Drug trials in pet dogs with cancer may speed advances in human oncology

June 16 2015

University of Illinois veterinary clinical medicine professor Timothy Fan, pictured here with his dog, Ember, describes the advantages of testing potential cancer therapies on pet dogs with spontaneously occurring cancers. Credit: L. Brian Stauffer

Pet dogs may be humans' best friends in a new arena of life: cancer

treatment, said University of Illinois veterinary clinical medicine professor Timothy Fan. Physiological similarities between dogs and humans, and conserved genetics between some dog and human cancers, can allow pet dogs to serve as useful models for studying new cancer drugs, he said.

In a meeting sponsored by the National Cancer Policy Forum of the National Academies' Institute of Medicine in Washington, D.C., Fan and 15 other experts in the field described the benefits of using pet dogs with naturally occurring (rather than laboratory-induced) tumors in early cancer drug trials.

"We have a lot of dogs in the United States, approximately 70 million of them, and it's believed that about 25 percent of pet dogs will develop some form of cancer in their lifetime," he said. "We're using dogs to help guide drug development for people, but at the same time we're offering new, innovative therapies that would otherwise never be available to dogs, to help them as well."

Several attributes make pet dogs attractive subjects for such studies, Fan said.

"Dogs tend to develop cancer as a geriatric population, just like people," he said. "Because the tumors develop spontaneously, there is heterogeneity in that tumor population, as a human being would have. The size of the tumors and the speed of growth of those tumors are comparable in dogs and human beings. So there are many attributes of a dog that develops cancer spontaneously that recapitulate the biology that we see in people."

Some studies have already begun using dogs to test new cancer therapies. Starting in 2007, for example, Fan began testing an anti-cancer drug called PAC-1 (developed by U. of I. chemistry professor Paul

Hergenrother) in pet dogs with naturally occurring lymphomas and osteosarcomas. The results in dogs allowed the scientists to advance PAC-1 as a potential therapy against human cancers. The drug is now in phase I human clinical trials at the U. of I. Cancer Center in Chicago.

Other investigational therapeutics historically piloted in pet dogs with cancer include muramyl tripeptide, an immune-stimulating agent that could not be tested in immune-deficient mice or rats with induced cancers, Fan said.

"Because you're taking a human cancer tissue and implanting it in a mouse, that's a foreign tissue, and the mouse's immune system will reject it," he said. "So you have to transplant those tissues into an immunocompromised mouse. Dogs are immunocompetent, and so were an ideal study subject for testing immunomodulatory cancer therapies.

"Another example in which dogs have been important in demonstrating drug activity was an anti-cancer compound produced by the pharmaceutical company Gilead Sciences," he said. "The company produced a pro-drug, which must be activated by a naturally occurring enzyme in human leukocytes before it can become effective. Mice and rats lack this enzyme, but dogs have it, so the compound was tested in dogs."

Fan also addressed the strengths and limitations of using mice and rats in preclinical trials of cancer drugs.

"We've relied almost exclusively on murine preclinical models, and we've been able to show that investigational agents are very good at fighting cancer in these models," he said. "But only about one in 10 of the agents that show great activity in mice will show similar activity in humans. So the question that we begin to ask is: Why is the hit rate so low?"

It may be that laboratory-induced cancers in mice fail to mimic the natural process of cancer development in humans, he said. "The formation of cancer in those mice is very artificial, it's very accelerated, and it's in the context of an incompetent immune system," Fan said. "So we can easily understand as scientists why there would be some limitations to that model."

There also are limitations to the use of pet dogs in cancer drug trials. "There are some tumors that will not be that relevant," Fan said. "Colon cancer, for example, is heavily driven by diet, and we don't see much colon cancer in dogs. So pet dogs might not be a suitable model for colon cancer in humans."

Mice and rats will likely always be used in preclinical trials of cancer drugs and do offer some significant advantages, Fan said. They are cheaper to rear, their lifespans are shorter, and genetic manipulations of these animals can produce specific and uniform traits. That genetic homogeneity allows researchers to identify how a drug agent is working "without having to deal with a lot of confounding factors," he said.

"But are human beings genetically identical? Absolutely not," Fan said. "There is heterogeneity in the human population and in dogs. So I would argue that if your drug agent produces positive results in dogs, that would give me greater confidence that those findings would be translatable to people."

More information: A webcast of the presentation, "The Role of Clinical Studies for Pets with Naturally Occurring Tumors in Translational Cancer Research" is available online (see Day 1, Session 3, under "Other Meeting Resources: Videos")

Provided by University of Illinois at Urbana-Champaign