

ISSN 1996-0700

Asian Journal of
Biotechnology

Age Doesn't Matter: New Genes Are as Essential as Ancient Ones

New genes that have evolved in species as little as one million years ago -- a virtual blink in evolutionary history -- can be just as essential for life as ancient genes, startling new research has discovered.

Evolutionary biologists have long proposed that the genes most important to life are ancient and conserved, handed down from species to species as the "bread and butter" of biology. New genes that arise as species split off from their ancestors were thought to serve less critical roles -- the "vinegar" that adds flavor to the core genes.

But when nearly 200 new genes in the fruit fly species *Drosophila melanogaster* were individually silenced in laboratory experiments at the University of Chicago, more than 30 percent of the knockdowns were found to kill the fly. The study, published December 17 in *Science*, suggests that new genes are equally important for the successful development and survival of an organism as older genes.

"A new gene is as essential as any other gene; the importance of a gene is independent of its age," said Manyuan Long, PhD, Professor of Ecology & Evolution and senior author of the paper. "New genes are no longer just vinegar, they are now equally likely to be butter and bread. We were shocked."

The study used technology called RNA interference to permanently block the transcription of each targeted gene into its functional product from the beginning of a fly's life. Of the 195 young genes tested, 59 were lethal (30 percent), causing the fly to die during its development. When the same method was applied to a sample of older genes, a statistically similar figure was found: 86 of 245 genes (35 percent) were lethal when silenced.

Because the young genes tested only appeared between 1 and 35 million years ago, the data suggests that new genes with new functions can become an essential part of a species' biology much faster than previously thought. A new gene may become indispensable by forming interactions with older genes that control important

functions, said Sidi Chen, University of Chicago graduate student and first author of the study.

"New genes come in and quickly interact with older genes, and if that interaction is favorable by helping the organism survive or reproduce better, it is favored by natural selection and stays in the genome," Chen said. "After a while, it becomes essential, and the organism literally cannot live without the gene any more. It's something like love: You fall in love with someone and then you cannot live without them."

The indispensable nature of new genes also questions long-held beliefs about the shared features of development across different species. In 1866, German zoologist Ernst Haeckel famously hypothesized that "ontogeny recapitulates phylogeny" after observing that the early steps of development are shared by animals as different as fly and man.

Biologists subsequently predicted and confirmed that the same ancient, essential genes would be the conductors of this early development in all species. This principle enabled the use of model organisms, including flies, mice, and rats, to be used for research on the mechanisms of human disease.

Intriguingly, in the new study, deleting many of the new genes causes flies to die during middle or late stages of development, while older genes were lethal during early development. So while ancient genes essential for the early steps of development are shared, newer genes unique to each species may take over the later developmental stages that make each species unique. For example, many new genes in the study were found to be involved with metamorphosis, the mid-life stage that drastically transforms the body plan in animals.

"This may change the way we view the developmental program," Long said. "Each species has a different species-specific developmental program shaped by natural selection, and we can no longer say that from *Drosophila* to humans the development of different organisms is just encoded by the same genetic program. The story is much more complicated than what we used to believe."

As such, a full understanding of biological diversity may require a new focus on genes unique to each organism.

"I think it has important implications on human health," Chen said. "Animal models have proven to be very useful and important for dissecting human disease. But if our intuition is correct, some important health information for humans will reside in the unique parts of the human genome."

The newfound importance of young genes and unique developmental programs may have a dramatic impact on the field, Long said. The discovery will also inspire new

research directions examining how quickly new genes can become essential and their exact role in species-specific development.

"Biologists have long assumed, quite reasonably, that ancient genes have survived natural selection because they are essential to life and that new genes are generally less critical to an organism's development," said Irene Eckstrand, PhD, who manages Dr. Long's and other evolutionary biology grants at the National Institutes of Health. "This important study suggests that this assumption is flawed, unlocking new questions that could lead to a deeper understanding of evolutionary processes and their impact on human health."

The work was funded by grants from the National Institute of General Medical Sciences, the National Science Foundation, and the Chicago Biomedical Consortium.

Sidi Chen, Yong E. Zhang, and Manyuan Long. New genes in *Drosophila* quickly become essential. *Science*, 17 December 2010: 1682-1685 DOI: 10.1126/science.1196380