Medical Xpress

Canine compulsive disorder gene identified in dogs

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A canine chromosome 7 locus that confers a high risk of compulsive disorder susceptibility has been identified through a collaboration between the Behavior Service at the Cummings School of Veterinary Medicine, the Program in Medical Genetics at the University of Massachusetts Medical School and the Broad Institute at the Massachusetts Institute of Technology. The findings are published in the January 2010 edition of *Molecular Psychiatry*.

Obsessive compulsive disorder is characterized by time consuming, repetitive behaviors and affects about 2 percent of humans, while the equally distressing canine equivalent, canine compulsive disorder, or CCD, seems to target certain dog breeds, especially Dobermans and Bull Terriers. For over a decade, behaviorists Drs. Dodman and Moon-Fanelli, at Tufts Cummings School of Veterinary Medicine collected blood samples from carefully characterized Doberman patients exhibiting flank- and/or blanket-sucking compulsive behaviors, as well as healthy, unaffected Doberman. In 2001, Edward Ginns, PhD, MD, head of the Program in Medical Genetics at UMass Medical School, joined the effort, enabling genetic studies that culminated in the genome wide association study that began in 2007 using the canine Affymetrix genotyping array at the Broad Institute.

The chromosome 7 location most significantly associated with CCD is located within the neural cadherin-2 gene, CDH2. CDH2 is widely expressed, mediating synaptic activity-calcium flux related neuronal adhesion. Dogs showing multiple compulsive behaviors had a higher

frequency of the "risk" associated DNA sequence than dogs with a less severe phenotype (60 and 43%, respectively, compared with 22% in unaffected dogs). This highly significant association of CCD with the CDH2 gene region on chromosome 7 is the first genetic locus identified for any animal compulsive disorder, and raises the intriguing possibility that CDH2 and other neuronal adhesion proteins are involved in human compulsive behaviors, including those observed in autism spectrum disorder. The neural cadherin-2 gene, CDH2, is an especially attractive candidate disease gene as it is involved in mediating presynaptic to postsynaptic neuronal junction adhesion, neuronal axon outgrowth and guidance in the central nervous system during development when critical brain nerve networks are established.

"The CDH2 gene is expressed in the hippocampus, a brain region suspected to be involved in OCD. In addition, this gene oversees structures and processes that are possibly instrumental in propagating compulsive behaviors - for example, the formation and proper functioning of glutamate receptors," said Dr. Nicholas Dodman, professor of clinical sciences at Cummings School of Veterinary Medicine at Tufts University and the study's lead author. Dr. Dodman added that "this finding is congruent with current evidence that NMDA blockers are effective in the treatment of OCD."

"The occurrence of repetitive behaviors and similarities in response to drug treatments in both canine CCD and human OCD suggest that common pathways are involved" said Dr. Ginns, professor of Clinical Pathology, Neurology, Pediatrics, Psychiatry and Neuroscience at UMass Medical School. Dr. Ginns is hopeful that "our finding will lead to a better understanding of the biology of compulsive disorder and facilitate development of genetic tests, enabling earlier interventions and even treatment or prevention of compulsive disorders in at-risk canines and humans." "This lead is so intriguing that we look forward to working with Dr. Dodman's group to extend our current findings to other

populations." added Dr. Marzena Galdzicka, assistant professor of Clinical Pathology at UMass Medical School. Collaborations are already in progress with Dr. Dennis Murphy's group at the National Institute of Mental Health to determine the extent to which CDH2 confers risk for human OCD and autism spectrum disorders.

Provided by Tufts University