Protein may help diagnose and treat lymphoma in people and dogs

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A protein that appears to play a key role in the formation of lymphoma and other tumors by inhibiting a tumor-suppressing gene has been identified by a team of veterinary and human medicine researchers at the University of California, Davis.

The researchers suggest that the newly identified protein may be a potential target for diagnosing and treating lymphoma in humans and animals. They will report their findings July 15 in the journal *Genes & Development*.

"Results from this study suggest that a gene known as RNPC1 may play a key role in the development of lymphoma," said Xinbin Chen, a veterinary oncologist with appointments in the UC Davis School of Veterinary Medicine and the UC Davis School of Medicine. Chen led the study.

About Lymphoma

Lymphoma refers to a group of blood cancers that start in the lymphatic system, a network of lymph vessels and lymph nodes that play a vital role in the body's immune system.

Lymphoma occurs when a type of white cell, known as a lymphocyte, undergoes a malignant change and begins to multiply out of control. As the lymphocytes multiply rapidly, they eventually crowd out normal,

healthy cells. In time, the cancerous lymphocytes accumulate in the lymph nodes, liver, spleen and other locations in the body.

Lymphoma occurs spontaneously in dogs, representing 6 percent of all canine cancers. It is remarkably similar to lymphoma in humans.

Cancer and the P53 Gene

For three decades, researchers have known that a gene referred to as p53 plays an important role in suppressing cancer. This tumor suppressor gene checks cells' DNA for mutations that might cause cancer and then stops cell growth until the mutations can be repaired. If the mutations can't be repaired, P53 triggers cell death to prevent cancer from developing.

But if something goes awry, p53 itself can mutate and produce undesirable proteins. Earlier studies have shown that mutated proteins produced by p53 are present in 60 percent of all cancerous human tumors. More recent studies have also shown that p53 can be inactivated in human cancers by means other than mutation. In short, when p53 and the process it controls are damaged, cancer often occurs.

In recent years, scientists, including Chen and his colleagues at UC Davis, have found that p53 mutations also are active in the formation or cancerous tumors in other mammals, including dogs, cats and horses.

About the RNPC1 gene

Because defects in p53 are so common in human and animal cancers, researchers have been extremely interested in how the activity of the gene is regulated. This led the UC Davis team to examine the RNPC1 gene.

RNPC1 is known to be an RNA-binding protein, regulating how other genes produce proteins. The UC Davis researchers suspected that RNPC1 might play a role in causing lymphomas by inactivating the p53 gene.

Findings from the UC Davis study

In their new study, the researchers examined several types of human cancer cells as well as cells isolated from a mouse embryo, known as embryonic mouse fibroblasts.

The team showed that the RNPC1 gene inhibited the activity of the p53 gene and reduced levels of the p53 protein in these cells. Conversely, p53 protein levels increased when RNPC1 was out of the picture.

Because the RNPC1 gene is located at a chromosome that is frequently overexpressed in human cancers, including lymphomas, the researchers examined the expression of RNPC1 in spontaneously occurring dog lymphomas and in non-cancerous canine lymph node tissue. (The dog lymph node samples were provided with the permission of the owners; all of the dogs in the study were patients at the UC Davis Veterinary Medical Teaching Hospital.)

Data from the dog lymphoma tests showed that the RNPC1 gene is frequently overactive in dog lymphomas and may, as suspected, play a role in the formation of lymphomas by inactivating the p53 gene.

Implications for human medicine

"Our findings are consistent with data from other cancer studies, which showed that RNPC1 is highly expressed in human cancers," Chen said. "This suggests that further studies are needed to analyze the expression

of patterns of both RNPC1 and p53 in human tumor tissues."

He noted that because dogs and humans alike are vulnerable to lymphoma, and similar gene processes may be at work in each species, the dog may serve both as a valuable sentinel for environmental causes of the disease and as a model for exploring its causes and treatments.

Provided by University of California - Davis