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## Simple Developmental Changes Gave Bats Flight

A change in a single gene may be in large part responsible for the evolution of flight in bats, according to new studies by Howard Hughes Medical Institute researchers. The findings not only help explain the emergence of flight in these animals, but also illustrate how alterations in genes that govern development can lead to the abrupt, dramatic changes in body shape frequently seen throughout evolution.

The fossil record indicates that bats, the only mammals with powered flight, date back to the Eocene, an era that began approximately 55 million years ago. Notably, bat wing anatomy has not changed substantially over the past 50 million years - an observation that served as a starting point for the new work, which was published April 17, 2006, in an advanced online publication of the *Proceedings of the National Academy of Sciences*.

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"We saw that the evolution of flight was quite sudden," said Lee A. Niswander, a Howard Hughes Medical Institute investigator at the University of Colorado Health Sciences Center who led the study. "That means there could be just a few key changes in limb development that resulted in more dramatic downstream consequences."

To find those key changes, Niswander and colleagues focused on the third, fourth, and fifth digits of the bat forelimb. These digits — equivalent to a human's middle, ring, and pinky fingers — are highly elongated and provide the support necessary for the wing membrane to be used for flight.

The group compared the embryonic development of bat forelimbs with that of bat hind limbs, which have much shorter digits than those in the wing. They also compared the bat forelimbs to mouse forelimbs so that they would have a similarly sized reference group.

During digit development in both species, cartilage cells (chondrocytes) divide and mature in areas called growth plates. The unique shape of the bat's forelimb is due to higher rates of both chondrocyte division and terminal maturation. Terminal chondrocyte maturation occurs in a part of the growth plate known as the hypertrophic zone, which is correspondingly larger in bat forelimbs than in mouse forelimbs. This difference in size, the researchers found, is due in large part to the expression of a single gene: bone morphogenetic protein 2, or *Bmp2*.

The researchers found that developing digits in the bat forelimb expressed more *Bmp2* than those in either bat hind limbs or mouse forelimbs. The group tested several other genes associated with chondrocyte maturation, but didn't find differences in expression.

Then, Niswander and colleagues found that if they cultured a growing bat forelimb in a soup of Bmp2 protein, the hypertrophic zone was larger and the digits grew longer than forelimbs grown without extra Bmp2. Forelimbs cultured with a Bmp2 blocking protein, on the other hand, developed a smaller hypertrophic zone and shorter digits than those grown normally.

The group's findings have implications not only for bat evolution, but also for mammalian evolution in general.

"What we seem to see is punctuated changes in morphology over evolutionary time," said Karen E. Sears, the first author on the research, who is also at UCHSC. Species will be in stasis for millions of years and then very quickly we get brand new species. That hints at just a few changes in key developmental genes."

That observation supports the theory of punctuated equilibrium, put forth in 1972 by Niles Eldredge and Stephen Jay Gould. Punctuated equilibrium states that evolutionary change is not gradual and geologically "slow"; instead, long periods of stability can be punctuated by periods of dramatic evolutionary change, and new species can appear relatively rapidly.

Other authors on the study are Richard R. Behringer, of the Department of Molecular Genetics at the University of Texas M.D. Anderson Cancer Center, Houston; and John J. Rasweiler IV, of the Department of Obstetrics and Gynecology, State University of New York Downstate Medical Center, Brooklyn.