EVOLUTION

Bursts in skull evolution weakened with time

The skull shapes of mammals diversified more rapidly early in their history

By **Sharlene E. Santana**[1,2] *and* **David M. Grossnickle**[1]

Evolutionary biologists generally agree that placental mammals began as small-sized animals that ate insects, and later evolved to become more varied in size and morphology. Today, the morphologies of placental mammals are incredibly diverse, ranging from the bumblebee bat to the blue whale (*1*–*3*). There is considerable debate over how the small, insect-eating ancestors of placental mammals gave rise to such incredibly divergent lineages. Among the competing hypotheses are varying opinions on the timing and pace of early placental mammal evolution, especially in the context of major environmental changes such as the Cretaceous-Paleogene (K-Pg) mass extinction event 66 million years ago and the Paleocene-Eocene Thermal Maximum (PETM) 56 million years ago. On page 377 of this issue, Goswami *et al.* (*4*) contribute to this discussion by reconstructing the patterns and possible drivers of placental mammal morphological diversification with a quantitative analysis of skull shape spanning over 70 million years of evolution.

Different traits tell different evolutionary stories about how mammals diversified (*3*). The skull is an informative structure for studying mammal evolution because of the multiple functions it serves that are critical to survival, such as feeding, protecting the brain, and supporting various sensory organs. For example, the shape of the skull can reflect dietary adaptations (consider the long snouts of anteaters) and thus inform how skull shape evolved across lineages with different diets. Despite these advantages, whole skulls are rarely used to study diversification in mammal evolution. This is partly because of their exceptional variation, which ranges from the elongated skulls in dolphins to the round skulls in primates, making direct and quantitative comparison difficult (*5*). In addition, well-preserved skull fossils are rare for extinct mammal species, which makes them less ideal for comprehensive studies.

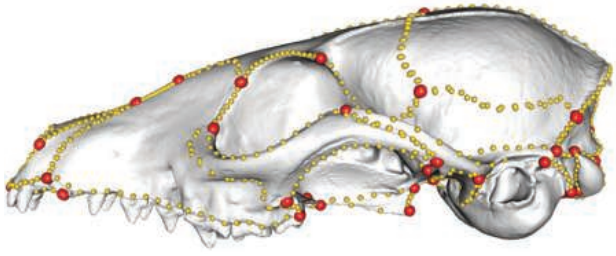
Goswami *et al.* used geometric morphometrics, a method based on the placement of marks on specific anatomical features, and a library of hundreds of three-dimensional models of skulls to quantify and compare the skull shape of placental mammals (see the figure). To account for uncertainties in the evolutionary relationships among extinct placental mammal lineages, the authors also simulated the evolution of skull shape across nearly 2000 evolutionary trees relating the 322 mammal species analyzed in the study.

Without the possibility of directly studying the behavior and physiology of extinct species, evolutionary biologists often use the geologic timing and pace of anatomical changes to identify major factors or events that influenced the diversification of a lineage. According to their data, Goswami *et al.* find that the ancestors of major placental mammal lineages likely had nonspecialized skull shapes and habits until shortly before or after the K-Pg mass extinction, when their skull shapes changed and diversified at a fast rate. After this initial phase of rapid change, skull shape evolved much more slowly within most lineages, albeit with occasional smaller bursts in evolution potentially related to climate changes, such as during the PETM, when the global temperature increased considerably in a relatively short amount of time. Their results are consistent with previous hypotheses that placental mammals began to ecologically diversify shortly before or at the K-Pg boundary, taking advantage of ecological opportunities in the wake of the mass extinction event (*3*). Goswami *et al.* also found that placental mammals that are aquatic, herbivorous, precocial, or social showed the fastest evolutionary rates. For example, skull shape evolved quickly for whales and dolphins as they adapted to a fully aquatic lifestyle.

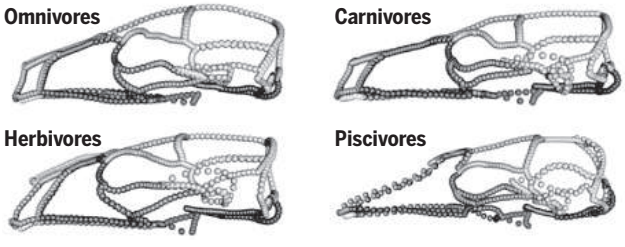
The authors overcame many of the challenges faced by other similar studies. For instance, discrepancies in the patterns recovered from fossil versus molecular data are a common point of controversy in studies of early mammal evolution (*6*). They solved this problem by sampling both fossil and modern placental mammals to provide a comprehensive dataset. Many studies on the diversification of early mammals also tend to rely on single traits, such as body size or a specific ecological trait (e.g., nocturnal versus diurnal behavior). By exam-

Tracking mammalian evolution with skulls

Placental mammal skulls can be compared to examine rates and patterns of anatomical diversification over evolutionary time.



The skulls are digitally mapped in three dimensions and analyzed by using markers (shown here in red and gold) that track the shape of various anatomical features.



Because mammalian skull shape is influenced by many important functions, such as dietary preference, the analysis of skull shapes is informative for examining the environmental changes that could have affected the evolution of diverse mammalian lineages.

GRAPHIC: BASED ON GOSWAMI *ET AL.* (*4*)

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ining the skull shape, which encompasses many anatomical traits, the study simultaneously examined a multitude of ecological and functional drivers of diversification. The breadth of the sample size analyzed by Goswami *et al.* is also impressive, containing species across all of Placentalia, rather than more restricted taxonomic groups, as is often the case for most studies of mammalian morphological evolution.

Despite the many insights provided by their extensive data and analyses, Goswami *et al.* cannot quantifiably verify if placental mammals experienced a diversification burst in the immediate wake of the K-Pg mass extinction. Similar to other studies (*7*), the authors are uncertain about the exact timing of placental mammal origins. When basing their analysis on evolutionary trees with relatively early origins of placental mammals (about 100 to 80 million years ago), the authors find evidence of rapid diversification before the K-Pg boundary. This could be interpreted as a refutation of the assumption that these mammals diversified rapidly after the K-Pg boundary and supports an earlier estimated date for when they first diversified (*3*). However, analyses using evolutionary trees with a more recent divergence time (about 80 to 70 million years ago) produce a pattern of rapid diversification at or immediately after the K-Pg boundary. The contradictory conclusions because of the different assumed timing of placental mammal origins highlight the need for a better understanding of early mammal evolution.

Elucidating how, when, and why mammals diversified will continue to require integrative and multidisciplinary approaches. Goswami *et al.* advance the understanding of placental mammal diversification and set a foundation for future work to examine the lineages of other modern and extinct groups and the evolution of other anatomical systems. In the context of pronounced ecological changes, including those induced by humans in recent history, the fossil record can provide clues about the functional mechanisms that could facilitate or constrain the evolution of animals. ■

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10.1126/science.add8460

GENETICS

Stealing genes and facing consequences

The human genome contains a domesticated viral envelope gene with antiviral activity

By **Ricky Padilla Del Valle** *and* **Richard N. McLaughlin Jr.**

Sequencing the human genome delivered the surprising finding that endogenous retroviruses (ERVs) and other genomic parasites dominate the genetic code. Perhaps more surprising was the discovery that this "junk" DNA does not merely contain the scars from millions of years of (ongoing) coevolution of genomes and transposable elements. Instead, the human genome contains numerous genes and regulatory sequences that were once part of replicating transposable elements, particularly ERVs, but have been "domesticated" by the host genome—once viral, now human (*1, 2*). Less is known about the cost of using part of a virus's genome to execute critical organismal functions. On page 422 of this issue, Frank *et al.* (*3*) uncover hundreds of transcribed retroviral envelope genes that are primed for co-option. They demonstrate that a domesticated envelope gene called *Suppressyn* restricts viral infections when expressed in trophoblasts of the human placenta, a tissue where another domesticated envelope gene promotes the fusion of cells required for placental function.

"...domestication will happen, but... it comes with trade-offs that impose additional constraints in the future."

Transposable elements are DNA sequences that encode all the information they need to replicate themselves within the environment of their host's genome. One class of transposable elements, the ERVs, come from retroviruses that infected germline cells and became "trapped" within the host's genome. These genome-bound parasites encode a few proteins but must steal cellular resources to complete their replication within the germline and their passage to the offspring of their host. Replicating ERVs impose a burden on the host genome because they can be potent mutagens. However, these parasites bring both challenges and opportunities. ERV replication creates abundant new DNA sequences—a pool of raw materials that could, by chance, benefit the afflicted host. Indeed, domestications of these sequences have contributed to fundamental aspects of organismal biology. For example, V(D)J recombination of immunoglobulin genes in jawed vertebrates is carried out by recombination-activating gene 1 (RAG1) and RAG2, which were domesticated from a RAG-like transposon (*4*). Additionally, the coordinated expression of immune genes in primates uses interferon-responsive enhancers that were domesticated from the MER41 family of ERVs (*5*). Even programmed genome rearrangement in ciliates requires transposase genes that are domesticated from piggyBac transposons (*6*).

In a key innovation within mammals, domestication of a viral envelope gene over 100 million years ago created the *Syncytin* gene, which became an essential part of the emergence of the placenta (*7, 8*). The first *Syncytin* gene was likely domesticated in the last common ancestor of placental mammals from an ERV that used the encoded envelope protein for fusion and entry into host cells. Now co-opted, this fusogenic activity mediates the formation of the multinucleate syncytium of the placenta (the syncytiotrophoblast), an essential barrier that enables transfer of nutrients from maternal blood to fetal blood while preventing passage of viruses to the fetus (*7, 8*). This evolutionary innovation may have been key to the emergence, diversification, and success of placental mammals. However, domestication of tools created by viral pathogens comes with an unavoidable cost.

The study of Frank *et al.* tackles the consequences of this co-option. The alanine, serine, cysteine-preferring transporter 2 (ASCT2) receptor, which binds primate Syncytin-1, must be expressed by trophoblasts to allow cellular fusion and formation of the syncytiotrophoblast. However, viruses that use Syncytin-1–like envelope genes can still recognize and bind ASCT2. Thus, Syncytin-1–mediated cell

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Science, 378 (6618), • DOI: 10.1126/science.add8460