food or drink; 4) concomitant development of suckling behavior, localized areolar regions, and an increased nutritional value of the maternal secretions. Although they are not mutually exclusive, the available hypotheses differ with respect to the primary adaptive benefit ascribed to the hypothetical protolactal secretions. The presumed advantages currently fall into three classes: 1) thermoregulation of eggs or young via evaporative cooling (Haldane, 1965) or heat transfer from the mother (Bresslau, 1907; Gregory, 1910); 2) maintenance of water balance of the eggs or hatchlings, e.g., prevention of desiccation (Haldane, 1965); 3) maintenance of proximity of the mother and her offspring (egg or young) either mechanically via albuminous glue (Gregory, 1910), or behaviorally via aggregation pheromones simultaneously operating as milk precursors (Graves and Duvall, 1983). As an addition to this list we propose a hypothesis that ties the molecular evolution of a major component of the milk synthesis system to the functional modifications accompanying the evolution of lactation from preexisting systems. These systems may have served very different roles in the lives of the earliest mammals and their ancestors.

We hypothesize that protolactal secretions helped protect the eggs or young from bacterial, protozoal, or fungal infection. The genesis of this hypothesis lies in the already documented (Brew et al., 1967,

1970; Smith, 1970; Gordon, 1971; Dayhoff, 1976) evolution of a gene for α -lactalbumin from a duplication of the genetic material for lysozyme. α -lactalbumin has been found only in therian mammals and is a subunit of the lactose synthetase system within the mammary gland (Brew, 1969; Jones, 1977). Lysozyme is a bactericidal and fungicidal enzyme (Tizard, 1981; Marquis et al., 1982) which is found in all major groups of organisms (Dayhoff, 1976) and is also present in mammalian milk (Hopper and McKenzie, 1974). α -lactalbumin has not been found in the egg-laying mammals, the platypus and the echidna. However, echidna milk possesses a lysozyme that not only has the antibacterial and structural properties, but also has activity in the lactose synthetase system (Hopper and McKenzie, 1974). Thus, monotremes appear to have a protein which is a structural and functional intermediate between that of lysozyme and α -lactalbumin. Following Dickerson and Geis (1969), and Gould and Vrba (1982), we envision the duplication of the genetic material for lysozymes occurring perhaps as early as 300 million years ago (Dayhoff, 1976). Subsequently, the duplicated material evolved, and its product was used in the milk-producing system perhaps via an intermediate form that possessed both functions as does the lysozyme in echidna milk. This suggests that although the gene for lysozyme may have duplicated much earlier, the evolution of α -lactalbumin did not occur until after the prototherian/therian split.

The probable evolution of α -lactalbumin from lysozyme implies that lysozyme was secreted by the mammary gland precursors, just as it is currently secreted by certain other glands of ectodermal origin (e.g., lacrimal glands, Sapse et al., 1968; salivary glands, Miyauchi, 1984). The precursors to other milk proteins with anti-microbial properties, i.e., lactoferrin and lactoperoxidase (Morrison and Allen, 1966; Arnold et al., 1977), may also have been present.

We suggest that the protolactal secretion enhanced the survival of the eggs or young by virtue of its anti-microbial properties. The microbial environment surrounding the eggs is probably im-

portant to offspring survival in all oviparous vertebrates (Board and Fuller, 1974). Specializations for protection of the eggs from microbial attack are exhibited by representative reptiles (Movchan and Gabaeva, 1967; Packard and Packard, 1980), birds (Board and Fuller, 1974), amphibians (Gabaeva, 1962; Movchan and Gabaeva, 1967; Salthe and Mecham, 1974), and fish (Bell et al., 1971). In addition, the pouch flora of at least one marsupial is known to vary with the reproductive cycle (Charlick et al., 1981). In reptiles, a major selective advantage of viviparity may be the reduced exposure of the eggs to bacterial and fungal infection (Fitch, 1970), while in avian ancestors intense predation by soil microbes may have been the selective pressure favoring calcified egg shells (Packard and Packard, 1980). These examples and others (Janzen, 1977) suggest that microbial predation constitutes an important selective pressure.

Our hypothesis suggests that the nutritional importance of milk has obscured the original protective function of the protolacteal secretions. In addition to lysozyme, other milk proteins (e.g., lactoferrin and lactoperoxidase) also have anti-microbial properties. The anti-microbial properties of the milk of extant species imply that this function is still important (McClelland et al., 1978; Butler, 1979; Gillin et al., 1983).

The evolution of lactation required the complex integration of many microevolutionary changes involving several levels of organization: molecular, developmental, morphological, physiological, and behavioral. Our hypothesis focuses on molecular changes associated with the origin of lactation, but it also has morphological and physiological ramifications. The hypertrophy of glandular tissue under the control of reproductive hormones would enhance the value of anti-microbial protolacteal secretions. In addition, if the secretions were accidentally imbibed, they may have enhanced offspring survival either by controlling enterobacterial levels or by supplying additional protein. This would provide some selective pressure for the evolution of suckling behavior.

Our hypothesis cannot be tested directly because, regrettably, there are no surviving therapsids. However, one testable corollary of our hypothesis would be that microbial predation constitutes an important selective pressure on reptilian eggs. Likewise, we would predict that egg or offspring survival in monotremes is enhanced by microbial inhibitors of cutaneous or mammary gland origin. In addition, clarification of the following issues may provide information bearing indirectly upon our hypothesis: mammary gland origins, the nature of the protolacteal secretions, the transition from these early secretions to milk, and the reproductive characteristics of the cynodont reptiles, which presumably first produced these secretions. In sum, we suggest that microbial predation on eggs or neonates was an early selective force for the evolution of what has become the hallmark of the mammalian radiation—lactation.

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ON IRREVERSIBLE EVOLUTION

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Evolutionary biology commonly addresses how and why organisms change. It also addresses how and why they do not change. Some types of change do not occur because of constraints—the evolution is simply prevented. The limitations on organic evolution are necessarily to be found at the levels of phenotypic variation, inheritance, and selection, just as the process of evolutionary change is also to be understood at these levels. Although some important constraints have already been discovered at these levels (e.g., inheritance is often Mendelian),

further observations are needed in developing a comprehensive theory of evolutionary restrictions.

An extreme type of evolutionary restriction is irreversibility—the inability of a population to reacquire a (recent) ancestral state; this is sometimes known as Dollo's law (Simpson, 1953; Dobzhansky, 1970; Gould, 1970; see Discussion for a review). As a biological problem, irreversibility has two features distinguishing it from the much larger class of general evolutionary restrictions. First, irreversibility involves restrictions with respect to a