In the developing ears of opossums, echoes of evolutionary history

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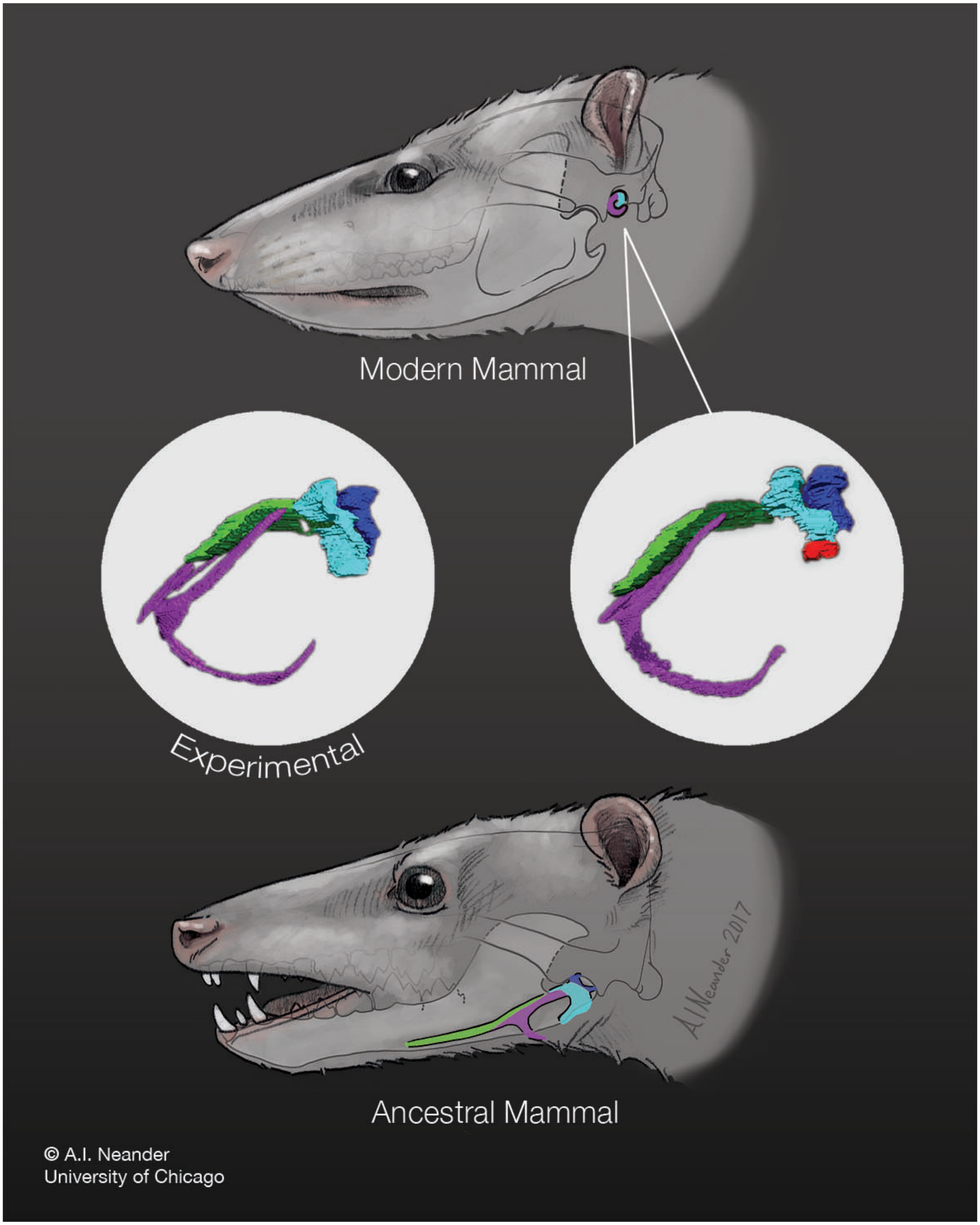

When mammalian middle ear bones develop, they begin as part of the arch of cartilage that makes up the embryonic jaw. In reptiles, these structures remain connected to the jaw as developmental processes gradually convert the cartilage to bone. Credit: A.I. Neander, University of Chicago

When we are confronted with the remarkable diversity and complexity of forms among living things—the lightweight and leathery wings of a bat, the dense networks of genes that work together to produce a functional cell—it can be hard to imagine how chance mutations and selective processes produced them. If we could rewind evolutionary time, what would we see?

In a new study published in *Proceedings of the Royal Society B*, animal scientists at the University of Illinois at Urbana-Champaign, King's College London, and the University of Chicago have discovered that hidden in the development of opossums is one possible version of the evolutionary path that led from the simple ears of reptiles to the more elaborative and sensitive structures of mammals, including humans.

Three tiny bones in the middle ear of mammals form a mechanism that converts the air vibrations of sound into the electrical impulses understood by the brain. Three of these bones are known by names that describe their shapes, either in Latin or in English: the malleus (hammer), incus (anvil), and stapes (stirrup). In the simpler ears of reptiles, as well as the shared ancestors of both groups, only the stapes is found in the middle ear, while analogs of the malleus and incus form part of the jaw.

The sharp contrast between the precise structure of these tiny mammalian bones and their non-auditory reptilian counterparts drew the attention of Associate Professor of Animal Biology Karen Sears and postdoctoral researcher Daniel Urban, who led the study. Sears is a member of the Carl R. Woese Institute for Genomic Biology (IGB);

Urban is an IGB Fellow.

"We came at this project through the approach of evolutionary developmental biology (evo-devo), which looks at the development of an organism . . . to help understand its evolutionary history," said Urban, explaining their experimental approach. An exciting aspect of the project for him was that it integrated "aspects of paleontology, cellular and molecular biology, developmental biology, and more. We're looking at the problem from more than one angle, utilizing all of these methods to solve the puzzle."

When mammalian middle ear bones develop, they begin as part of the arch of cartilage that makes up the embryonic jaw. In reptiles, these structures remain connected to the jaw as developmental processes gradually convert the cartilage to bone. In mammals, cells within a section of the developing jaw called Meckel's cartilage disappear as the animal grows, freeing the malleus and incus (the hammer and anvil) to reach their positions in the middle ear.

To get a better idea of how the mammalian ear might have evolved, Sears, Urban and their colleagues chose to study the gray short-tailed opossum, a small and charismatic South American marsupial whose key stages of jaw and ear development take place gradually and after birth.

The group first detailed the anatomical progression of middle ear development in their opossums, capturing images that revealed the changing architecture of cartilage and bone. They observed that the progression of structures in the developing opossum jaw and ear appeared to re-enact the evolutionary progression of these structures in the mammalian fossil record.

"It was truly remarkable how well the developmental stages of our extant opossum model organism matched up with the transitional fossils . . .

this makes our study organism, the gray short-tailed opossum, a fantastic living model to aid in the understanding of development of long extinct taxa," Urban said. "By using this modern analogue, we can learn so much more about these earlier species and the origins of mammals."

The team also explored changes in gene activity and individual cells that occurred during the breakdown of Meckel's cartilage. They identified a set of genes whose increased activity was correlated with the self-destruction of the cells that connect the future jaw to the future ear.

Among these genes, the researchers focused on a gene called TGF-β for further investigation. When they treated developing opossums with a drug that blocks the signaling of the TGF-β protein, the death of cells within Meckel's cartilage was prevented, and the malleus and incus remained a part of the jaw. With one tweak of gene activity, this one detail of anatomy appeared to have slid backward through evolutionary time.

TGF-β signaling is also known to play a role in the middle ear development of mice. However, the breakdown of cells in Meckel's cartilage in this study of opossums occurred via a different mechanism than that observed in mice: the cells self-destructed, rather than being engulfed by other cells.

"It was both surprising and intriguing to find evidence suggesting that two different cellular mechanisms may be responsible for separating middle ear elements from the jaw in placental and marsupial mammals . . . combined with previous fossil evidence, this implies the [mammalian middle ear] has independently evolved at least four times in total," Urban said. "This would initially seem improbable, except that when we performed functional testing, we showed that this connection (between the middle ear and jaw) can actually be preserved or broken by a relatively minor change in the expression of a single gene."

This power of a single molecular change, one that could be produced by a chance mutation in a key gene, to alter the trajectory of development provides one possible answer for how the ear might have evolved. Although the group's present study did not address why this change might have been adaptive, Urban offered one hypothesis to explain the successful spread through multiple populations of early mammals that roughly resembled his mealworm-munching opossums.

"The improved auditory sensitivity of these newly freed middle ear ossicles would have been a remarkable boon for early mammals. Most of these would have been very small, nocturnal insectivores," he said. "Confinement to activity during the night hours would have helped them avoid becoming prey, while at the same time, improved hearing would have aided in their own predatory abilities."

More information: Daniel J. Urban et al, A new developmental mechanism for the separation of the mammalian middle ear ossicles from the jaw, *Proceedings of the Royal Society B: Biological Sciences* (2017). DOI: 10.1098/rspb.2016.2416

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