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Dogs, humans, put heads together to find cure for brain cancer

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Pinpointing the genes involved in human brain cancer can be like looking for a needle in a haystack, and sometimes the needle you find may not be the right one. By comparing human and canine genomes, researchers at North Carolina State University have discovered that a gene commonly believed to be involved in meningiomas-tumors that affect the meninges, or thin covering, of the human brain and account for one out of four adult brain tumors -may not be as key for tumor formation as previously thought, and they've narrowed the search for the real culprit.

Meningiomas are intracranial tumors, meaning that they do not grow within brain tissue itself, but in the space between the brain and the skull. In humans, they are associated with genetic defects of large segments of chromosomes, which makes isolating the specific genes involved extremely difficult. Humans suffering from meningioma frequently lose one copy of almost the entire length of human chromosome 22. This chromosome is made of almost 50 million base pairs of DNA that code for more than 500 genes.

"The dog has been man's best friend for centuries, and now the genome of the dog could well be man's next best friend," says Dr. Matthew Breen, professor of genomics at NC State.

"With so much genetic material to consider, one can see why figuring out which genes play a key role in meningiomas is extremely difficult," says Breen. "By looking at tumors seen in both humans and dogs we have

a simple way to narrow the search: we compare the affected areas of a human chromosome with related areas on dog chromosomes. This works because dogs and humans are genetically similar and both get the same kinds of cancers. While we share much of our genetic material, the DNA of a dog is organized differently to our own and this makes it possible to isolate smaller 'shared' regions of genetic data rather than looking at an entire chromosome."

Breen, NC State colleagues Rachael Thomas and veterinary neurologist Natasha Olby, along with researchers from the University of California-Davis and the Wellcome Trust Sanger Institute in Cambridge, UK collaborated on the project, sharing samples of canine meningiomas for research. Their results were published in the *Journal of Neurooncology*.

Previous researchers had pinpointed a particular tumor-suppressing gene on human chromosome 22, known as NF2, as a possible contributor to meningioma. They believed that the deletion of NF2, with its tumor suppressing abilities, could trigger tumor growth.

In looking at genetic changes across the whole genome, Breen's team compared human chromosome 22 to its canine counterpart. In dogs, the region shared with 22 is "split up" across three separate dog chromosomes - numbers 10, 26 and 27- with the NF2 gene appearing on dog chromosome 26. The researchers discovered that in dogs with meningioma, chromosome 26, and hence NF2, was rarely affected, casting doubt on this gene as playing a significant role in the disease. Instead, dogs with meningioma frequently showed loss of parts of dog chromosome 27. This led the researchers to focus on the portion of human chromosome 22 that corresponds to canine chromosome 27.

"Now, instead of looking at 50 million base pairs that contain several hundred genes, we can focus on the portion of human chromosome 22 that is evolutionarily conserved with dog chromosome 27," Breen says.

"By looking at dog and human meningiomas together we reduce the amount of searching we need to do 50-fold. It's the old needle/haystack dilemma, except that using information from dog and human tumors allows us to concentrate our search on the two percent of the haystack that actually contains the needle, and not spend time and resources on the other 98 percent."

Breen also noticed that the other chromosome involved for canines that suffer from meningioma is dog chromosome 17, which correlates with part of human chromosome 1. Defects of this chromosome are involved in almost 70 percent of human meningioma cases and are associated with a poor patient outcome. He hopes that he can use this correlation to further narrow the search for specific genes involved with the disease.

In addition the team looked also at gliomas, another kind of brain tumor, and have shown common genetic features shared between human and canine tumors that are now under further investigation.

"The data support that dog and human tumors are very similar at the genetic level, so both species will benefit from this research," Breen says. "It's proof of the 'One Medicine' concept - the idea that human and animal health relies on a common pool of medical and scientific knowledge and is supported by overlapping technologies and discoveries."

Source: North Carolina State University (news : web)

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