Research gains toehold on skeletal evolution

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The developmental rules for forming a foot just got a little simpler. New research led by UMass Dartmouth Biology faculty member Dr. Kathryn Kavanagh and Harvard Medical School Professor Cliff Tabin, joined by Professor Uri Alon and Oren Shoval, of Israel's Weizmann Institute of Science's Department of Molecular Cell Biology, Akinori Kan of Harvard Medical School's Department of Genetics, and UMass Dartmouth's Dr. Benjamin Winslow and graduate student Brian Leary, studied the toe bones, or phalanges, of animals in order to test an idea that has been debated by evolutionary biologists for centuries—that the developmental process itself can guide evolution.

"Most bones in the skeleton evolve relatively independently from other bones, meaning that the size of each bone has freedom to evolve to suit any particular adaptive need. However, the toe bones seemed to be an exception," said Professor Kavanagh. "We first noticed that phalanges size proportions seemed to vary in predictable ways, from a gradient large-to-small, to a more equal-sized pattern, suggesting some coordination among parts."

Using chicken embryos as a model, the team used small foil barriers placed in the edge of the developing chick digit to prevent molecular signals from communicating with the still-developing tips. They found that this interference set up a shift in joint positioning that continued to reverberate during the rest of the digit's development. In contrast, when the barrier was placed in the metatarsal (the major bones of the foot's sole), only the metatarsal was altered with no reverberation into the phalanges.

The final test was then to see if this developmental connectedness influenced evolutionary patterns. The researchers used museum collections and previously published descriptions to measure a large sample of phalanges. The sample came from species from every major group of animal, including the oldest fossils that have any toe bones to measure. Remarkably, among all these creatures—some with over 15 phalanges—the variations were extremely predictable, such that if one knows the size of two phalanges, one can predict the others with confidence. Given this discovery, the researchers propose that the developmental construction rules for phalanges have remained consistent since the first origin of toes.

As usual in nature, there was a notable exception. Animals that don't need to use phalanges to walk, but do use them to grasp (for example, birds of prey) have unexpectedly long bones at the tips. The researchers concluded that when the functional constraint of walking is removed, such as in bird flight, the developmental system is freed to evolve a new variation.

The research further concludes that the formation of each phalanx bone, rather than being on its own, is part of a larger developmental unit. This ancestral developmental system has been fine-tuned over hundreds of millions of years of vertebrate evolution to work within a very simple set of variations regardless of whether the animal uses its feet to jump, swim, run, dig, or grasp.

The data provides a better understanding of the working relationship between developmental systems and natural selection; meaning that our internal systems will guide the evolution of our skeleton at least partly due to our deep ancestral history. Further, understanding these "construction rules" of the skeleton can help researchers use the natural tendencies of the skeletal system to facilitate skeletal and joint regeneration in the future.

"Such incredible consistency shows our bodies are capable of 'toeing' the line," concluded Dr. Kavanagh.

The study is published in the *Proceedings of the National Academy of Sciences*.

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