

# DOG GENOME SEQUENCE AND ANALYSIS PUBLISHED IN NATURE

*Analysis unlocks genetic variation among dog breeds; evolutionary conservation with human reveals regulatory controls of key genes*

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## MEDICAL MATTERS

*This article has been approved by the AKC's Canine Health Committee and its distribution is encouraged. Copies may be downloaded at [www.akcchf.org/research/perspectives.cfm](http://www.akcchf.org/research/perspectives.cfm).*

### **B**ay Colony Cluster Dog Show, Boston, MA, December 7, 2005

An international research team led by scientists at the Broad Institute of MIT and Harvard announced today the completion of a high-quality genome sequence of the domestic dog.

Funded in part by grants from the AKC Canine Health Foundation, the genome sequence will provide a catalog of 2.5 million specific genetic differences across several dog breeds.

"The completion of the canine genome sequence has been the number one priority of the Board of the Canine Health Foundation," says Wayne E. Ferguson, president of the CHF. "This incredible tool will no doubt become the standard for researchers worldwide who are contributing to the fight against canine disease."

"We survive on our visions and prosper by their fulfillment," echoes Robert L. Kelly, CHF Grants Committee chair and founding board member. "Utilization of the Dog Genome will alleviate suffering for both man and dog and augur healthier lives for future generations of these two most bonded species. The AKC Canine Health Foundation is honored to have worked with the Scientists who achieved this exemplary cooperative Genomic milestone."

Published in the December 8 issue of *Nature*, the dog research sheds light on both the genetic similarities between dogs and humans and the genetic differences between dog breeds. Comparison of the dog and human DNA reveals key secrets about the regulation of the master genes that control embryonic development. Comparison among dogs also reveals the structure of genetic variation among breeds, which can now be used to unlock the basis of physical and behavioral differences, as well the genetic underpinnings of diseases common to domestic dogs and their human companions. "Of the more than 5,500 mammals living today, dogs are arguably the most remarkable," said senior author Eric Lander, director of the Broad Institute, professor of biology at MIT and systems biology at Harvard Medical School, and a member of the Whitehead Institute for Biomedical Research. "The incredible physical and behavioral diversity of dogs from Chihuahuas to Great Danes is encoded in their genomes. It can uniquely help us understand embryonic development, neurobiology, human disease and the basis of evolution."

#### **Similarities to humans**

Dogs not only occupy a special place in human hearts, they also sit at a key branch point in the evolutionary tree relative to humans. By tracking evolution's genetic footprints through the dog, human and mouse genomes, the scientists found that

humans share more of their ancestral DNA with dogs than with mice, confirming the utility of dog genetics for understanding human disease.

Most importantly, the comparison revealed the regions of the human genome that are most highly preserved across mammals. Roughly 5% of the human genome has been well preserved by evolution over the past 100 million years and must encode important biological functions. The researchers discovered that the most highly conserved of these sequences are not randomly distributed throughout the genome. Instead, they are crowded around just a tiny fraction (about 1%) of the genes that encode crucial regulatory proteins involved in development (such as transcription factors or axon guidance receptors). "The clustering of regulatory sequences is incredibly interesting," said Kerstin Lindblad-Toh, first author of the *Nature* paper and co-director of the genome sequencing and analysis program at Broad. "It means that a small subset of crucial human genes is under much more elaborate control than we had ever imagined."

#### **Differences between dog breeds**

Dogs were domesticated from gray wolves as long as 100,000 years ago, but selective breeding over the past few centuries has made modern dog breeds a testament to biological diversity. Obvious examples include the contrasting body sizes of 6-pound Chihuahuas and 120-pound Great Danes, the hyperactivity of Jack

