The Human/Canine Connection

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Humans and dogs have coexisted for thousands of years, during which time we have developed a unique bond, centered primarily on companionship. Along the way, we have developed purebred dog breeds, each of which have their own special combination of physical and behavioral characteristics. An unfortunate consequence is that much of the breeding has been conducted in a manner that has resulted in many dog breeds being affected by serious genetic disorders including cancers. Studies of the human and canine genome assemblies have shown that at the genetic level we are remarkably similar. In addition, clinical and pathological data provide strong evidence that humans and dogs share many common diseases. With this knowledge and armed with a well stocked genomics 'toolbox', we and our pet dogs continue, side by side, along our journey of mutually beneficial scientific discovery. For example, it is anticipated that the genetic study of cancers in dogs will identify genes of significance to dogs and that with the pathophysiological and genome similarity between dog and human cancers, this research may also translate to provide benefit to humans. In this presentation examples will be provided of how this close genomic association is already starting to provide insights into both canine and human health.

It is evident that the unique bond shared between human and dog extends now beyond one of an emotional basis; it is now a bond that is made even more rigid by the biomedical relationship that we share. Study of the canine genome may ultimately provide many of the keys to unlock some of nature's most intriguing biomedical puzzles. The domestic dog and its genome, quite rightly, continue to be Man's best friend.

Biographical Profile

Dr. Matthew Breen completed his PhD in cytogenetics in 1990 and then spent two years as a Post Doc in Molecular Genetics at the UK Medical Research Council's Human Genetics Unit in Edinburgh, Scotland, where he was responsible for developing novel ways to map genes to chromosomes as part of the Human Genome Project. Dr. Breen then spent four years working for the research arm of the Australian Thoroughbred industry, returning to the UK in 1996 where his laboratory developed molecular cytogenetics reagents, resources and techniques for application to canine genome mapping, comparative cytogenetics and cancer studies. In 2002 Dr. Breen relocated his laboratory to North Carolina State University's College of Veterinary Medicine, where he is Professor of Genomics and also a member of the Center for Comparative Medicine and Translational Research (CCMTR). He also serves as Director of the CCMTR's Clinical Genomics Resources Laboratory.

Dr. Breen's major research interests continue to focus on the genomics, genome mapping and the comparative aspects of canine cancer. Dr. Breen played a key role in the mapping of the canine genome and now used his skills and resources to focus on the molecular cytogenetic evaluation of canine tumors as a means to discover the genes involved in the initiation and progression of cancers. Dr. Breen's lab is the recipient of numerous grants from a variety of agencies including

the AKC-Canine Health Foundation, Morris Animal Foundation, National Canine Cancer foundation and the National institutes of Health.

In addition to his activities at NCSU, Dr. Breen was a founder member and now serves on the Board of Directors of the Canine Comparative Oncology and Genomics Consortium Inc. The CCOGC is a national organization that serves to gather tumor tissues that mat be used for the advancement of canine (and human) cancer research. He also serves on the Scientific Advisory Board of the Morris Animal Foundation and the National Canine Cancer Foundation.

Dr. Breen's research has been supported by the following grants:

2038T: The Molecular Cytogenetics of Canine Lymphosarcoma: Correlating Chromosomal Changes with Clinical Disease
2214T: Identification of a 5-10Mb BAC Set as a Cytogenetic Resource andfor the Development of an Ordered CGH Microarray for Cancer Studies in the Dog
2254B: Heritable and Sporadic Genetic Lesions in Canine Lymphoma and Osteosarcoma 249: Genomics of Canine BrainNeoplasia
2667: *Cellular Genomics - Molecular Cytogenetic Investigation of Canine Soft Tissue Sarcomas*
403: Application of the 7.5X Canine Genome Assembly to Generate a 1Mb Cytogenetic BAC-Map of the Canine Genome
613: *The Prognostic Significance of Chromosome Aneuploidy in Canine Lymphoma 615B: Heritable and Sporadic Genetic Lesions in Canine Lymphoma*
760: Cellular Genomics - Molecular Cytogenetic Investigation of Canine Soft Tissue Sarcomas
947A: Heritable and Sporadic Genetic Lesions in Canine Osteosarcoma

The Human Dog Bond – Emotions, Purines and Pyrimidines – conference notes

Why work with dogs? Not humans?

Need a bigger model than a mouse – why not use a rat?

What is a domestic dog?

Humans started to co-exist many many thousands of years ago.

Ancient Egyptians recorded over seventy dog names. Many animals depicted in the middle kingdom era (c 2040 – 1640 bce) on tombstones, artwork, etc.

Dogs with collars, men walking dogs, King Tutankamen with a “saluki” killing a lion/panther

Move forward in time – 1873, The Kennel Club held the first dog show. This started a process of developing dogs that we like how they look. Therefore defining and developing genetic pools. This also was the time that we invited dogs into our homes and our lives.

We now take our dogs everywhere we go. We have trained them to understand us. They continue to provide an early warning system for intruders – trained to protect.

From the wolf to now having 155 AKC recognized breeds.

Popularity in different breeds wanes and waxes over the years. Because our tastes change the popularity of breeds changes.

Comparative Genomics …

We all have the same genes; they are just "shuffled" differently. The power of using dogs to study genetics is the fact we can have multiple generations alive and can study them all, when you cannot do that easily in humans. As well as in human pedigrees, individuals will only be present in a "pedigree" once. Whereas in dogs, we line-breed and therefore focus genes and less genetic variability. Breen cautions that this could lead to genetic crises because of limited gene pools. – Litter size could be reduced, could lead to fertility problems.

Canine genetic diseases … now affect our dogs because they are living longer because we are keeping them alive longer. 25% of dogs carry a gene for major genetic disorder whereas humans this is 1% in humans.

In helping find genes for diseases, it is easier to find in canines because there is less genetic variability.

Dogs are plagued by the greatest number of documented naturally occurring genetic diseases. Because the canine genome is available, the dog is truly mans best friend.

How is canine genome informing human health – for example, narcolepsy. Much of what we know about narcolepsy comes from studies on Dobermans that had a similar genetic defect resulting in comparable symptoms. – The gene was found and the dogs were used to test treatments

Lafora's disease – inherited progressive epilepsy. Autosomal recessive … found in dogs, and tested.

Cancer … studies have shown that human and dog cancers present with the same, evolutionary conserved chromosome aberration and that genes within regions are deregulated in the same way. We are finding regions of the dog genome that contain potential cancer associated genes that may also advance human cancer research.

Humans and dogs have co-existed for 1000s of years

During that time the dog has been our best friend … the irony is that the keys to unlocking these puzzles are in our dogs.

They new warning system – will not be barking – but their genome.

Breen and Jaime Modiano have received a $1 million/five year grant to study lymphoma in dogs!!! This came from studies and work done by funds provided by the Canine Health Foundation.