

# Molecular evolution of limb length

January 14 2008

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In the January 15th issue of G&D, a research team led by Dr. Richard Behringer at MD Anderson Cancer Center reports that they have successfully switched the mouse Prx1 gene regulatory element with the Prx1 gene regulatory region from a bat – and although these two species are separated by millions of years of evolution -- the resulting transgenic mice displayed abnormally long forelimbs.

While forelimb length is just one of several key morphological changes that occurred during the evolution of the bat wing, this unprecedented finding demonstrates that evolution can be driven by changes in the patterns of gene expression, rather than solely by changes in the genes, themselves.

Prx1 is a paired-box homeodomain transcription factor, with an established role in limb bone growth. Dr. Behringer and colleagues identified a conserved Prx1 enhancer domain, which regulates expression of Prx1 in the developing forelimb.

To study the evolutionary contribution of the Prx1 enhancer to the morphological differences between the bat and mouse forelimb, Dr. Behringer and colleagues replaced the endogenous mouse Prx1 enhancer with that of the bat. The transgenic mice showed higher expression levels of Prx1 in the perichondrium, increased chondrocyte proliferation, and ultimately, longer forelimbs.

Dr. Behringer describes the significance of his finding as such: “Darwin suggested that "successive slight modifications" would ultimately result

in the evolution of diverse limb morphologies, like a hand, wing, or fin. The genetic change we engineered in mice may be one of those "slight modifications" to evolve a mammalian wing."

Source: Cold Spring Harbor Laboratory

Citation: Molecular evolution of limb length (2008, January 14) retrieved 2 May 2024 from <https://phys.org/news/2008-01-molecular-evolution-limb-length.html>

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