

SOUTHWESTERN NEWS

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EMBARGOED UNTIL 4 P.M. CST MONDAY, DEC. 13, 2004

Research points to new theory driving evolutionary changes

DALLAS – Dec. 13, 2004 – Researchers at UT Southwestern Medical Center at Dallas have used canine DNA to identify a genetic mutation mechanism they believe is responsible for rapid evolutionary changes in the physical appearance of many species.

The findings, based on data gathered from hundreds of museum specimens of dogs and from blood samples of volunteered live dogs, offer a new explanation for the sudden, rapid rise of new species found in the fossil record. They also help explain the variability in appearance among individual members of a species, such as the length of the nose in different breeds of domestic dogs.

The findings will appear in an upcoming issue of the *Proceedings of the National Academy of Sciences* and are available online.

“We’re offering an explanation for a lot of different components of evolution, one that goes against the central dogma that currently explains how certain aspects of evolution take place,” said Dr. Harold “Skip” Garner, professor of biochemistry and internal medicine at UT Southwestern and one of the authors of the study, which involved only small, non-invasive blood draws from dogs by licensed veterinarians.

The chemical units that make up an organism’s DNA, or genetic code, are abbreviated with the letters A, C, T and G. Strings of these letters spell out the genetic instructions needed to carry out all of life’s functions.

Most scientists agree that over very long periods of time, mutations in the genetic code are responsible for driving evolutionary changes in species. One widely accepted hypothesis is that random, so-called single-point mutations – a change from one letter to another among the billions of letters contained in the code – minutely but inexorably change an organism’s appearance.

UT Southwestern scientists, however, believe the single-point mutation process is much too slow and happens much too infrequently to account for the rapid rise of new species found in the fossil record, or for the rapid evolutionary changes occurring in species such as the domestic dog, whose various breeds have evolved relatively quickly from a not-too-distant common ancestor.

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The scientists combined extensive genetic data from different dog breeds and data on the shapes of dog skulls with computer programs developed by study co-author Dr. John “Trey” Fondon, a research fellow in the Eugene McDermott Center for Human Growth and Development and biochemistry at UT Southwestern. The researchers found a correlation between the length and angle of the dogs’ noses and specific regions in their genetic code that are prone to mutate often.

These genetic regions, called tandem repeat sequences, consist of the same series of letters repeated many times over, for example, A-C-T-A-C-T-A-C-T. Mutations happen in these regions when such units – the A-C-T in the above example – are mistakenly added or subtracted by the proteins responsible for “reading” and “copying” the letters in the genetic instructions. Such additions or deletions can result in changes in the proteins made by cells, which then affects how the cells function and, over time, the physical appearance of an animal.

The researchers found that in a dog gene involved in determining muzzle length, the number of times specific tandem repeat units were repeated could be used as a predictor of what the dog looked like – long muzzle or short.

In the same genetic region from wild coyotes and wolves, the researchers also found variations in repeat lengths, but these animals do not have nearly the wide range of variation in repeat length that domestic dogs do. Consequently, they also don’t have the range in physical variation in muzzle length.

Mutations in tandem repeat sequences occur much more frequently than single point mutations – up to 100,000 times as often – and are much more likely to result in significant morphological changes, or changes in physical appearance, in an organism, said Dr. Fondon, an evolutionary biologist.

“I was struck by the prevalence of very highly mutable tandem repeats in the coding regions of genes responsible for development,” he said. “That’s when it occurred to me that this may be an important mechanism whereby our genomes are able to create lots of useful variations in genes that are important for our development, our shape and structure, and our overall appearance.

“Many of the shape difference that we see in evolution are not suddenly adding a wing or a leg. They are distortions, the stretching or squishing of a body part. Mutations in these repeat

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sequences are responsible for such incremental, quantitative changes.”

The researchers say the same processes may play an important role in the subtle variations between people. In addition, in humans and in other animals, tandem repeat sequences are found in genes responsible for neurological development, an area where humans have evolved rapidly.

“We have demonstrated that the tandem repeat sequences found in many genes are probably responsible for rapidly evolving physical traits that affect a species’ ability to survive,” Dr. Garner said. “Dogs have been rapidly bred to have many different shapes and traits that are pleasing to humans, enabling them to survive. Humans rapidly evolved big brains, which helped them survive as well.”

The next step in the research is to determine whether tandem repeat mutations behave in a similar manner in other animals, such as mice, and whether such genetic information can be used to predict what an animal will look like.

The research was funded by the National Cancer Institute and the M.R. and Evelyn Hudson Foundation.

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