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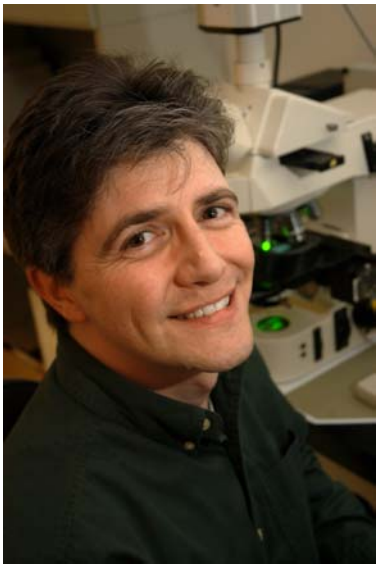
Completed Dog Genome Sequence Shows New Promise for Canine, Human Health

FOR IMMEDIATE RELEASE

Man's best friend may soon offer humans more than loyal companionship. Dogs could help scientists "sniff out" diseases such as cancer that afflict both humans and canines.



Dr. Matthew Breen

Researchers at the Broad Institute of Harvard and Massachusetts Institute of Technology, North Carolina State University's College of Veterinary Medicine, and from universities and hospitals around the globe have successfully sequenced the canine genome, or set of all genes. The results of the team's work are published in the Dec. 8 issue of the journal *Nature*.

"Our pet dogs could hold the keys to unlocking some of the puzzles that perplex us about human health," says Dr. Matthew Breen, associate professor of genomics at NC State and co-investigator of the dog genome project. "Some of the answers to the health questions we have been struggling to answer for decades may have been sitting right beside us all along."

Having the canine genome sequenced will help researchers identify disease-causing genes in both humans and dogs. Several diseases found in humans, such as cancers, heart disease, cataracts, epilepsy and deafness, are also prevalent in dogs. Dogs make good models for studying human diseases, Breen says, because the genetic makeup of dogs and humans are so similar, plus they both share the same environment.

"Our dogs are our companions, therefore they share our environment," Breen says. "They breathe the same air, drink the same water and walk across the same lawns that we do.

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Cancers that dogs get are exactly the same as the cancers that we get. The only difference is that the genetic structure of dog populations allows us to identify the underlying genetic cause of the disease."

Identifying the genes that cause cancers and other diseases will likely be easier in the dog genome, Breen says, because for centuries, dogs have been bred to meet stringent standards, which has resulted in a reduction in the level of genetic variation within different dog breeds.

"One has to look at significantly more points throughout the human genome than in the dog genome to find out what's happening in a specific disease," Breen says. "After identifying which parts of the dog genome are involved, one can narrow it down from a piece that's a mile long to a piece that's a foot long. Instead of investigating 200 to 300 possible genes, we can focus on maybe just two or three possible genes."

Additionally, some dog breeds have a considerably higher predisposition to certain cancers than others. That's because over the generations, as breeders selected for specific physical characteristics, they may also have unknowingly selected for genes with certain adverse characteristics, such as cancer or other diseases, due to the proximity of the genes in the sequence. So the gene that gives a dog a desirable trait may be sitting next to a gene that causes cancer. Select for the desirable trait and you may also select for the cancer.

"We have also begun to identify genetic changes in a variety of canine tumors that are restricted to individual dog breeds," Breen says. "Using this information, we can delve into the code and determine what it is about the organization of the genetic code in these particular breeds that make them more susceptible to cancer. We are then a few steps away from designing ways to halt the cancer process and maybe even preventing it from starting."

The breed of dog that was sequenced was the boxer. Breen's role in dog genome sequencing project involved reassembling the more than 2.5 billion pieces of DNA, or genetic information, in the proper order after researchers at the Broad Institute decoded each individual piece.

"The information in a genome is similar to the information contained in a book," Breen says. "If you think of pieces of the genome as pieces of paper that result from all the pages of the book passing through a paper shredder, the scientists at the Broad Institute analyzed each shred and then assembled the pieces back into pages. Our lab's role contributed to putting all the pages of the book back together in the proper order."

Funding for the dog genome project came from that National Human Genetics Research Institute and the Canine Health Foundation. The sequence of the dog genome will be publicly available for other biomedical and veterinary researchers to use to work on treating and perhaps curing human and canine diseases.

"The real power of having the canine genome sequenced is that it really will help us understand more about veterinary health and welfare, but at the same time it will help us understand significantly more about our own human health and welfare," Breen says. "The

availability of the canine genome sequence has opened up a completely new avenue into all kinds of genetic research."

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Note to editors: An abstract of the *Nature* paper follows.

"Genome sequence, comparative analysis and haplotype structure of the domestic dog"

Authors: Kerstin Lindbald-Toh, Eric S. Lander, Broad Institute of Harvard and MIT; Matthew Breen, North Carolina State University; et al

Published: Dec. 8, 2005, in *Nature*

Abstract: Here we report a high-quality draft genome sequence of the domestic dog (*Canis familiaris*), together with a dense map of single nucleotide polymorphisms (SNPs) across breeds. The dog is of particular interest because it provides important evolutionary information and because existing breeds show great phenotypic diversity for morphological, physiological and behavioural traits. We use sequence comparison with the primate and rodent lineages to shed light on the structure and evolution of genomes and genes. Notably, the majority of the most highly conserved non-coding sequences in mammalian genomes are clustered near a small subset of genes with important roles in development. Analysis of SNPs reveals long-range haplotypes across the entire dog genome, and defines the nature of genetic diversity within and across breeds. The current SNP map now makes it possible for genome-wide association studies to identify genes responsible for diseases and traits, with important consequences for human and companion animal health.